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Effects of Psychological Treatments on Functioning in People With Schizophrenia: Systematic Review and Meta-Analysis

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Index of Abbreviations

ACT	Acceptance and commitment therapy
CBSST	Cognitive behavioural social skills training
CBT	Cognitive behavior therapy
CCMD	Cochrane Common Mental Disorders (formerly Cochrane Collaboration Depression, Anxiety and Neurosis Group [CCDAN])
CCDAN	Cochrane Collaboration Depression, Anxiety and Neurosis Group
DGPPN	Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde [German Association for Psychiatry, Psychotherapy and Psychosomatics]
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, 4 th edition, text revision
GAF	Global Assessment of Functioning
GAS	Global Assessment Scale
I^2	Measure of the degree of inconsistency
ICD	International Statistical Classification of Diseases and Related Health Problems
M	Mean
N	Number of studies
n	Number of participants
OPCRIT	Operational Criteria Checklist
p	Level of statistical significance
PANSS	Positive and Negative Syndrome Scale
PSP	Personal and Social Performance scale
RCT	Randomized controlled trial
SANS	Scale for the Assessment of Negative Symptoms
SAPS	Scale for the Assessment of Positive Symptoms
SD	Standard deviation
SFS	Social Functioning Scale

SLOF	Specific Levels of Functioning
<i>SMD</i>	Standardized mean difference
SOFAS	Social and Occupational Functioning Assessment Scale
TAU	Treatment as usual
WHO	World Health Organization

1 Introduction

1.1 Schizophrenia: A Societal and Individual Burden

1.1.1 *Burden for Society*

Schizophrenia is a severe mental disorder with relevant consequences for the individual and society. Its worldwide median lifetime prevalence amounts to 0.48%, with estimates ranging from 0.06% to 1.54% in different countries (Simeone et al., 2015, p. 8). People affected by schizophrenia have a 2 to 3 times elevated risk of dying compared to the general population (McGrath et al., 2008, pp. 71–72). Possible explanations for the higher mortality are, among others, an increased cardiovascular morbidity in people with schizophrenia and the considerable suicide risk which is raised by factor 22 compared to the overall population (Hjorthøj et al., 2017, pp. 298–299). Altogether, the lifetime suicide risk of individuals suffering from schizophrenia amounts to 5% (Hor & Taylor, 2010, p. 86). In the age between 25 and 49 years, schizophrenia is among the top 25 reasons for disability worldwide (Vos et al., 2020, p. 1211). Its disease burden is expected to further increase due to population growth and ageing (Charlson et al., 2018, p. 1201). Frequent inpatient treatment and lack of employment bring forth total annual costs of schizophrenia in Europe of 93.9 billion Euros (Olesen et al., 2012, p. 155). Hence, the substantial burden of schizophrenia on society necessitates systematic research in order to provide optimal evidence-based treatment.

1.1.2 *Burden for the Individual*

The numbers mentioned above show the heavy impact of schizophrenia on society and economy. Focusing on such abstract statistics summarizing the situation of a population as a whole brings the danger of losing sight of the suffering of the individual behind the numbers, that needs to be acknowledged and alleviated. For example, a point prevalence of schizophrenia of 0.28% corresponds to more than 20 million individuals worldwide struggling with this debilitating disorder and its consequences (Charlson et al., 2018, p. 1195). Typically, the first symptoms of schizophrenia appear in the age between 20 and 30 years (Bäumel et al., 2018, p. 78), interrupting the young adult's life in a time that can be used to pursue further education and to begin establishing oneself in a work environment as well as to form meaningful relationships. It is

incomparably harder to fulfil the different expectations emerging in this phase of life when facing symptoms of schizophrenia. Delusions, auditory hallucinations, disturbed thinking processes or a blurring line between the self and the environment – symptoms summarized as positive symptoms (Bäumel et al., 2018, pp. 81–82) – make it nearly impossible to fully socially participate or even to take care of oneself, not even talking about promoting oneself in a job interview. In severe cases, aggression towards self and others is the result of those delusions and hallucinations, often leading to unemployment or even imprisonment (Torrey, 1994, pp. 654–656). Poverty of affect and speech, social isolation and lack of motivation, the so-called negative symptoms (Bäumel et al., 2018, p. 84), are especially problematic as they predict a more chronic course of illness (Bäumel et al., 2018, p. 95). Antipsychotic treatment does not always work to a satisfying degree, especially concerning negative symptoms (Leucht, Arbter et al., 2009, pp. 439–442). Besides, it can create new difficulties. Metabolic syndrome and prolongation of QT interval leading to increased cardiovascular mortality, as well as sexual dysfunction and dyskinesia are common side-effects of antipsychotic medication (Leucht, 2018, pp. 285–287). Many second-generation antipsychotics failed to fulfil the hopes of addressing negative symptoms more effectively than first-generation drugs (Leucht, Corves et al., 2009, p. 31). On the contrary: antipsychotics themselves can produce side-effects such as akinesia that mimic negative symptoms (Leucht & Davis, 2017, p. 1077). On top of psychotic symptoms and side-effects of medication, people with schizophrenia frequently have to face stigma and prejudice, more than in most if not all other mental disorders (Angermeyer & Matschinger, 2003, pp. 532–533). Schizophrenia stigma is enabled by sensationalist receptions in art and media such as the “homicidal maniac” character that is seen frequently in contemporary movies (Owen, 2012, pp. 657–658). In spite of their more profound knowledge, mental health care professionals display equally high social distance towards people with schizophrenia as the general public (Nordt et al., 2006, p. 712). Efforts to reduce stigma are reflected by the ongoing debate about changing the name of the disorder (Gaebel & Kerst, 2019, p. 259), with suggestions like “neuro-emotional integration disorder” (Levin, 2006, p. 324).

1.2 Diagnosis and Treatment of Schizophrenia

1.2.1 Concept and Diagnosis

The complexity of schizophrenia is reflected by conceptual changes and desperate treatment attempts over the years. Even though retrospectively, the history of the diagnosis of schizophrenia is depicted linear, it is far more complex and one concept is not just the logical consequence of its precursor (Berrios et al., 2003, p. 117). Nevertheless, some milestones on the way from dementia praecox (Kraepelin, 1896, p. 426) to the contemporary concept of schizophrenia (Bleuler, 1911, p. 2) shall be mentioned.

The contemporary concept of schizophrenia is largely based on Kraepelin's understanding. He combined the pre-existing concepts of Hecker's hebephrenia and Kahlbaum's catatonia with his own idea of dementia paranoia. Kraepelin's description entails psychological and physical symptoms, among which auditory hallucinations take a prominent role and an emphasis is put on neuroanatomical correlates. Kraepelin developed and adapted his concept over time in detailed ways. Eugen Bleuler, a Swiss psychiatrist, established the term schizophrenia. He took distance from the neuropathological approach and used a more psychological one by defining fundamental and accessory psychological symptoms. The name he chose could be translated as "split mind" and refers to the fundamental symptoms, the cognitive disturbances such as loose associations, ambivalence and inattention – also understood as fragmented thinking processes. Delusions and hallucinations were counted among the accessory symptoms by Bleuler. Kurt Schneider introduced first and second-rank symptoms, with first rank symptoms being hallucinations and ego-distortions. (Lavretsky, 2008, pp. 3–5)¹

Today, the diagnosis of schizophrenia is given with the help of operational criteria set out in manuals such as the Diagnostic and Statistical Manual of Mental Disorders, currently in the fifth edition (DSM-5), or the International Classification of Diseases, currently in the 11th edition (ICD-11). The DSM-5 mentions delusions, hallucinations, disorganized thinking and speech, grossly

¹ Following the recommendations by the university library of the Technical University of Munich, the source indicated by a parenthetical citation placed after the end of the sentence refers to the whole preceding paragraph (Technische Universität München, Universitätsbibliothek, 2020, p. 15).

disorganized or abnormal motor behavior including catatonia and negative symptoms as core defining features (American Psychiatric Association., 2013, pp. 87–88). In the ICD-11, abnormal motor behavior is not considered a core feature. Here, the core symptoms are: persistent delusions, persistent hallucinations, thought disorder, and experiences of influence, passivity, or control (World Health Organization, 2019).

1.2.2 Somatic Treatment

Not even 100 years ago, reckless treatments were carried out in people suffering from schizophrenia. Examples are insulin shock therapy and lobotomy (Lavretsky, 2008, pp. 5–6). Another somatic treatment is electroconvulsive therapy, first promoted by Cerletti in the late 1930s (McClintock et al., 2008, p. 196). It is still applied, however with an unclear evidence base (Sinclair et al., 2019, p. 732). Well into the 20th century, the treatment of patients with schizophrenia was affected by “therapeutic nihilism” and “dehumanization” of the patients (McNally, 2016, p. 209).

An important turning point was marked by the introduction of antipsychotic medication, beginning with chlorpromazine that was investigated for schizophrenia in 1952 by Delay and Deniker (Lavretsky, 2008, p. 6; Leucht, 2018, p. 278). Today, antipsychotic medication is considered the most important part of schizophrenia therapy (Bäumel et al., 2018, p. 87). Yet this paradigm continues to be challenged in ongoing discussions (Morrison et al., 2012, pp. 83–84).

There is a wide range of different antipsychotic drugs with different routes of administration. As there are no tremendous differences in efficacy – except for clozapine – the choice of drug is a pragmatic one. Criteria to consider are, if applicable, how well the medication worked and was tolerated in a previous episode as well as its general side-effect profile or if the medication is planned to be administered in depot form later on. In a shared decision-making process, the patient’s preference may be taken into account to improve compliance. Second generation antipsychotics are presumed to produce less extrapyramidal motoric side effects and potentially work better for negative symptoms. However, many of them lead to weight gain and the associated risks. (Bäumel et al., 2018, p. 87) Thus, albeit not as invasive as the earlier methods, pharmacological treatment is still not free of side-effects and adverse events. For instance, in a large recent meta-analysis, an increased risk of serious somatic adverse events for people taking

antipsychotic medication was found compared to placebo (Schneider-Thoma et al., 2019, pp. 757–764). Given the age-dependence they found for somatic adverse events, the authors still recommend antipsychotic medication for physically fit adults.

The mechanism by which antipsychotics work is in regulation of dopamine metabolism, mostly as dopamine-receptor-antagonists. There are, however, also a few partial agonists. That they work corroborates the dopamine hypothesis by Carlsson and Snyder. They postulate a dopaminergic hyperfunction in D2-receptors in mesolimbic pathways that is responsible for the positive symptoms such as delusions and hallucinations. Concerning D1-receptors, a hypofunction in mesofrontal pathways is assumed, causing negative symptoms. Other neurotransmitters that play a role are glutamate and serotonin. (Bäumel et al., 2018, pp. 79–80) Hence, schizophrenia is one of the most popular examples for biological psychopathology concepts.

1.3 Psychotherapy for the Prime Example Disorder of Biological Psychiatry?

So, if a mostly biological etiology is assumed, the question arises why psychological methods should be applied at all. There are different possible reasons why psychotherapy indeed for a long time played a minor role in schizophrenia treatment and is just recommencing to grow more and more important and become more often object of research.

1.3.1 Apprehension About Psychotherapy in Schizophrenia

It appears plausible that because of the possibly confronting nature and invoking of psychological processes, the vulnerable schizophrenia patients might get worse when participating in psychotherapy. Another reason for hesitation may be that due to the commonness of cognitive impairment in patients with schizophrenia, practitioners do not think that the patients understand the psychological reasoning. Critics of psychotherapy for schizophrenia argue that important meta-analyses did not provide satisfying results and that the recommendations are based on old and low-quality evidence (Jauhar et al., 2019; Kinderman et al., 2015; Laws & Gournay, 2018).

Some advocates of biological psychiatry doubt psychotherapy as a matter of principle. But if the concept that all psychological processes have biological correlates and are changed by biological agents is thought through, it is evident that talking and reflecting about one's experience have a

biological correlate too and might as well be able to change biochemical processes in a measurable way. Thus, biological and psychological psychiatry are only seemingly opposites. (Gabbard, 2000, p. 117) This point of view goes in line with the current neuroscientific model of brain function integrating insights from neuroscience, psychology and cognitive sciences and supported by neuroimaging studies: the free-energy framework. Differences between the brain's model of reality – such as beliefs and goals – and environmental input – such as psychotherapeutic interventions – are supposed to be minimized by processes of neuroplasticity. (Prosser et al., 2016, pp. 309–310)

1.3.2 Rationale for Psychotherapy in Schizophrenia

In spite of claims that there is a lack of convincing evidence for psychological interventions in schizophrenia, there are justifications for its use and research as there are some unique strengths of psychotherapy when compared to pharmacotherapy.

Psychological interventions activate and include the patients in treatment and help them regain a sense of autonomy. Patients get a feeling of self-efficacy because the healing power gets internalized instead of externalized into a magic pill that does something with the otherwise passive patient. So, even if psychotherapy was not effective for positive and negative symptoms, dimensions such as self-esteem, quality of life and functioning could profit.

Another argument for investigating psychological interventions are the good results in other mental disorders such as depressive disorders. The encouraging results might be translated to schizophrenia.

In 1952, the same year in which chlorpromazine became popular, Beck published a case study about successful cognitive therapy for delusions (TARRIER & WYKES, 2004, p. 1378).

Marder (2000, p. 88) suggests a complementary effect of combining pharmacological and psychological treatments in schizophrenia, stating that the effects are “more than additive since each would enhance the effectiveness of the other”. He argues that whereas drugs may improve symptoms, psychological treatments may improve social and vocational skills. Furthermore, he suggests that psychosocial treatment may lead to improved medication adherence and reduced

drug doses and that adequate medication may help patients to tolerate more intensive psychological treatments. Guidi et al. (2018, p. 279) describe interaction between pharmacotherapy and psychotherapy in general with four different types: addition, inhibition, reciprocation and potentiation. Note that they also mention inhibition as possible interaction, acknowledging potential disadvantages of a combination.

1.4 Developments in Psychotherapy

Psychotherapy in the stricter sense was introduced with the development of psychoanalysis by Sigmund Freud in the end of the 19th century. Although Freud himself did not consider it a suitable treatment for patients with schizophrenia, many of his disciples attempted to treat them with psychoanalysis and developed different theories of etiology and psychoanalytic intervention. Psychoanalysis reached its peak between 1945 and 1965 and then made way for pharmacotherapy and other emerging psychological treatments. (Brenner et al., 2000, p. 246)

Nowadays, one of the most influential psychological interventions for schizophrenia is cognitive behavior therapy (CBT).

As suggested by its name, CBT can be understood as the fusion of two distinct therapy models, namely behavior therapy and cognitive therapy. In the 1950s and 1960s, behavioral therapy originated from the application of behaviorism to facilitate behavior modification in humans. Behaviorism was characterized by the ambition of using experimental approaches to explain and control behavior, first especially concerning non-human animals. This focus on empirical methods and effort to establish psychology as a natural science stood in opposition to classical psychoanalysis whose hypotheses of hidden phenomena were hard to prove at the time. (Thoma et al., 2015, p. 424)

Cognitive therapy was coined amongst others by Albert Ellis and Aaron Beck. With his rational emotive therapy, Ellis created an alternative to psychoanalysis, in which he was originally trained. His new approach was designed to help clients achieve a more realistic viewpoint on their issues and incorporate behavioral improvements in their lives, if necessary in a confrontational way. As opposed to Ellis, rather than confrontation, Beck in his cognitive therapy adapted a framework of

cooperative exploration with the patient. Key feature is cognitive restructuring: detecting negative automatic thoughts, identifying the cognitive distortion at play and then working to attain a more functional perspective on their experience. (Thoma et al., 2015, pp. 429–430)

If described as waves, the first wave of CBT consists in the strictly behavioral approach and the second is characterized by the implementation of a cognitive model. In the current third wave, an emphasis is put on metacognition and how the patient relates to thoughts and emotions. Examples for third wave therapies are dialectical behavior therapy, acceptance and commitment therapy (ACT), mindfulness-based treatments, metacognitive therapy and several others. In addition to new techniques, a greater emphasis is put on the processes of therapy as well as moderators and mediators of change, rather than an exact diagnosis and treatment protocol. This new focus might lead to less strict positions of therapy schools and to a more collaborative evidence-based search for effective transformational processes. Furthermore, it permits a less deficit-oriented and more holistic concept of health being more than the mere absence of sickness. (Hayes & Hofmann, 2017, p. 245)

1.5 Functioning: An Important Outcome

A famous example for a holistic definition of health is the definition by the World Health Organization (International Health Conference, 1948, p. 100): *Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.* Social well-being might not be a synonym for functioning – the outcome parameter investigated in this thesis. However, there is an inseparable relation between social well-being and functioning.

Together with the replacement of a dualistic view of sanity and insanity by a more differentiated perception, a development took place from taking people with mental illness out of society and placing them in remote asylums to establishing such institutions inside the patients' communities (Millon et al., 2004, pp. 103–104).

Efforts to reintegrate people with mental disorders into society are one of the key aspects of social psychiatry. With the rise and general acceptance of the bio-psycho-social model of disease, social psychiatry is nowadays deemed one of three essential dimensions of psychiatry interconnected with

biological psychiatry and psychotherapy. A central task of social psychiatry is rehabilitation. This is where the outcome functioning becomes relevant as it includes important goals of rehabilitation: employment, independent housing, autonomy in everyday life and cultivation of social contacts. (Wancata et al., 2007, pp. 58–63)

Especially concerning schizophrenia with its severe social consequences, it is important to estimate to which extents these goals of rehabilitation have been reached when recommending cost-intensive pharmacological and psychological interventions. Particularly the latter require not only financial, but also enormous personal resources. To measure progress towards the goals of rehabilitation mentioned above, a multitude of functioning scales are available that are described in Chapter 3.4. This work aims to find out in which ways psychological interventions can help improve functioning in people affected by schizophrenia.

One might argue that the term functioning is somewhat mechanistic. To meet such objections, some aspects have to be pointed out. First, functioning does not only focus on employment and economical contribution. Social behavior and participation are included in most of the rating scales as well as activities of daily living and self-care (see Chapter 3.4). It is in the interest of each individual patient to be able to lead a self-guided life and manage their daily life themselves without being dependent from others, to regain autonomy. Second, when considering employment as a domain of functioning, one has to acknowledge that work is more than contributing to economy. Work provides a social context in which people interact with each other, build a team, have a sense of self-efficacy and ideally develop new skills and knowledge that go in line with individual strengths and values. Improving functioning in its educational, occupational, self-care and social domains promotes social participation and contribution as well as personal development and autonomy. Thus, ultimately good functioning does not only benefit society but it also ameliorates the individual's quality of life.

The importance of functioning improvement as therapeutic goal in schizophrenia is backed up by statements of the scientific community. Jones, Hacker, Meaden et al. (2018, p. 37) called functioning the “ultimate aim of clinical intervention” and the German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) formulated functioning as treatment goal as well in their guideline for the treatment of schizophrenia (Deutsche Gesellschaft für Psychiatrie und

Psychotherapie, Psychosomatik und Nervenheilkunde, 2019, p. 22). Guidi et al. (2018, p. 280) criticize the often symptom-focused approach in psychotherapy research and emphasize that, among other variables, functioning has a relevant impact on the clinical presentation of mental illness.

1.6 Need for Research in This Field

As functioning is an important and interesting outcome in schizophrenia, and psychotherapy is getting more attention as well, there is already some research in this field. Laws et al. investigated the effect of CBT on functioning in patients with schizophrenia (Laws et al., 2018, p. 1). They did, however, not include psychological treatments other than CBT and no so-called integrated treatments that combine multiple therapies in their meta-analysis (Laws et al., 2018, p. 3). To get a comprehensive overview, in this thesis, not only the effect of CBT on functioning in patients with schizophrenia is investigated, but also the effect of several other psychological treatments. Jones, Hacker, Meaden et al. (2018) investigated other psychosocial treatments as well - but only if they were comparators to CBT. In the present work, different psychological interventions are investigated regardless of their comparator. In a project, to which the author contributed, Bighelli, Salanti, Huhn et al. (2018) investigated the effect of different psychological interventions in schizophrenia, but considered functioning only a secondary outcome. Furthermore, that work was focused on a population with positive symptoms. This makes sense because primary outcome was the effect of psychological interventions on positive symptoms. But when investigating functioning, it is important to not leave out patients with predominant or prominent negative symptoms. Therefore, in the present work studies focusing on negative symptoms are included as well.

In clinical practice, especially in inpatient settings, often multiple treatments are administered together, including expressive and creative treatments such as art and music therapy. Furthermore, third wave therapies are on the rise. The evidence, especially of meta-analytical nature, is scarce so far in these areas – even though these treatments are already recommended and used nowadays. To better estimate the usefulness and justify or re-evaluate the use of creative, third wave and integrated treatments, they all are included in this review and meta-analysis. It is important to know if patients, relatives and society can benefit from wider spread application of psychological

treatments for schizophrenia, and which treatments specifically. Therefore, the systematic review and meta-analysis conducted for this thesis give an overview over different psychological interventions and their effect on functioning in people with schizophrenia. Furthermore, the methodological quality of the included studies is evaluated and suggestions are made to improve future research and practice in this field.

2 Material and Methods

The systematic review and meta-analysis carried out for this thesis are largely based on data from a research project to which the author contributed as a co-worker. That project was funded by the European Union's Horizon 2020 Research and Innovation Programme. It investigated the effect of psychological interventions on positive symptoms in schizophrenia with a network meta-analysis. A network meta-analysis holds the powerful advantage of being able to compare treatments that have not yet been investigated in a head-to-head comparison so far, providing a comprehensive overview of all the available evidence as well as a hierarchy of treatments concerning efficacy and acceptability. The study protocol has a priori been registered in the PROSPERO database, number CRD42017067795 (Bighelli et al., 2017), and published in *BMJ Open* (Bighelli, Salanti, Reitmeir et al., 2018). Results have been published by Bighelli, Salanti, Huhn et al. (2018), Bighelli, Huhn et al. (2018) and Bighelli et al. (2020). (Klinik und Poliklinik für Psychiatrie und Psychotherapie, 2021)

Other doctoral theses as part of the above-mentioned project are being undertaken by Cornelia Reitmeir and Felicitas Schwermann. They use very similar methodology because of the same original dataset and the standards and statistical approach applied in this workgroup and in the field of meta-analysis in general. However, they examine other outcome domains. The review and meta-analysis carried out for this thesis focused on the effect of psychological interventions on functioning in patients with schizophrenia. As opposed to Bighelli, Salanti, Huhn et al. (2018), the author does not consider functioning as secondary outcome, but as main outcome, and the population is not limited to patients with positive symptoms, but includes patients with a diagnosis of schizophrenia regardless if positive or negative symptoms dominate the clinical presentation. All data have been checked and organized again as well as analyzed in detail by the author of this thesis. The approach used in this thesis is also somewhat similar to that used by Rabaioli in 2018 in his dissertation, as that work also focused on social functioning in patients with schizophrenia, but on the effects of antipsychotic medication (Rabaioli, 2018).

2.1 Inclusion and Exclusion Criteria

The inclusion and exclusion criteria described here are largely based on the standards enabling good scientific practice used in the working group in which this thesis project was conducted. Therefore, there is a considerable amount of similarities to the inclusion and exclusion criteria in the works of Bighelli et al. and Rabaioli (Bighelli et al., 2020; Bighelli, Huhn et al., 2018; Bighelli, Salanti, Huhn et al., 2018; Bighelli, Salanti, Reitmeir et al., 2018; Bighelli, Salanti, Reitmeir et al., 2017; Rabaioli, 2018).

Table 1 *Inclusion and Exclusion Criteria*

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none">- randomized controlled trials- at least 80% of patients with a diagnosis of schizophrenia or related disorder- psychological intervention	<ul style="list-style-type: none">- first-episode psychosis- somatic or psychiatric comorbidity

In the present work randomized controlled trials (RCTs) that met the following inclusion criteria and did not meet any of the exclusion criteria were included (Table 1). There was no time limit as to when the studies were conducted. Trial duration and number of participants were not limited either.

Open label trials were not excluded because blinding is often difficult to do in psychological treatments. In Table 3 and *Figure 3*, information about blinding is given for every study that provided such information.

Regarding the diagnosis, all studies were included that enrolled adult patients of which at least 80% had a diagnosis of schizophrenia or schizophrenia-related disorders, like schizoaffective disorder, schizophreniform disorder, delusional disorder or non-affective psychotic disorder. There was no restriction concerning the diagnostic criteria that were used. If individuals with different diagnoses were included and data for patients with the above-mentioned diagnoses was available separately, that separate data was used. In Table 3 *Study and Patient Characteristics*, information about the type of diagnosis that was used is given for every trial.

Studies were excluded if they focused on patients that had a medical or psychiatric comorbidity, that experienced their first episode of psychosis or that were in the prodromal stage of psychosis. First-episode patients were excluded because they tend to show significantly higher response rates to treatments than chronic patients (Leucht et al., 2017, p. 933; Zhu et al., 2017). (Bighelli, Salanti, Reitmeir et al., 2018, p. 4)

One inclusion criterion was that patients had to receive a psychological treatment. The Cochrane Common Mental Disorders Group (CCMD) (formerly Cochrane Collaboration Depression, Anxiety and Neurosis Group [CCDAN]) published a list of psychological treatments, the “CCDAN Topic List: Intervention – Psychological therapies” (The Cochrane Collaboration Depression, Anxiety and Neurosis Group [CCDAN], 2013). For this thesis, all treatments were considered “psychological” that the CCMD considered so. This varies from ACT over music therapy to supportive therapy. More about the treatments is explained in Chapter 3.3 Description of Treatments.

The psychological treatment could be compared to another psychological treatment, wait-list, inactive control conditions or to treatment as usual (TAU).

The outcome functioning was measured in the included studies with different rating scales. The results of rating scales have only been used if the instrument has been published in a peer-reviewed journal. This is a conservative approach, since non-published rating scales have been found to exaggerate differences in schizophrenia trials (Marshall et al., 2000, pp. 249-251).

2.2 Search Strategy

For this systematic review and meta-analysis, the same search strategy was applied that was used by Bighelli, Salanti, Huhn et al. (2018, Appendix, pp. 3-23). The following databases were searched: EMBASE, MEDLINE, PsycINFO, PubMed, BIOSIS, Cochrane Library, World Health Organization’s International Clinical Trials Registry Platform and ClinicalTrials.gov. This broad search looked for any RCT about patients with schizophrenia or a related disorder that received any psychological treatment. The complete search strategy can be found in detail in Chapter 10 Search Strategy.

2.3 Study Selection Process

Two independent reviewers, one of whom was the author of this thesis, first screened for eligibility the identified records' titles and abstracts that were found in the search. Disagreements were discussed and resolved between the two reviewers and in case of remaining disagreement the full-text was retrieved. This screening in double is an essential necessity in systematic reviews and meta-analyses to ensure high quality in this field of research. Duplicates were deleted and records that did not meet the inclusion criteria or that met one or more of the exclusion criteria were excluded.

For the remaining records, the full-texts were retrieved from different sources. When possible, they were retrieved online via the eAccess option of the university library of the Technical University of Munich or the Bavarian State Library. If the text was not available online, the print versions of the texts were retrieved and scanned. If this was not possible either, the articles were purchased. Furthermore, authors were contacted via e-mail and asked if they could provide unpublished data that was relevant for this analysis.

The full-texts were then screened again thoroughly by two independent reviewers for inclusion and exclusion criteria and only included if they met inclusion criteria and did not meet exclusion criteria. To ensure high quality, disagreements were discussed with a third reviewer or an expert in the field such as Prof Dr Stefan Leucht. This screening in double and resolution of disagreement with the help of an expert is essential to ensure high quality and consistent decisions concerning study selection for a systematic review and meta-analysis.

2.4 Data Extraction Process

The data extraction followed the methodology used by Bighelli and colleagues (Bighelli, Salanti, Reitmeir et al., 2018): The full articles of the included studies were read carefully by the author and another independent co-worker. The studies were allotted randomly to the members of the Section Evidence Based Medicine in Psychiatry and Psychotherapy, Department of Psychiatry and Psychotherapy, Klinikum rechts der Isar, Technical University of Munich, led by Prof Dr Stefan Leucht. All members of this working group were trained in the same structured way to ensure high

quality in data extraction. Detailed instructions for data extraction were provided in the internal handbook “Beschreibung Parameter der Datenbank_Psychotherapie” in which the parameters of the database were described (Section Evidence Based Medicine in Psychiatry and Psychotherapy, 2017). Data was extracted from each study by both reviewers independently, and all the relevant numbers were inserted in a Microsoft Access form, explicitly created for studies in the field of schizophrenia, and specifically adapted for studies on psychological treatments. The software allows automatic detection of inconsistencies between the two versions, so that they can be discussed in order to have a final agreed version. In case of disagreement between the author and the second reviewer, it was discussed further with a third senior reviewer or an expert in the field such as Prof Dr Stefan Leucht. This double-check procedure is a standard in meta-analysis, and ensures high quality in the data extraction. Data were extracted from the main study reports as well as from supplementary material and all authors were contacted via e-mail to ask if they could provide additional unpublished data. See Table 2 for the types of data that were collected.

Table 2 *Types of Collected Data*

Overall study characteristics	<ul style="list-style-type: none"> - study citation - study duration - registration number to trial registries - year of publication - location - setting - number of centers - sample size - diagnostic criteria - funding/sponsor (industry or academic)
Methodology	<ul style="list-style-type: none"> - study design - number of arms - risk of bias
Characteristics of participants	<ul style="list-style-type: none"> - gender - age - details on diagnosis - number randomized to each arm - sociodemographic characteristics - whether naïve to psychological treatments at baseline or with previous experience with the experimental intervention

Characteristics of intervention	<ul style="list-style-type: none"> - number and frequency of sessions - therapy setting - expertise of therapist - researcher allegiance
Outcome measures	<ul style="list-style-type: none"> - information on whether an intention-to-treat approach has been used and how it was defined - scale used - number of patients for which data are available - mean change score between endpoint and baseline - mean score at endpoint - standard deviation - baseline score

The information in the previous paragraph and table has been published by Bighelli et al. in 2018 (Bighelli, Salanti, Reitmeir et al., 2018) and their methodology was used for this thesis as well as it corresponds to the high scientific standards used in the working group to which the author of this thesis belongs.

2.5 Risk of Bias Assessment

For every study, the risk of bias was assessed using the Cochrane Collaboration’s risk of bias assessment tool (Higgins et al., 2017, pp. 8:10-8:23). The tool consists of seven items. The items are “random sequence generation”, “allocation concealment”, “blinding of participants and personnel”, “blinding of outcome assessment”, “incomplete outcome data”, “selective reporting” and “other bias”. For the calculation of the overall risk of bias the method described by Furukawa et al. (2016, Appendix p. 136) was used: if no domain was rated as having a high risk of bias and three or less studies were rated as unclear, the overall risk of bias was considered low; if one domain was rated as having a high risk of bias or four or more domains were rated as having an unclear risk of bias, the overall risk of bias was considered moderate; in all other cases, the overall risk of bias was considered high. There were two adaptations of the above described procedure for the present review: the domain “blinding of participants and personnel” was not considered, as it is very difficult to obtain in psychotherapy because of the personal nature of psychotherapy; and the

domain “researcher allegiance” was added as it is a common source of bias in psychotherapy trials. This evaluation was performed by the author and a second reviewer independently, and the disagreements discussed with a third senior reviewer as suggested by Munder and Barth (2017, p. 353).

2.6 Statistical Analyses

2.6.1 Type of Data

In meta-analyses, it is differentiated between dichotomous and continuous outcome data. Continuous data means that any value in a given interval can be obtained. To be precise, as a consequence of the scale that is used, it may occur that only discrete values can result. But as the data is not dichotomous, meaning there are not only the two options “yes” or “no”, it makes sense to proceed as if the data was continuous. (Higgins, Thomas et al., 2019, p. 156; Rabaioli, 2018, p. 14) Applying that definition, outcome data for functioning is usually of continuous nature.

2.6.2 Effect Size

To present the effect size, the standardized mean difference (*SMD*) is used. It is standardized because different scales, used in the different RCTs, are to be compared. To obtain the *SMD*, the difference in mean outcome between groups, the mean difference (*MD*), is divided by the standard deviation (*SD*) of outcome among participants (Higgins, Thomas et al., 2019, pp. 157–158):

$$SMD = MD/SD$$

Missing standard deviations were imputed using the following parameters, from most to least preferred: standard error (*SE*), *p*-value, mean of all *SD*s, confidence interval (*CI*).

A negative *SMD* favors the treatment condition, a positive *SMD* favors the control condition.

The effect size was judged using Cohen’s classification, according to which an effect size is considered small from 0.2 to 0.5, medium from 0.5 to 0.8 and large if higher than 0.8 (Cohen, 1988, pp. 25–27).

To assess the level of significance of the results, both 95% CIs and p -values (p) are used. The 95% CI can be roughly described as the interval in which with a probability of 95% the true value lies. If this interval does not include zero, a difference is considered statistically significant. (Higgins, Thomas et al., 2019, p. 408)

A p -value below 0.05 means that the probability that a difference has been detected without there being a difference in reality (error of the second kind) is below 5%. If this is the case, a result is considered statistically significant. As this threshold is an arbitrary one and may be misleading, exact p -values are given for every result. (Higgins, Thomas et al., 2019, pp. 409–410)

Both change and endpoint data were used for the analysis. Change data was preferred, but only used if originally given, not calculated from endpoint and baseline data.

A random effects model following the approach by DerSimonian and Laird (1986) was used as it does not seem likely that there is one true treatment effect that is identical for all the studies. It seems more likely that in reality there is a variety of effects across the different studies. (Higgins, Thomas et al., 2019, p. 262)

2.6.3 Heterogeneity

Statistical heterogeneity describes the variability of intervention effects in different studies. It is a result of the clinical and methodological diversity of the analyzed studies. Heterogeneity was described and assessed using the Tau^2 , the Chi^2 and the I^2 . The Tau^2 is defined as the variation in effect estimates. The Chi^2 test describes if the variability of the results exists due to heterogeneity of the studies or due to chance. If its p -value is below 0.05, there is evidence that the variability of results is a consequence of heterogeneity. As there is always some amount of clinical and methodological diversity and therefore heterogeneity when comparing different studies, another measure can be helpful to assess its relevance: the I^2 -value. The I^2 describes how much of the variability in effect estimates can be traced back to heterogeneity and is calculated as following:

$$I^2 = \left(\frac{Q - df}{Q} \right) * 100\%$$

Q stands for the Chi^2 statistics and df for its degrees of freedom. Heterogeneity was considered probably not important for an I^2 of up to 40%, moderate for an I^2 from 30 to 60%, substantial for an I^2 from 50 to 90% and considerable if over 75%. Possible sources for heterogeneity were explored using sensitivity analyses, subgroup analyses and meta-regression analyses. (Higgins, Thomas et al., 2019, pp. 257–261)

2.6.4 Sensitivity Analyses

Sensitivity analyses were carried out for comparisons with five or more studies to explore heterogeneity (Higgins, Thomas et al., 2019, p. 261). Different factors may lead to heterogeneity. Open label studies, that means studies without blinding of outcome assessment, may be subject to detection bias (Higgins, Thomas et al., 2019, p. 626). High researcher allegiance may lead to the Rosenthal effect in which better results are obtained because of a self-fulfilling prophecy of positive expectations (Faller & Lang, 2019, p. 79). Studies focused on treatment resistant patients may also contribute to heterogeneity in results. Therefore, sensitivity analyses excluding studies focused on treatment resistant patients, open label studies, studies with high researcher allegiance or studies with high overall risk of bias were carried out. This choice of studies to be excluded for sensitivity analyses is based on the reasoning used by Bighelli and colleagues (Bighelli, Salanti, Reitmeir et al., 2018, p. 8).

2.6.5 Subgroup Analyses

Another way of exploring heterogeneity is by conducting subgroup analyses. The principle of subgroup analyses is splitting up the total sample according to predefined criteria and then running analyses for the subsamples independently. Then, the effect sizes and significance measures of the subgroups are compared and tests for heterogeneity between the subgroups are carried out to see if the variation in results is a consequence of the subgroup difference. As subgroup analyses do not make sense when there is not enough material, they were carried out only for comparisons with 10 or more studies. (Higgins, Thomas et al., 2019, pp. 265–268)

As both studies with group and individual setting were included, this might account for some heterogeneity and was investigated with a subgroup analysis regarding treatment setting. Group

setting means that sessions were conducted with groups of patients and individual setting means that treatment sessions were conducted individually. Another possible moderator is therapist expertise which was explored with a subgroup analysis with one subgroup in which trainee therapists are allowed and another subgroup with the studies in which only expert therapists provided the intervention. This choice of effect modifiers to be investigated follows the methodology used by Bighelli and colleagues. (Bighelli, Salanti, Reitsma et al., 2018, pp. 7–8)

2.6.6 Meta-Regression Analyses

Subgroup analyses are especially helpful for categorical variables, like the ones mentioned above. For continuous variables, their moderating effect can be better explored with meta-regression analyses. The method of regression has the aim to investigate if and how the value of an explanatory variable predicts the value of the outcome variable. The explanatory variable can be a patient or treatment characteristic, the outcome variable is the effect size. In a meta-regression, the studies are weighted according to their numbers of participants. The result of a meta-regression analysis is the regression co-efficient. It shows by how many units the outcome variable increases per unit increase of the explanatory variable. Significance tests for meta-regressions indicate if the relationship between the two variables is linear. (Higgins, Thomas et al., 2019, pp. 267–268)

Meta-regression analyses were carried out for comparisons with 10 or more studies to explore the role of the possible moderators treatment duration, age, quantity of male and female participants, number of sessions and baseline severity in Positive and Negative Syndrome Scale (PANSS) equivalents (Leucht, Rothe et al., 2013, Webtable 2). All these characteristics may influence how well the treatments work. These variables were also considered in the meta-analysis undertaken by Bighelli et al. 2018. (Bighelli, Salanti, Reitsma et al., 2018, pp. 7–8)

2.6.7 Publication Bias

Publication bias means that studies preferably get published when they show big effects favoring the treatment condition and the results are statistically significant (Faller & Lang, 2019, p. 105).

This may lead to distorted conclusions in meta-analyses. Therefore, it is important to assess the risk of missing studies. One way to do this is by using funnel plots. Funnel plots are scatter plots,

where each study is represented according to its effect estimate that is shown on the horizontal axis and *SE* that is shown on the vertical axis. Normally, the resulting form is an inverted funnel. If the graph is asymmetric, it is likely for studies to be missing. Funnel plots were carried out for comparisons comprising 10 or more studies, as they are based on symmetry and the tests for funnel plot asymmetry have a low power when there are less studies. (Higgins, Thomas et al., 2019, pp. 362–365)

Egger’s test for funnel plot asymmetry was applied (Egger et al., 1997). It measures the bias shown by funnel plot asymmetry and indicates its significance. The trim and fill method by Duval and Tweedie (2000) was used to give an estimate of the effect size after correcting for publication bias. (Bighelli, Salanti, Huhn et al., 2018, Appendix, p. 75)

2.6.8 Graphic Presentation

The continuous outcome variable “functioning” is graphically illustrated using forest plots.

The effect size of each study, here the *SMD*, is depicted by a square whose size depends on the weight of the trial. The 95% CI is depicted by a horizontal line that runs through the square. The result of the meta-analysis is depicted by a diamond. The graph is divided by a vertical axis. On the horizontal axis, the scale and direction of effect estimates is defined. Usually, results on the left side of the axis mean that the treatment condition is favored, results on the right side mean that the control condition is favored. If a result would be right on the axis it would mean that no difference is found between intervention and control. If the line of the 95% CI or the corner of the diamond touches or crosses the vertical axis, it means that the confidence interval includes the possibility of no difference between the treatments. (Higgins, Thomas et al., 2019, p. 243; Lewis & Clarke, 2001, pp. 1479–1480)

2.6.9 Software

Data extraction was carried out with “Microsoft Access 2013”. Statistical analyses were carried out with “Review Manager 5.3” (The Cochrane Collaboration, 2014) and “RStudio version 1.3.959” (RStudio Team, 2020).

3 Results

3.1 Study Selection Process

By January 10, 2018, 21772 records that possibly investigated psychological interventions in schizophrenia were identified by the search. After title-abstract screening, 2754 full-text articles were assessed for eligibility, of which 462 articles corresponding to 192 studies met inclusion criteria. Of these studies, 44 had usable data for the outcome functioning and were included in this meta-analysis (*Figure 1*).

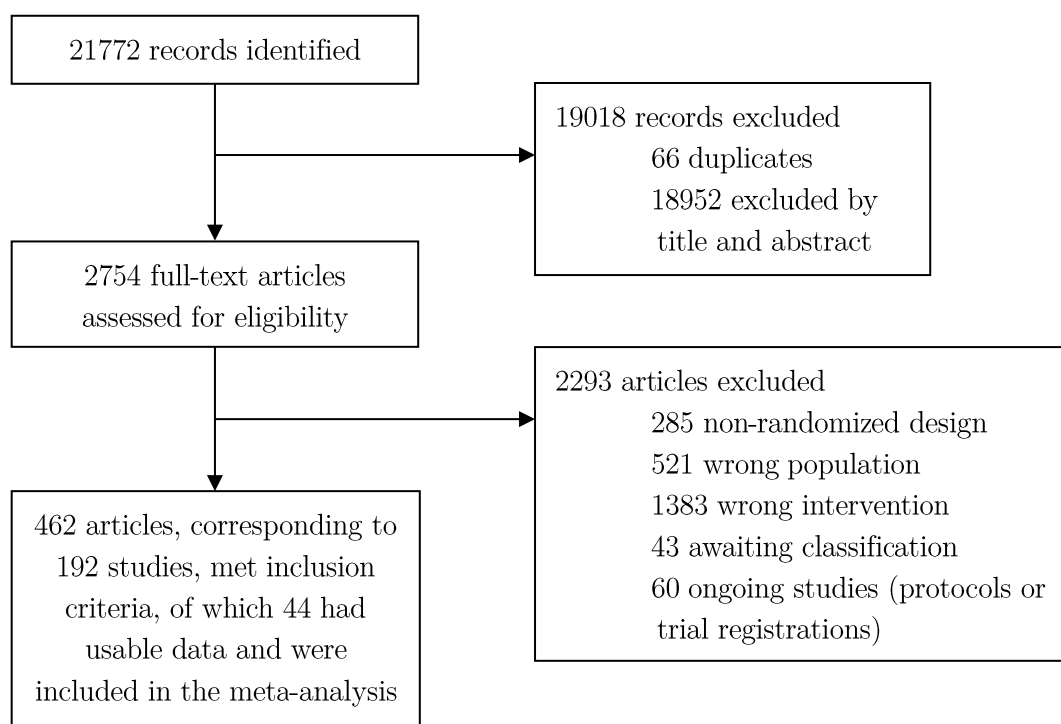


Figure 1. Flow chart depicting the study selection process (adapted from Bighelli, Salanti, Huhn et al., 2018).

3.2 Characteristics of Included Studies

Details about the included studies investigating psychological interventions for schizophrenia and containing outcome data on functioning are given in Table 3.

Table 3 *Study and Patient Characteristics*

	Overall study characteristics	Characteristics of patients
Barrowclough et al., 2006	<p><u>Country</u>: UK</p> <p><u>Study treatments (number of patients)</u>: cognitive behavior therapy (CBT) ($n = 57$), treatment as usual (TAU)($n = 56$)</p> <p><u>Trial duration</u>: 26 weeks</p> <p><u>Number of sessions</u>: 10.4</p> <p><u>Study design</u>: single blind</p> <p><u>Risk of bias*</u>: moderate</p> <p><u>Functioning scale</u>: Global Assessment of Functioning (GAF)</p>	<p><u>Diagnosis (criteria)</u>: schizophrenia or schizoaffective disorder (DSM-IV)</p> <p><u>Gender</u>: 82 (73%) men, 31 women (27%)</p> <p><u>Mean age</u>: 38.83 years</p> <p><u>Baseline severity</u>: Positive and Negative Syndrome Scale (PANSS) total score: 63.8, positive symptoms 17.4, negative symptoms 14.1;</p> <p><u>Duration of illness</u>: 13.67 years</p>
Bradshaw, 2000	<p><u>Country</u>: not available (author's affiliation in the USA)</p> <p><u>Study treatments (number of patients)</u>: CBT ($n = 12$), day treatment program ($n = 12$)</p> <p><u>Trial duration</u>: 156 weeks</p> <p><u>Number of sessions</u>: not available</p> <p><u>Study design</u>: single blind</p> <p><u>Risk of bias</u>: high</p> <p><u>Functioning scale</u>: Role Functioning Scale</p>	<p><u>Diagnosis</u>: schizophrenia (DSM-IV)</p> <p><u>Setting</u>: outpatients</p> <p><u>Mean age</u>: 32 years</p> <p><u>Duration of illness</u>: 11 years</p> <p><u>Medication</u>: 100% taking antipsychotics</p>

<p>Cather et al., 2005</p>	<p><u>Country:</u> USA</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 16$), psychoeducation ($n = 14$)</p> <p><u>Trial duration:</u> 16 weeks</p> <p><u>Number of sessions:</u> 15</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Social Functioning Scale (SFS)</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder, depressed type (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 17 (57%) men, 13 (43%) women</p> <p><u>Mean age:</u> 40.4 years</p> <p><u>Baseline severity:</u> PANSS total score 51.1, positive symptoms factor 13.53, negative symptoms factor 14.32;</p> <p><u>Duration of illness:</u> 18 years</p> <p><u>Medication:</u> 100% of CBT arm taking antipsychotics</p>
<p>Chadwick et al., 2009</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> mindfulness ($n = 11$), wait-list ($n = 11$)</p> <p><u>Trial duration:</u> 10 weeks</p> <p><u>Number of sessions:</u> 10</p> <p><u>Study design:</u> open label</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Clinical Outcomes in Routine Evaluation</p>	<p><u>Diagnosis:</u> psychotic disorder (criteria not available [NA])</p> <p><u>Mean age:</u> 41.6 years</p> <p><u>Duration of illness:</u> 17.7 years</p> <p><u>Medication:</u> 100% taking antipsychotics</p>
<p>Chien & Lee, 2013</p>	<p><u>Country:</u> Hongkong</p> <p><u>Study treatments (number of patients):</u> mindfulness-based psychoeducation ($n = 48$), TAU ($n = 48$)</p> <p><u>Trial duration:</u> 36 weeks</p> <p><u>Number of sessions:</u> 12</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> Specific Levels of Functioning (SLOF)</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 53 (55%) men, 43 (45%) women</p> <p><u>Mean age:</u> 25.9 years</p> <p><u>Baseline severity:</u> Brief Psychiatric Rating Scale (BPRS) total score 63.35</p> <p><u>Duration of illness:</u> 3.1 years</p> <p><u>Medication:</u> 84.38% taking antipsychotics</p>

<p>Chien & Thompson, 2014</p>	<p><u>Country:</u> Hongkong</p> <p><u>Study treatments (number of patients):</u> mindfulness-based psychoeducation ($n = 36$), TAU ($n = 35$), psychoeducation ($n = 36$)</p> <p><u>Trial duration:</u> 27 weeks</p> <p><u>Number of sessions:</u> 12</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> SLOF</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 61 (57%) men, 46 (43%) women</p> <p><u>Mean age:</u> 25.63 years</p> <p><u>Baseline severity:</u> BPRS-18 total score 31.40</p> <p><u>Duration of illness:</u> 2.6 years</p> <p><u>Medication:</u> 87.85% taking antipsychotics</p>
<p>Chien et al., 2017</p>	<p><u>Country:</u> Hongkong</p> <p><u>Study treatments (number of patients):</u> mindfulness-based psychoeducation ($n = 114$), TAU ($n = 114$), psychoeducation ($n = 114$)</p> <p><u>Trial duration:</u> 24 weeks</p> <p><u>Number of sessions:</u> 12</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> SLOF</p>	<p><u>Diagnosis:</u> schizophrenia and other psychotic disorders (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 216 (63%) men, 126 (37%) women</p> <p><u>Mean age:</u> 25.63 years</p> <p><u>Baseline severity:</u> PANSS total score 80.77, positive symptoms 20.23, negative symptoms 19.83</p> <p><u>Duration of illness:</u> 2.6 years</p> <p><u>Medication:</u> 89.77% taking antipsychotics</p>
<p>Crawford et al., 2012</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> art therapy ($n = 140$), activity group ($n = 140$), TAU ($n = 137$)</p> <p><u>Trial duration:</u> 52 weeks</p> <p><u>Number of sessions:</u> 52</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia (clinical diagnosis)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 279 (67%) men, 138 (33%) women</p> <p><u>Mean age:</u> 41 years</p> <p><u>Baseline severity:</u> PANSS total score 74.08, positive symptoms 17.84, negative symptoms 18.63</p> <p><u>Duration of illness:</u> 19.33 years</p> <p><u>Medication:</u> 96% taking antipsychotics</p>

<p>Durham et al., 2003</p>	<p><u>Country:</u> Scotland</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 22$), supportive therapy ($n = 23$), TAU ($n = 21$)</p> <p><u>Trial duration:</u> 39 weeks</p> <p><u>Number of sessions:</u> 20</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Global Assessment Scale (GAS)</p>	<p><u>Diagnosis:</u> schizophrenia, schizoaffective disorder, delusional disorder (ICD-10 and DSM-IV)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 45 (68%) men, 21 women (32%)</p> <p><u>Mean age:</u> 36.3 years</p> <p><u>Baseline severity:</u> PANSS total score 96.63, PSYRATS total 35.57</p> <p><u>Duration of illness:</u> 13 years</p> <p><u>Medication:</u> 100% taking antipsychotics</p>
<p>Farhall et al., 2009</p>	<p><u>Country:</u> Australia</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 45$), TAU ($n = 49$)</p> <p><u>Trial duration:</u> 52 weeks</p> <p><u>Number of sessions:</u> 17.05</p> <p><u>Study design:</u> open label</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Life Skills Profile</p>	<p><u>Diagnosis:</u> schizophrenia, schizoaffective disorder, delusional disorder, or mood disorder with psychotic features (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 54 (59%) men, 38 (41%) women</p> <p><u>Mean age:</u> 32.85 years</p> <p><u>Baseline severity:</u> PANSS total score 59.31, positive symptoms 14.63; negative symptoms 14.78</p> <p><u>Medication:</u> 90.43% taking antipsychotics</p>

<p>Garety et al., 2008 (total sample)</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 133$), family intervention ($n = 28$), TAU ($n = 140$)</p> <p><u>Trial duration:</u> 39 weeks</p> <p><u>Number of sessions:</u> 14.3 (CBT), 13.9 (FI)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> Social and Occupational Functioning Assessment Scale (SOFAS)</p>	<p><u>Diagnosis:</u> non-affective psychosis (ICD-10 and DSM-IV)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 211 (70%) men, 90 (30%) women</p> <p><u>Mean age:</u> 37.54 years</p> <p><u>Baseline severity:</u> PANSS total score 65.16, positive symptoms 18.15, negative symptoms 13.27</p> <p><u>Duration of illness:</u> 10.8 years</p>
<p>Garety et al., 2008 (sample a)</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 27$), family intervention ($n = 28$), TAU ($n = 28$)</p> <p><u>Trial duration:</u> 39 weeks</p> <p><u>Number of sessions:</u> 13.9</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> SOFAS</p>	<p><u>Diagnosis:</u> non-affective psychosis (DSM-IV and ICD-10)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 60 (72%) men, 23 (28%) women</p> <p><u>Mean age:</u> 36.4 years</p> <p><u>Baseline severity:</u> PANSS total score 67.31, positive symptoms 17.16, negative symptoms 15.58</p> <p><u>Duration of illness:</u> 11.57 years</p>

<p>Garety et al., 2008 (sample b)</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 106$), TAU ($n = 112$)</p> <p><u>Trial duration:</u> 39 weeks</p> <p><u>Number of sessions:</u> 14.3</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> SOFAS</p>	<p><u>Diagnosis:</u> non-affective psychosis (DSM-IV and ICD-10)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 151 (69%) men, 67 (31%) women</p> <p><u>Mean age:</u> 38.1 years</p> <p><u>Baseline severity:</u> PANSS total score 64.29, positive symptoms 18.51, negative symptoms 12.38</p> <p><u>Duration of illness:</u> 10.4 years</p>
<p>Gottlieb et al., 2017</p>	<p><u>Country:</u> USA</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 19$), TAU ($n = 18$)</p> <p><u>Trial duration:</u> 24 weeks</p> <p><u>Number of sessions:</u> 10</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> Specific Levels of Functioning</p>	<p><u>Diagnosis:</u> schizophrenia, schizoaffective disorder, or psychosis not otherwise specified diagnosis (NA)</p> <p><u>Setting:</u> outpatients; 23 (62%) men, 14 women (38%)</p> <p><u>Mean age:</u> 42.04 years</p> <p><u>Baseline severity:</u> BPRS-24 total score 54.92, Psychotic Symptom Rating Scales (PSYRATS) 53.06, BPRS negative symptoms 6.23</p> <p><u>Medication:</u> 100% taking antipsychotics</p>
<p>Granholtm et al., 2005</p>	<p><u>Country:</u> USA</p> <p><u>Study treatments (number of patients):</u> cognitive behavioural social skills training (CBSST)($n = 37$), TAU ($n = 39$)</p> <p><u>Trial duration:</u> 24 weeks</p> <p><u>Number of sessions:</u> 24</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> Independent Living Skills Survey</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 56 (74%) men, 20 (26%) women</p> <p><u>Mean age:</u> 53.78 years</p> <p><u>Baseline severity:</u> PANSS total score 53.37, positive symptoms 12.73, negative symptoms 14.66</p> <p><u>Duration of illness:</u> 29.23 years</p> <p><u>Medication:</u> 87.5% taking antipsychotics</p>

<p>Granholm et al., 2013</p>	<p><u>Country:</u> USA</p> <p><u>Study treatments (number of patients):</u> CBSST ($n = 41$), goal-focused supportive contact ($n = 38$)</p> <p><u>Trial duration:</u> 36 weeks</p> <p><u>Number of sessions:</u> 30.3 (CBSST), 29.6 (goal-focused supportive contact)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Independent Living Skills Survey</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 44 (56%) men, 35 (44%) women</p> <p><u>Mean age:</u> 55 years</p> <p><u>Baseline severity:</u> PANSS total score 64.63, positive symptoms 18.06</p> <p><u>Medication:</u> 94.94% taking antipsychotics</p>
<p>Granholm et al., 2014</p>	<p><u>Country:</u> USA</p> <p><u>Study treatments (number of patients):</u> CBSST($n = 73$), goal-focused supportive contact ($n = 76$)</p> <p><u>Trial duration:</u> 36 weeks</p> <p><u>Number of sessions:</u> 12.2 (CBSST), 15.6 (goal-focused supportive contact)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Independent Living Skills Survey</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 99 (66%) men, 50 (34%) women</p> <p><u>Mean age:</u> 41.36 years</p> <p><u>Baseline severity:</u> PANSS total score 72.42, positive symptoms 19.81</p> <p><u>Duration of illness:</u> 21.35 years</p> <p><u>Medication:</u> 97.32% taking antipsychotics</p>
<p>Grant et al., 2012</p>	<p><u>Country:</u> USA</p> <p><u>Study treatments (number of patients):</u> cognitive therapy ($n = 31$), standard treatment ($n = 29$)</p> <p><u>Trial duration:</u> 18 months</p> <p><u>Number of sessions:</u> 50.5</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> GAS</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 40 (67%) men, 20 (33%) women</p> <p><u>Mean age:</u> 38.46 years</p> <p><u>Baseline severity:</u> Scale for the Assessment of Positive Symptoms (SAPS) score 17.33</p> <p><u>Duration of illness:</u> 15.52 years</p>

<p>Haddock et al., 2009</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 38$), social activity therapy ($n = 39$)</p> <p><u>Trial duration:</u> 26 weeks</p> <p><u>Number of sessions:</u> 17 (CBT), 17.4 (social activity therapy)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-VI)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 66 (86%) men, 11 (14%) women</p> <p><u>Mean age:</u> 34.8 years</p> <p><u>Baseline severity:</u> PANSS total score 63.81, positive symptoms 27.6, negative symptoms 13.04</p> <p><u>Medication:</u> 100% taking antipsychotics</p>
<p>Jenner et al., 2004</p>	<p><u>Country:</u> Netherlands</p> <p><u>Study treatments (number of patients):</u> hallucination focused integrative treatment ($n = 39$), TAU ($n = 39$)</p> <p><u>Trial duration:</u> 39 weeks</p> <p><u>Number of sessions:</u> 11</p> <p><u>Study design:</u> open label</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Groningen Social Disabilities Schedule</p>	<p><u>Diagnosis:</u> non-affective psychosis, including schizophrenia, schizoaffective or psychotic disorder not otherwise specified (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 41 (54%) men, 35 (46%) women</p> <p><u>Mean age:</u> 36.35 years</p> <p><u>Baseline severity:</u> PANSS total score 60.2, positive symptoms 16.05, negative symptoms 13.25</p>
<p>Klingberg et al., 2011</p>	<p><u>Country:</u> Germany</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 99$), cognitive remediation ($n = 99$)</p> <p><u>Trial duration:</u> 36 weeks</p> <p><u>Number of sessions:</u> 16.6 (CBT), 13.7 (cognitive remediation)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 87 women (43.94%), 111 men (56.06%)</p> <p><u>Mean age:</u> 36.9 years</p> <p><u>Baseline severity:</u> PANSS total score 59.45, positive symptoms 10.5, negative symptoms 18.55</p> <p><u>Duration of illness:</u> 12.5 years</p> <p><u>Medication:</u> 100% taking antipsychotics</p>

<p>Kråkvik et al., 2013</p>	<p><u>Country:</u> Norway</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 23$), wait-list ($n = 22$)</p> <p><u>Trial duration:</u> 26 weeks</p> <p><u>Number of sessions:</u> 20</p> <p><u>Study design:</u> open label</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia, schizoaffective disorder, or persistent delusional disorder (ICD-10)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 29 (64%) men, 16 (36%) women</p> <p><u>Mean age:</u> 36.36 years</p> <p><u>Baseline severity:</u> BPRS-24 score 49.49</p> <p><u>Duration of illness:</u> 10.9 years</p>
<p>Kuipers et al., 2004</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> CBT and family intervention ($n = 32$), TAU ($n = 27$)</p> <p><u>Trial duration:</u> 39 weeks</p> <p><u>Number of sessions:</u> not available</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> any functional psychosis (OPCRIT)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 45 (76%) men, 14 (24%) women</p> <p><u>Mean age:</u> 27.8 years</p> <p><u>Baseline severity:</u> PANSS total score 73.11, positive symptoms 17.39, negative symptoms 16.86</p>
<p>Lee et al., 2014</p>	<p><u>Country:</u> Korea</p> <p><u>Study treatments (number of patients):</u> group music therapy ($n = 12$), control ($n = 12$)</p> <p><u>Trial duration:</u> 12 weeks</p> <p><u>Number of sessions:</u> 18</p> <p><u>Study design:</u> not available</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 25 (75%) men, 5 (25%) women</p> <p><u>Mean age:</u> 40.55 years</p> <p><u>Baseline severity:</u> PANSS total score 94.5, positive symptoms 21.25, negative symptoms 23.2</p>

Li et al., 2015	<p><u>Country:</u> China</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 96$), supportive therapy ($n = 96$)</p> <p><u>Trial duration:</u> 24 weeks</p> <p><u>Number of sessions:</u> 15</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> Personal and Social Performance scale (PSP)</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 72 (38%) men, 120 (63%) women</p> <p><u>Mean age:</u> 31.36 years</p> <p><u>Baseline severity:</u> PANSS total score 72.6, positive symptoms 23.43, negative symptoms 20.4</p> <p><u>Duration of illness:</u> 8.21 years</p> <p><u>Medication:</u> 100% taking antipsychotics</p>
Lincoln et al., 2012	<p><u>Country:</u> Germany</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 40$), TAU ($n = 40$)</p> <p><u>Trial duration:</u> 38 weeks</p> <p><u>Number of sessions:</u> 28.9 (CBT), 2 (TAU)</p> <p><u>Study design:</u> open label</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia, schizoaffective disorder, delusional disorder, or brief psychotic disorder (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 45 (56%) men, 35 (44%) women</p> <p><u>Mean age:</u> 33.15 years</p> <p><u>Baseline severity:</u> PANSS total score 63.15, positive symptoms 14.95, negative symptoms 14.15</p> <p><u>Duration of illness:</u> 10.4 years</p> <p><u>Medication:</u> 96.25% taking antipsychotics</p>
Martin, Koch et al., 2016	<p><u>Country:</u> Germany</p> <p><u>Study treatments (number of patients):</u> dance and movement therapy and body psychotherapy ($n = 44$), TAU ($n = 24$)</p> <p><u>Trial duration:</u> 10 weeks</p> <p><u>Number of sessions:</u> 20</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia spectrum disorder (ICD-10)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 36 (53%) men, 32 (47%) women</p> <p><u>Mean age:</u> 39.8 years</p> <p><u>Baseline severity:</u> BPRS total score 38.16, SANS 25.03</p> <p><u>Medication:</u> 100% taking antipsychotics</p>

Matthews, 1981	<p><u>Country:</u> USA</p> <p><u>Study treatments (number of patients):</u> psychotherapy ($n = 28$), TAU ($n = 14$)</p> <p><u>Trial duration:</u> 8 weeks</p> <p><u>Number of sessions:</u> 8</p> <p><u>Study design:</u> not available</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia (NA)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 21 (50%) men, 21 (50%) women</p> <p><u>Mean age:</u> 24.95 years</p> <p><u>Medication:</u> 100% taking antipsychotics</p>
Montag et al., 2014	<p><u>Country:</u> Germany</p> <p><u>Study treatments (number of patients):</u> psychodynamic art therapy ($n = 29$), TAU ($n = 29$)</p> <p><u>Trial duration:</u> 6 weeks</p> <p><u>Number of sessions:</u> 12</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> inpatients</p> <p><u>Gender:</u> 38 (72%) men, 15 (28%) women</p> <p><u>Mean age:</u> 38.1 years</p> <p><u>Baseline severity:</u> SAPS total score 60.15, Scale for the Assessment of Negative Symptoms (SANS) 45.6</p> <p><u>Duration of illness:</u> 12.6 years</p>
Morrison et al., 2014	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> cognitive therapy ($n = 37$), TAU ($n = 37$)</p> <p><u>Trial duration:</u> 39 weeks</p> <p><u>Number of sessions:</u> 13.3</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> PSP</p>	<p><u>Diagnosis:</u> schizophrenia, schizoaffective disorder, or delusional disorder; diagnostic uncertainty in early phases of psychosis (Early intervention for psychosis service) (ICD-10 or PANSS)</p> <p><u>Gender:</u> 39 (53%) men, 35 (47%) women</p> <p><u>Mean age:</u> 31.32 years</p> <p><u>Baseline severity:</u> PANSS total score 71.76, positive symptoms 20.98, negative symptoms 14.52;</p> <p><u>Medication:</u> 0% taking antipsychotics</p>

<p>Naeem et al., 2016</p>	<p><u>Country:</u> Canada</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 18$), TAU ($n = 15$)</p> <p><u>Trial duration:</u> 16 weeks</p> <p><u>Number of sessions:</u> 14</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> low</p> <p><u>Functioning scale:</u> WHODAS 2.0</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 17 (52%) men, 16 (48%) women</p> <p><u>Mean age:</u> 40.45 years</p> <p><u>Baseline severity:</u> PANSS total score 50.24, positive symptoms 13.54, negative symptoms 12.18</p>
<p>Ochoa et al., 2017</p>	<p><u>Country:</u> Spain</p> <p><u>Study treatments (number of patients):</u> metacognitive training ($n = 65$), psychoeducation ($n = 57$)</p> <p><u>Trial duration:</u> 8 weeks</p> <p><u>Number of sessions:</u> 5.53 (metacognitive training), 4.95 (psychoeducation)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia, psychotic disorder not otherwise specified, delusional disorder, schizoaffective disorder, brief psychotic disorder, or schizophreniform disorder (DSM-IV-TR)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 85 (70%) men, 37 (30%) women</p> <p><u>Mean age:</u> 27.59 years</p> <p><u>Baseline severity:</u> PANSS total score 54.33, positive symptoms 12.22, negative symptoms 14.63</p> <p><u>Duration of illness:</u> 2.29 years</p>
<p>Penadés et al., 2006</p>	<p><u>Country:</u> Spain</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 20$), cognitive remediation ($n = 20$)</p> <p><u>Trial duration:</u> 16 weeks</p> <p><u>Number of sessions:</u> 40</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> Life Skills Profile</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 23 men (57.5%), 17 women (42.5%)</p> <p><u>Mean age:</u> 35.1 years</p> <p><u>Baseline severity:</u> PANSS score 66.99, positive symptoms 11.27, negative symptoms 20.17</p> <p><u>Duration of illness:</u> 13.8 years</p> <p><u>Medication:</u> 100% taking antipsychotics</p>

Penn et al., 2009	<p><u>Country:</u> USA</p> <p><u>Study treatments:</u> CBT ($n = 32$), supportive therapy ($n = 33$)</p> <p><u>Trial duration:</u> 12 weeks</p> <p><u>Number of sessions:</u> 8.3</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> low</p> <p><u>Functioning scale:</u> SFS</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 33 (51%) men, 32 (49%) women</p> <p><u>Mean age:</u> 40.65 years</p> <p><u>Baseline severity:</u> PANSS total score 61.75, positive symptoms 17.55, negative symptoms 13.9</p> <p><u>Duration of illness:</u> 15.4 years</p>
Pot-Kolder et al., 2018	<p><u>Country:</u> Netherlands</p> <p><u>Study treatments (number of patients):</u> virtual-reality exposure therapy for psychosis ($n = 58$), wait-list ($n = 58$)</p> <p><u>Trial duration:</u> 12 weeks</p> <p><u>Number of sessions:</u> 16</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> low</p> <p><u>Functioning scale:</u> SOFAS</p>	<p><u>Diagnosis:</u> psychotic disorder (DSM-IV)</p> <p><u>Gender:</u> 82 (71%) men, 34 (29%) women</p> <p><u>Mean age:</u> 38 years</p> <p><u>Duration of illness:</u> 14.1 years</p> <p><u>Medication:</u> 95.5% taking antipsychotics</p>
Richardson et al., 2007	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> art therapy ($n = 43$), TAU ($n = 47$)</p> <p><u>Trial duration:</u> 12 weeks</p> <p><u>Number of sessions:</u> 12</p> <p><u>Study design:</u> open label</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> SFS</p>	<p><u>Diagnosis:</u> chronic schizophrenia (NA)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 59 (66%) men, 31 (34%) women</p> <p><u>Mean age:</u> 41.17 years</p> <p><u>Baseline severity:</u> BPRS total score 15.57, SANS 8.44</p>

<p>Schrank et al., 2016</p>	<p><u>Country:</u> UK</p> <p><u>Study treatments (number of patients):</u> group psychotherapy ($n = 47$), TAU ($n = 47$)</p> <p><u>Trial duration:</u> 11 weeks</p> <p><u>Number of sessions:</u> 7</p> <p><u>Study design:</u> open label</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> Health of the Nation Outcome Scale</p>	<p><u>Diagnosis:</u> diagnosis of psychosis defined as schizophrenia and other psychoses including schizoaffective and delusional disorder, but not depressive psychosis or psychosis due to substance misuse (clinical diagnosis)</p> <p><u>Setting:</u> inpatients and outpatients</p> <p><u>Gender:</u> 56 (60%) men, 38 (40%) women</p> <p><u>Mean age:</u> 42.5 years</p> <p><u>Baseline severity:</u> BPRS-18 total score 32.14</p> <p><u>Duration of illness:</u> 13.5 years</p>
<p>Shawyer et al., 2012</p>	<p><u>Country:</u> Australia</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 21$), befriending ($n = 22$)</p> <p><u>Trial duration:</u> 15 weeks</p> <p><u>Number of sessions:</u> 14.3 (CBT), 14.4 (Befriending)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia or related condition (DSM-IV)</p> <p><u>Gender:</u> 24 (56%) men, 19 (44%) women</p> <p><u>Mean age:</u> 39.8 years</p> <p><u>Baseline severity:</u> PANSS total score 62.89, positive symptoms 15.99, negative symptoms 14.15</p> <p><u>Duration of illness:</u> 14.71 years</p>
<p>Shawyer et al., 2016</p>	<p><u>Country:</u> Australia</p> <p><u>Study treatments (number of patients):</u> acceptance and commitment therapy ($n = 49$), befriending ($n = 47$)</p> <p><u>Trial duration:</u> 13 weeks</p> <p><u>Number of sessions:</u> 7</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> low</p> <p><u>Functioning scale:</u> SFS</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-IV-TR)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 59 (61%) men, 37 (39%) women</p> <p><u>Mean age:</u> 34.3 years</p> <p><u>Baseline severity:</u> PANSS total score 78.25, positive symptoms 21.8, negative symptoms 18</p> <p><u>Medication:</u> 100% taking antipsychotics</p>

Startup et al., 2004	<u>Country:</u> UK <u>Study treatments (number of patients):</u> CBT ($n = 47$), TAU ($n = 43$) <u>Trial duration:</u> 26 weeks <u>Number of sessions:</u> 12.9 <u>Study design:</u> open label <u>Risk of bias:</u> high <u>Functioning scale:</u> GAF	<u>Diagnosis:</u> schizophrenia, schizophreniform, schizoaffective (DSM-IV) <u>Setting:</u> inpatients <u>Gender:</u> 68 (76%) men, 22 (24%) women <u>Mean age:</u> 30.8 years <u>Baseline severity:</u> BPRS-16 total score 45.75, SAPS positive symptoms 10.7, SANS negative symptoms 8.9; <u>Duration of illness:</u> 6.95 years
Talwar et al., 2006	<u>Country:</u> UK <u>Study treatments (number of patients):</u> music therapy ($n = 33$), TAU ($n = 48$) <u>Trial duration:</u> 12 weeks <u>Number of sessions:</u> 8 <u>Study design:</u> single blind <u>Risk of bias:</u> low <u>Functioning scale:</u> GAF	<u>Diagnosis:</u> schizophrenia, or schizophrenia-like psychoses (ICD-10) <u>Setting:</u> inpatients <u>Gender:</u> 60 (74%) men, 21 (26%) women <u>Mean age:</u> 37.36 years <u>Baseline severity:</u> PANSS total score 71.72, positive symptoms 16.36, negative symptoms 19.20
Tarrier et al., 2014	<u>Country:</u> UK <u>Study treatments:</u> CBT ($n = 25$), TAU ($n = 24$) <u>Trial duration:</u> 16 weeks <u>Number of sessions:</u> 24 <u>Study design:</u> single blind <u>Risk of bias:</u> moderate <u>Functioning scale:</u> GAF	<u>Diagnosis:</u> schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder or psychotic disorder not otherwise specified (DSM-IV) <u>Gender:</u> 31 (63%) men, 18 (37%) women <u>Mean age:</u> 34.9 years <u>Baseline severity:</u> PANSS total score 60.12, positive symptoms 15.44, negative symptoms 13.29 <u>Medication:</u> 100% taking antipsychotics

<p>Valencia et al., 2006</p>	<p><u>Country:</u> Mexico</p> <p><u>Study treatments (number of patients):</u> music therapy ($n = 18$), psychosocial therapy ($n = 18$), multiple therapies ($n = 18$)</p> <p><u>Trial duration:</u> 26 weeks</p> <p><u>Number of sessions:</u> 44 (music therapy), 44 (psychosocial therapy), 108 (multiple therapies)</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> GAF</p>	<p><u>Diagnosis:</u> schizophrenia (DSM-IV)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 33 (77%) men, 10 (23%) women</p> <p><u>Mean age:</u> 30.5 years</p> <p><u>Duration of illness:</u> 8.13 years</p> <p><u>Medication:</u> 100% taking antipsychotics</p>
<p>van der Gaag et al., 2011</p>	<p><u>Country:</u> Netherlands</p> <p><u>Study treatments (number of patients):</u> CBT ($n = 110$), TAU ($n = 106$)</p> <p><u>Trial duration:</u> 26 weeks</p> <p><u>Number of sessions:</u> 13</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> high</p> <p><u>Functioning scale:</u> SFS</p>	<p><u>Diagnosis:</u> schizophrenia or schizoaffective disorder (DSM-IV-TR)</p> <p><u>Gender:</u> 153 (71%) men, 63 (29%) women</p> <p><u>Mean age:</u> 36.99 years</p> <p><u>Baseline severity:</u> PANSS total score 69.3, PSYRATS total 31.35</p> <p><u>Duration of illness:</u> 10.58 years</p>
<p>Wang et al., 2016</p>	<p><u>Country:</u> Hong-Kong</p> <p><u>Study treatments (number of patients):</u> mindfulness-based psychoeducation ($n = 46$), psychoeducation ($n = 46$), TAU ($n = 46$)</p> <p><u>Trial duration:</u> 26 weeks</p> <p><u>Number of sessions:</u> 12</p> <p><u>Study design:</u> single blind</p> <p><u>Risk of bias:</u> moderate</p> <p><u>Functioning scale:</u> SLOF</p>	<p><u>Diagnosis:</u> schizophrenia or its subtypes (DSM-IV-TR)</p> <p><u>Setting:</u> outpatients</p> <p><u>Gender:</u> 72 (52%) men, 66 (48%) women</p> <p><u>Mean age:</u> 24.3 years</p> <p><u>Baseline severity:</u> PANSS total score 87.93, positive symptoms 26.57, negative symptoms 18.3</p> <p><u>Duration of illness:</u> 2.03 years</p> <p><u>Medication:</u> 85.51% taking antipsychotics</p>

Wykes et al., 2005	<u>Country:</u> UK <u>Study treatments (number of patients):</u> CBT ($n = 45$), TAU ($n = 40$) <u>Trial duration:</u> 10 weeks <u>Number of sessions:</u> 7 <u>Study design:</u> open label <u>Risk of bias:</u> high <u>Functioning scale:</u> Social Behaviour Schedule	<u>Diagnosis:</u> schizophrenia (DSM-IV) <u>Setting:</u> outpatients <u>Gender:</u> 50 (59%) men, 35 (41%) women <u>Mean age:</u> 39.7 years <u>Baseline severity:</u> PSYRATS hallucination score 27.95
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*The overall risk of bias was calculated using the Cochrane risk of bias tool (Higgins et al., 2017) and the approach described by Furukawa (2016). The domain “blinding of participants and personnel” was not considered as patients and therapists usually cannot be blinded in psychological interventions.

3.3 Description of Treatments

This analysis includes a variety of psychological interventions. They are described in detail in Table 4. The arrows in the left column indicate under which term the treatment was subsumed for the present work, if applicable. The decision which studies to put inside which treatment comparison or subgroup was made by two independent reviewers and then discussed, not solely based on the name the study authors gave to the intervention, but based on the description they provided about the treatment and control conditions.

Table 4 *Description of Treatments*

Acceptance and commitment therapy (ACT)	A manualized cognitive behavior therapy (Hayes et al., 2003, p. 79), which focuses more on the patient's relation to distressing symptoms than on the symptoms themselves. It encourages patients to be mindful of and accept instead of try and avoid negative experiences, such as distressing voices. At the same time, it is a goal to take value-guided action to enable positive change in spite of the difficulties the patients face (Pankey & Hayes, 2003, p. 325).
Activity group (⇒ inactive control)	Activity groups are used as control groups in the trial Crawford and colleagues conducted. They aim to control for potential effects of the group setting also used in group art therapy. Led by a group facilitator, the patients engage together in different activities varying from watching films to visiting local cafés. Psychological techniques as well as art materials are not employed. (Crawford et al., 2012, p. 6)
Art therapy	In art therapy, patients express their inner experience spontaneously and freely in a creative process using different art materials. Then they get the possibility to share and discuss their pictures helped by interventions of an art therapist. (Crawford et al., 2012, p. 6; Montag et al., 2014, p. 3)
Befriending (⇒ inactive control)	A manualized treatment designed to control for the therapist's attention and the patient's treatment expectancy. It includes conversation about everyday topics and, if conversation is too difficult to attain, neutral activities that do not provoke fear or negative emotions. For talking about symptoms and problems, the patient is referred to the treating clinician. (Shawyer et al., 2012, p. 113)

Cognitive behavior therapy (CBT)	A widely spread therapy approach aimed at changing thought processes and behavior. Initially a stable therapeutic relationship is to be built. The following treatment includes identifying dysfunctional cognitive and behavioral patterns, setting distinct and reachable therapy goals together and replacing dysfunctional patterns step by step with healthier ones. CBT for psychosis focusses especially on dealing with disturbing hallucinations and delusional thoughts as well as the identification of negative belief systems and the development of healthy coping strategies. (Hagen et al., 2011, pp. 3–7)
Cognitive behavioural social skills training (⇒ CBT)	An intervention integrating cognitive behavioral techniques and strategies from social skills training to help patients challenge their thoughts, ask for help in an appropriate way and problem-solve, tailored to the specific needs of patients suffering from schizophrenia. (Granholtm et al., 2005, p. 523)
Cognitive remediation	Applying the principles of errorless learning and immediate positive feedback, executive functioning, attention and memory are trained using techniques for structuring of information, verbalization and self-instruction. (Klingberg et al., 2011, p. S101)
Cognitive therapy (⇒ CBT)	An individualized goal-directed therapy approach aiming to motivate the patient to work on realistic long- and short-term goals. Dysfunctional believes are replaced by more functional ones using cognitive and behavioral strategies. Techniques introduced and practiced during the sessions are consolidated with homework for the patient to do between the sessions. (Grant et al., 2012, pp. 122–123)
Creative therapy	This term summarizes therapies that give patients the possibility to express themselves in a creative way, for example through art, music or body movement. For more detailed information about the treatments that are considered creative therapy, see their descriptions in this table.
Dance and movement therapy and body psychotherapy	See Movement therapy

Day treatment program (⇒ TAU)	A psychiatric service provided for a longer period of time to people with serious and chronic psychiatric conditions. It entails medication management and different group interventions. (Bradshaw, 2000, p. 494)
Family intervention	An intervention that aims at improving communication and problem-solving skills in the families of patients with schizophrenia. There are psychoeducational elements to enable a better understanding of the patients. On top of that, the patient and the relatives get the possibility to discuss and resolve conflicts with the help of a professional and work through difficult emotions that arise as a consequence of the disease. (Garety et al., 2008, p. 413)
Goal-focused supportive contact (⇒ inactive control)	Designed to control for frequency and amount of contact to the therapist and other group members, this intervention gives patients the opportunity to formulate goals and work on them through group discussion without specific therapist guidance. (Granholm et al., 2014, p. 1175)
Hallucination focused integrative treatment	This is a combination treatment containing psychoeducational, cognitive-behavioral, coping-oriented as well as family interventions and rehabilitative elements added to antipsychotic medication. The main purpose is to cope better with hallucinations. (Jenner et al., 2004, p. 134)
Inactive control	This term is utilized for any treatment that serves as a control condition regarding non-specific factors such as the therapist's attention, for example "activity group", "befriending", "social activity therapy" or "supportive counselling", which are also described in this table. (Bighelli, Salanti, Huhn et al., 2018, Appendix, p. 24)
Metacognitive training	A structured group intervention aimed at dismantling cognitive biases that contribute to psychotic exacerbations. There are multiple modules with different specific targets such as showing the importance of collecting enough information before making assumptions, strengthening theory of mind or also handling affective symptoms. The rationale behind metacognitive training is similar to and based on those of psychoeducation and cognitive behavior therapy. (Roberts & Penn, 2012, pp. 358–362)

Mindfulness	A third wave cognitive and experiential approach aimed at enabling a different pattern of relating to psychotic experiences such as thoughts, images and hallucinations. Core element are guided meditation sessions in which patients are motivated to focus on bodily sensations and their breath and bring a gentle attention to distressing symptoms. The aim is not to eliminate distressing sensations, but to alleviate distress that is generated by dysfunctional ways of relating to them. Mindfulness meditation integrated with discussion in a cognitive frame is believed to bring about metacognitive insights that enhance the process of relating more functionally to psychotic experiences. (Chadwick, 2006, pp. 78–92; Chadwick et al., 2009, p. 406)
Mindfulness-based psychoeducation (⇒ mindfulness)	Its aim is to increase the patient’s comprehension of schizophrenia and their illness insight as well as helping them to manage and accept their symptoms. Patients are taught to recognize and respond in a less involved way to their emotions, cognitions and perceptions instead of seeing them as exact representations of reality. (Chien & Lee, 2013, p. 377)
Movement therapy	Movement therapy is a therapy form that aims at alleviating psychotic symptoms by using body-oriented exercises. These can focus on perception of sensation on the one hand as well as on an active and expressive bodily movement on the other hand. Feeling and moving the body is used to enable the patients to develop a more embodied sense of self, a broader range of communicative behaviors and a more differentiated understanding and expression of their emotions. (Martin, Pohlman et al., 2016, p. 185)
Multiple therapies	Under this term, treatments that combine multiple fundamentally different therapeutic strategies, for example music therapy, family intervention or behavioral therapy, are subsumed.

Music therapy	An intervention that uses music to tackle psychotic symptoms. It can take place either individually or in a group setting. Usually, patients are encouraged to express themselves spontaneously by improvising on musical instruments. Therapeutic interventions can entail accompanying the patients' music, helping them to vary the course of the music and interpreting the music together through discussion. (Talwar et al., 2006, p. 405)
Positive psychotherapy	By using different exercises, patients shall be encouraged to make positive experiences, enhance their personal strengths and interpersonal relationships and get a more meaningful perspective on their lives. (Schrank et al., 2016, p. 237)
Psychodynamic therapy	Patients get the opportunity to describe the narratives of their lives. By doing so, they can make sense of the timing and nature of the illness and how it is related to strong and unbearable affects in their past personal history. Furthermore, transference phenomena in the therapeutic relationship can be described and worked through. (Durham et al., 2003, p. 305)
Psychoeducation	Psychoeducation is meant to teach patients about different aspects of their disease and its management. Topics vary from explanation models of disease development to the rationale for medication and different coping strategies as well as noticing and understanding warning signs for relapses. (Cather et al., 2005, p. 204)
Psychosocial therapy	Psychosocial therapy is an intervention based on social skills training with the aim to give patients behavioral alternatives that enrich their existing behavioral strategies. The focus lies on five areas: occupation, economical aspects and relationships with friends, partners and family. (Valencia et al., 2006, p. 538)
Psychotherapy not further specified	A therapy is considered not specified, if no further information is given about the specific form of psychological treatment, for example in the study undertaken by Matthews in 1981, where it was only mentioned that the patients received "psychotherapy", but no details were given.

Social activity therapy (⇒ inactive control)	Social activity therapy has the goal to support patients in finding activities they like doing and taking steps to actually engage in them. (Haddock et al., 2009, p. 154)
Standard treatment (⇒ TAU)	See “Treatment as usual”
Supportive therapy	In supportive therapy, a safe environment is created in which patients can talk about their problems (Durham et al., 2003, p. 305). The therapists support the patients emotionally without giving symptom specific interventions. More importance is given to non-specific therapeutic factors such as empathic attitude and creating a reliable therapeutic alliance. (Penn et al., 2009, p. 54).
Third wave cognitive behavior therapy	If described as waves, the first wave of CBT consists in the strictly behavioral approach and the second is characterized by the implementation of a cognitive model. In the current third wave, an emphasis is put on metacognition and how the patient relates to thoughts and emotions. Examples for third wave therapies are dialectical behavior therapy, acceptance and commitment therapy (ACT), mindfulness-based treatments, metacognitive therapy and several others. (Hayes & Hofmann, 2017, p. 245)
Treatment as usual (TAU)	Patients assigned to this group get the usual psychiatric care. What it exactly entails depends on the local guidelines. Usually, patients are offered medication and regular visits to doctors and nurses to talk about current issues. (Bighelli, Salanti, Huhn et al., 2018, Appendix, p. 24)
Virtual-reality exposure therapy for psychosis (⇒ CBT)	A cognitive behavior therapy using a virtual-reality environment for exposure exercises for fear and paranoia provoking social situations. (Pot-Kolder et al., 2016, p. 31)
Wait-list	If patients get assigned to the wait-list, this means that they get informed that there is a possible treatment, but they cannot yet engage in it. They can only get that specific treatment after waiting some weeks. (Bighelli, Salanti, Huhn et al., 2018, Appendix, p. 25)

3.4 Scales for Assessing Functioning

The presentation of functioning scales here follows the style adopted by Rabaioli to describe social functioning scales in his dissertation (Rabaioli, 2018).

In the included studies, different scales for assessing the patients' functioning were used. The most used scale was the Global Assessment of Functioning (GAF), which was used in 39% of the studies. The Social Functioning Scale (SFS) and the Specific Levels of Functioning (SLOF) were each used in 11% of the studies. The other scales used in the included studies can be seen in Table 5.

Table 5 *Scales Used in the Included Studies Ordered by Frequency of Occurrence*

Scale	Percentage of studies	Number of studies
Global Assessment of Functioning	38.64%	17
Social Functioning Scale	11.36%	5
Specific Levels Of Functioning	11.36%	5
Independent Living Skills Survey	6.82%	3
Global Assessment Scale	4.55%	2
Life Skills Profile	4.55%	2
Personal and Social Performance scale	4.55%	2
Social and Occupational Functioning Assessment Scale	4.55%	2
Clinical Outcomes in Routine Evaluation	2.27%	1
Groningen Social Disabilities Schedule	2.27%	1
Health of the Nation Outcome Scale	2.27%	1
Role Functioning Scale	2.27%	1
Social Behaviour Schedule	2.27%	1
World Health Organization Disability Assessment Schedule 2.0	2.27%	1

In the following paragraphs, the scales are described in chronological order. First, the evolution from the Global Assessment Scale (GAS) over the GAF scale and the Social and Occupational Functioning Assessment Scale (SOFAS) to the Personal and Social Performance (PSP) scale is described. In the second part, the other scales are presented. A summary of the characteristics of the scales is then presented in Table 6.

3.4.1 From Global Assessment Scale to Personal and Social Performance Scale

3.4.1.1 Global Assessment Scale

The Global Assessment Scale (GAS) was published by Endicott in 1976. Scores range from 0 to 100 and for each 10-point interval a description is given on the patient's symptom severity and functioning that determines which interval to choose. The rater, usually a healthcare professional, first chooses the interval according to the descriptions and second, depending on which neighbor interval is closer to the patient's state, the exact number is chosen. The lowest interval from 0 to 10 describes a functioning level in which the patient does not apply personal hygiene or constant supervision is needed to prevent harm. A score ranging from 51 to 60 stands for "moderate symptoms or generally functioning with some difficulty". Scores from 81 to 100 are reserved for the few patients that do not only function normally, but have traits of positive mental health such as broad interests, integrity and a very satisfying social life. (Endicott et al., 1976, pp. 766–768)

3.4.1.2 Global Assessment of Functioning

The Global Assessment of Functioning (GAF) was first introduced by the American Psychiatric Association in 1987 in the revised version of the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM III-R) as "Axis V" of the multiaxial evaluation and is a revision of the GAS and the Children's Global Assessment Scale (American Psychiatric Association., 1987, p. 20).

It is a global outcome measure looking at the patient's symptoms, psychological, social and occupational functioning. Scores range from 0 to 90. A score of 0 means that there is insufficient information, whereas a score from 1-10 means that there are "persistent danger of hurting self or others", serious hygiene problems or a "serious suicidal act", a score from 51 to 60 means "[moderate] symptoms [...] or moderate difficulty in social, occupational, or school functioning" and a score from 81 to 90 means "absent or minimal symptoms [...], good functioning in all areas, [...] generally satisfied with life". (American Psychiatric Association., 1987, p. 12) A modified version was developed by Hall in 1995. It contains the same 10-point ranges from 0 to 90, but with more detailed instructions to help the rater choose the right score inside the 10-point interval (Hall, 1995, pp. 270–273).

3.4.1.3 Social and Occupational Functioning Assessment Scale

The Social and Occupational Functioning Assessment Scale (SOFAS) was developed for the DSM-IV as a modification of the GAF which was used in the DSM-III-R. As opposed to the GAF, the SOFAS does not look at psychological functioning, but focuses on social and occupational functioning with the aim of reducing redundancy to Axis I diagnoses and improving user-friendliness. (Goldman et al., 1992)

Scores range from 0, which means that there is no usable data, to 100, which means superior functioning. It is divided in 10-point-intervals. There are definitions for each interval describing how severe the impairment is, from a lack of personal hygiene and self-harm or harm to others, which would equal 1 to 10 points, over “moderate difficulty in social, occupational, or school functioning” to “superior functioning in a wide range of activities” which would result in 91 to 100 points. (American Psychiatric Association., 1994, pp. 760–761)

3.4.1.4 Personal and Social Performance Scale

The Personal and Social Performance (PSP) scale is derived from the SOFAS. Functioning is assessed in the four areas “socially useful activities”, “personal and social relationships”, “self-care” and “disturbing and aggressive behaviours”. Scores range from 0 to 100, the higher the impairment, the lower the score. Scores above 91 mean that the functioning is not only not impaired, but more than adequate. (Morosini et al., 2000, pp. 323–324)

3.4.2 Other Scales

3.4.2.1 Social Functioning Scale

The Social Functioning Scale (SFS) was developed by Birchwood in 1983 and validated by him and his colleagues in 1990. Seven different areas are evaluated to assess social functioning. These are social engagement or withdrawal, interpersonal behavior, pro-social activities, recreation, independence competence and performance and employment. The interview is to be completed by an informant from the patient’s environment. (Birchwood et al., 1990)

It consists of 76 items in total. The response formats differ from dichotomous ratings to ratings on a Likert scale. The items are grouped into seven subscales corresponding to the areas described above. The subscale scores consist of the sum of the item scores. The results of Birchwood’s study

sample were standardized and normalized for each subscale so that 100 is the mean and the standard deviation is 15, with higher scores corresponding to better functioning. The total score is the mean of the subscale scores. (Iffland et al., 2015, p. 5)

3.4.2.2 *Specific Level of Functioning*

The Specific Level of Functioning (SLOF) assessment scale was developed in 1983 by Schneider and Struening. It consists of 43 items grouped in the 6 categories physical functioning, personal care skills, interpersonal relationships, social acceptability, activities and work skills. Each item is rated on a 5-point Likert scale by an assessor. (Schneider & Struening, 1983, p. 12) The points are then added so that resulting scores vary from 43 to 215 points, while higher scores equal better functioning (Harvey, 2012, p. 35).

3.4.2.3 *Social Behaviour Schedule*

The Social Behaviour Schedule (SBS) by Wykes and Sturt is rated by an interviewer depending on the information given about the patient by an informer. It covers 21 social behaviors, most of them rated from 0 (“no problem”) to 4 (“serious problem”). Included areas are, amongst others, communication and conversation, social mixing, over- or underactivity, self-harming and suicidal behavior and personal hygiene. (Wykes & Sturt, 1986, p. 2)

3.4.2.4 *Groningen Social Disabilities Schedule*

The Groningen Social Disability Schedule (GSDS) is a semi-structured questionnaire. Based on the patient’s and possibly other informers’ statements and his own observations, the interviewer rates functioning in eight different roles. These roles are “self-care”, “family role”, “kinship role”, “partner role”, “parental role”, “role as citizen”, “social role” and “occupational role”. How adequately each role is fulfilled is rated on a score from 0 (“excellent”) to 4 (“maximum disability”). If there is not enough information, the score 8 is given, and if it is not applicable, e.g. if the person has no children or no partner, the score 9 is given. (Wiersma et al., 1988, pp. 213–222)

3.4.2.5 *Life Skills Profile*

The Life Skills Profile (LSP) by Rosen et al. consists of 39 items arranged in 5 subscales called “self-care”, “nonturbulence”, “social contact”, “communication” and “responsibility”. The items are rated from 1 (“no difficulty”) to 4 (“extreme difficulty”), then all scores are added to build a

total. It is designed to be usable both by professional staff and non-professionals. (Rosen et al., 1989, pp. 325–329)

3.4.2.6 *Role Functioning Scale*

The Role Functioning Scale (RFS) is an interview carried out by health-care professionals with the patients. It comprises 4 subscales that can be rated from 1 to 7, resulting in total scores ranging from 4 to 28, where higher scores mean better functioning. The 4 subscales are “working productivity”, “independent living, self-care”, “immediate social network relationships” and “extended social network relationships”. (Goodman et al., 1993, pp. 122–125)

3.4.2.7 *Health of the Nation Outcome Scale*

The Health of the Nation Outcome Scale (HoNOS) contains 12 items, rated by clinicians in severity from 0 to 4, resulting in a maximum total score of 48. A lower score indicates a better functioning. The items are “aggression and overactivity”, “self-harm”, “substance use”, “cognition”, “physical health”, “hallucinations and delusions”, “depression”, “other symptoms”, “social relations”, “general functioning”, “housing” and “activities”. (Wing et al., 1998, pp. 11–12)

3.4.2.8 *Clinical Outcomes in Routine Evaluation*

The Clinical Outcomes in Routine Evaluation (CORE) is an interview to be filled out by the patients themselves. It consists of 34 items grouped in the four areas “well-being”, “problems and symptoms”, “social functioning” and “risk” to self and others. Each item is scored from 0 to 4 depending on how often the thought, feeling or behavior outlined in the item occurs. The total score consists of the sum of the item scores. (Evans et al., 2000)

3.4.2.9 *Independent Living Skills Survey*

There are two formats of the Independent Living Skills Survey (ILSS), the informant format ILSS-I and the self-report format ILSS-SR. There is also an interview version of the ILSS-SR. The ILSS-I contains 103 items that are arranged in the 12 following groups: personal hygiene, appearance and care of clothing, care of personal possessions and living space, food preparation, care of personal health and safety, money management, transportation, leisure and recreational activities, job seeking, job maintenance, eating behaviors and social interactions. Each item can be rated depending on how frequently a living skill is used from 0 (never) to 4 (always). If a skill cannot be performed because of a lack of opportunity, there is the option to tick “no opportunity”. For each

area, the mean is computed. The ILSS-SR contains 61 items when filled out by the patient and 70 items when administered as an interview. In this version, there are only three different answering options: 1 (yes), 0 (no) and “not apply”, if there is no opportunity to apply a skill. Then again, a mean is calculated for each area. (Wallace et al., 2000, p. 634)

3.4.2.10 World Health Organization Disability Assessment Schedule 2.0

The World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) assesses functioning with 36 items in the six domains “cognition”, “mobility”, “self-care”, “getting along”, “life activities” and “participation”. Each item is scored concerning the difficulty the patient has with an activity from 1 (“none”) to 5 (“extreme or cannot do”). Higher scores equal higher disability. Scores are then summed up first for each domain and then the domain scores are summed up to get the total score of up to 180. The total score can facultative be converted so that 0 means no disability and 100 means full disability. It can be administered in a self-reporting format as well as in an interview with the patient or an informer. (Üstün et al., 2010, pp. 4–41)

Table 6 *Functioning Scales (adapted from Rabaioli, 2018 and Burns et al., 2007)*

Name of scale and author	Items and domains	Scoring and reporting system
Clinical Outcomes in Routine Evaluation (Evans et al., 2000)	34 items in four areas: <ul style="list-style-type: none"> - well-being - problems and symptoms - social functioning - risk to self and others 	Self-administered by patient Single item rating: 0 to 4 Total score: sum of the item scores
Global Assessment of Functioning (American Psychiatric Association., 1987), modified by Hall, 1995	3 domains of functioning: <ul style="list-style-type: none"> - psychological - social - occupational 	Observer-rated Range: 0 – 90 0: no data 1-10: “persistent danger of hurting self or others” 81-90: “good functioning in all areas”

<p>Global Assessment Scale (Endicott et al., 1976)</p>	<p>Functioning is rated “on a hypothetical continuum of mental health-illness”</p>	<p>Observer-rated</p> <p>Range: 1 – 100 1: “hypothetically sickest individual” 81-100: “positive mental health” 100: “hypothetically healthiest individual”</p>
<p>Groningen Social Disabilities Schedule (Wiersma et al., 1988)</p>	<p>8 roles:</p> <ul style="list-style-type: none"> - self-care - family role - kinship role - partner role - parental role - role as citizen - social role - occupational role 	<p>Observer-rated from interview with patient, informer or both</p> <p>Fulfilment of each role is rated from 0 (excellent) to 4 (maximum disability)</p>
<p>Health of the Nation Outcome Scale (Wing et al., 1998)</p>	<p>12 items:</p> <ul style="list-style-type: none"> - aggression and overactivity - self-harm - substance use - cognition - physical health - hallucinations and delusions - depression - other symptoms - social relations - general functioning - housing - activities 	<p>Observer-rated</p> <p>Range: 0 to 48, every item rated from 0 to 4</p> <p>Lower score indicates better functioning</p>

Independent Living Skills Survey (Wallace et al., 2000)	61 to 103 items in 10 to 12 groups: <ul style="list-style-type: none"> - personal hygiene - appearance and care of clothing - care of personal possessions and living space - food preparation - care of personal health and safety - money management - transportation - leisure and recreational activities - job seeking - job maintenance - eating behaviours - social interactions 	Interview with patient or informant or self-reported Single item rating from 0 (never) to 4 (always), a mean is calculated for each area
Life Skills Profile (Rosen et al., 1989)	39 items, 5 subscales: <ul style="list-style-type: none"> - self-care - nonturbulence - social contact - communication - responsibility 	Observer-rated Range: 39-156 Single item scores: from 1 (no difficulty) to 4 (extreme difficulty)
Personal and Social Performance scale (Morosini et al., 2000)	4 areas: <ul style="list-style-type: none"> - social useful activities - personal and social relationships - self-care - disturbing and aggressive behaviors 	Observer-rated Range: 0-100, the higher the score, the better the functioning. Scores above 91 mean superior functioning
Role Functioning Scale (Goodman et al., 1993)	4 subscales: <ul style="list-style-type: none"> - working productivity - independent living, self-care - immediate social network relationships - extended social network relationships 	Interview Each subscale is rated from 1 to 7, resulting in a total score ranging from 4 to 28, higher scores mean better functioning
Social Behaviour Schedule (Wykes & Sturt, 1986)	21 social behaviors	Interview with informant 0 (no problem) to 4 (serious problem)

<p>Social Functioning Scale (Birchwood et al., 1990)</p>	<p>76 items in 7 domains:</p> <ul style="list-style-type: none"> - social engagement or withdrawal - interpersonal behavior - pro-social activities - recreation - independence - competence and performance - employment 	<p>Self-administered by informant</p> <p>Scores are standardized to 100, with a standard deviation of 15, single item scores are rated on a Likert scale</p>
<p>Social and Occupational Functioning Assessment Scale (Goldman et al., 1992)</p>	<p>Social and occupational respectively educational functioning</p>	<p>Observer-rated</p> <p>Range: 0-100</p> <p>0: no data</p> <p>1-10: lack of personal hygiene, harm to self or others</p> <p>91-100: superior functioning in a wide range of activities</p>
<p>Specific Levels of Functioning (Schneider & Struening, 1983)</p>	<p>43 items in 6 categories:</p> <ul style="list-style-type: none"> - physical functioning - personal care skills - interpersonal relationships - social acceptability - activities - work skills 	<p>Observer-rated</p> <p>Range: 43 to 215 points, higher scores equal better functioning (Harvey 2012, p. 35)</p> <p>Single item rating on a 5point Likert scale</p>
<p>World Health Organization Disability Assessment Schedule 2.0 (Üstün et al., 2010)</p>	<p>36 items in six domains:</p> <ul style="list-style-type: none"> - cognition - mobility - self-care - getting along - life activities - participation 	<p>Self-administered, interview, informant</p> <p>Single item ratings concerning difficulty: 1 (none), to 5 (extreme difficulty or cannot do), resulting in total scores ranging from 36 to 180.</p> <p>Total scores can be converted so that 0 means no disability and 100 means full disability</p>

3.5 Risk of Bias of Included Studies

For a graphical illustration of the percentages of risk of bias in each domain, see *Figure 2*. By inclusion criteria, none of the studies had high risk of bias concerning random sequence generation (Bighelli, Salanti, Reitmeir et al., 2018, p. 2); 65.9% of the studies had low risk of bias and the remaining 34.1% had unclear risk of bias. Concerning allocation concealment, 68.2% had an unclear risk of bias and 31.8% a low risk of bias. In the category blinding of participants and personnel, 100% had a high risk of bias. For blinding of outcome assessment, 40.9% of the studies had a low risk of bias, 36.4% had an unclear risk and 22.7% had a high risk of bias. Regarding incomplete outcome data, 70.4% of studies had a high risk of bias, for 18.2%, the risk of bias was judged as low, in 11.4%, it was not clear. In the category “selective reporting”, more than half of the studies (52.3%) had an unclear risk of bias, 29.5% had a high risk of bias, 18.2% had a low risk of bias. For researcher allegiance, 63.6% of studies had high risk of bias, 22.7% had unclear risk of bias and only 13.6% had a low risk of bias. Concerning other possible sources of bias, 84.1% of the studies had low risk, in 11.4% it was unclear and in 4.5% high. For comments on possible reasons for the high risk of bias percentages and possibilities to reduce the risk, see Chapters 4.4 and 4.6.

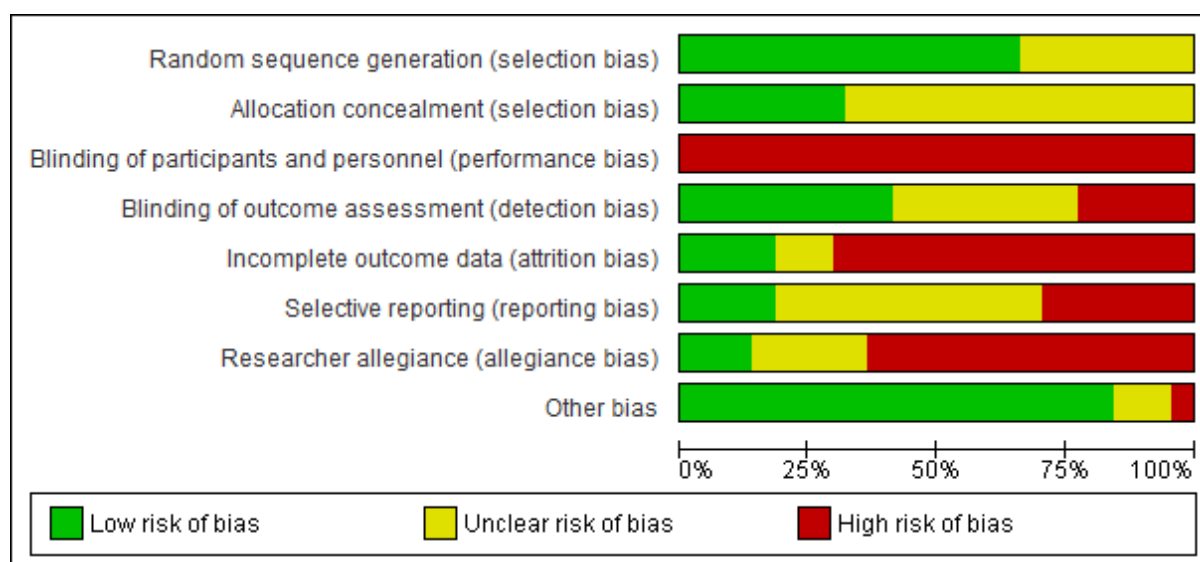


Figure 2. Risk of bias of included studies as judged by the reviewers using the Cochrane risk of bias tool for each domain, shown as percentage of included studies (created with Review Manager 5.3).

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Researcher allegiance (allegiance bias)	Other bias
Barrowclough 2006	+	+	+	+	+	?	+	+
Bradshaw 2000	?	?	+	?	+	+	+	+
Cather 2005	?	?	+	?	+	+	+	?
Chadwick 2009	?	+	+	+	+	?	+	+
Chien 2013	?	?	+	?	?	?	+	+
Chien 2014	+	+	+	?	+	+	?	+
Chien 2017	+	?	+	?	+	+	+	+
Crawford 2012	+	+	+	+	+	?	?	+
Durham 2003	+	+	+	+	+	+	?	?
Farhall 2009	+	?	+	+	+	?	+	+
Garety 2008	+	+	+	+	+	+	+	+
Garety 2008a	+	+	+	+	+	+	+	+
Garety 2008b	+	+	+	+	+	+	+	+
Gottlieb 2017	?	?	+	?	+	+	+	+
Granholm 2005	+	?	+	+	?	+	+	+
Granholm 2013	?	?	+	?	+	+	+	+
Granholm 2014	+	?	+	+	+	+	+	+
Grant 2012	+	?	+	+	+	+	+	+
Haddock 2009	+	?	+	+	?	?	+	+
Jenner 2004	+	+	+	+	?	+	+	+
Klingberg 2011	+	+	+	+	?	+	?	?
Krakovik 2013	?	?	+	+	+	+	?	?
Kuipers 2004	+	?	+	?	?	+	+	+
Lee 2014	?	?	+	?	?	?	?	+
Li 2015	+	+	+	?	?	+	+	+
Lincoln 2012	+	?	+	+	+	+	+	+
Martin 2016	+	?	+	?	+	+	+	+
Matthews 1981	?	?	+	+	?	?	?	+
Montag 2014	?	+	+	?	+	+	+	+
Morrison 2014	+	+	+	+	+	+	+	+
Naeem 2016	+	?	+	+	?	+	+	+
Ochoa 2017	+	?	+	?	+	+	+	+
Penades 2006	+	?	+	?	?	?	+	+
Penn 2009	+	?	+	?	?	?	+	+
Pot-Kolder 2016	+	+	+	+	?	?	+	+
Richardson 2007	+	?	+	+	?	?	+	+
Schrank 2016	?	+	+	+	+	+	+	+
Shawyer 2012	+	?	+	+	+	?	?	?
Shawyer 2016	+	+	+	+	+	+	+	+
Startup 2004	+	?	+	+	?	?	+	+
Talwar 2006	+	?	+	?	?	?	+	+
Tarrier 2014	?	?	+	+	?	?	+	+
Valencia 2006	?	?	+	?	?	?	+	+
van der Gaag 2011	?	?	+	?	?	?	?	+
Wang 2016	+	?	+	+	+	+	+	+
Wykes 2005	?	?	+	+	?	?	+	+

Figure 3. Risk of bias summary. Reviewers' judgements about each risk of bias item for each included study (created with Review Manager 5.3)

3.6 Effects of Psychological Treatments on Functioning in Schizophrenia

3.6.1 Psychological Treatment Versus Control

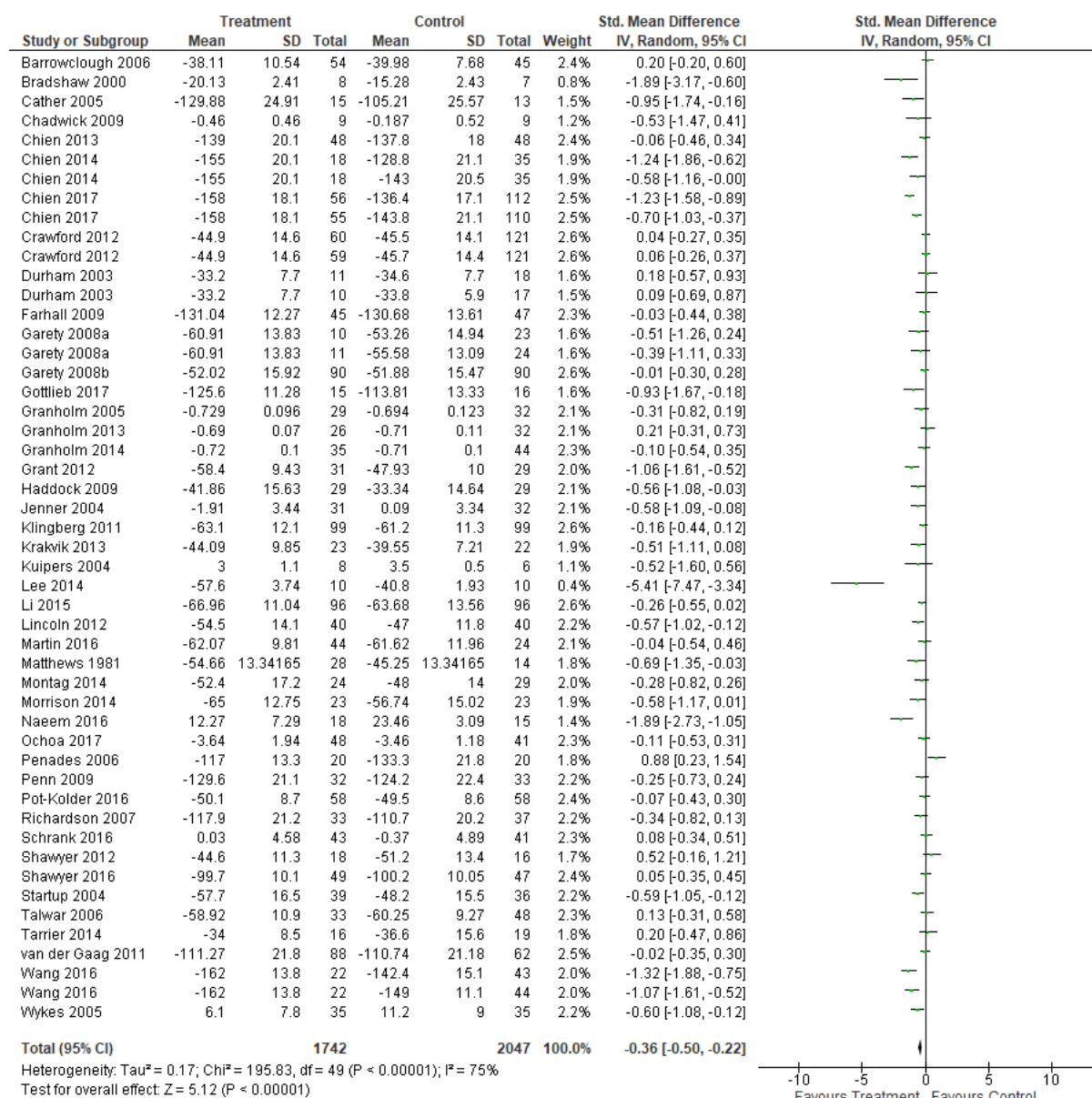


Figure 4. Forest plot of the comparison of psychological treatments versus control. Studies with three arms appear twice.

A total of 44 studies, providing data about 45 randomized samples, met the inclusion criteria for this meta-analysis and had usable data. The study by Valencia and colleagues was not included in the overall comparison, because it compared three different active treatment conditions and it was not clear which one to consider as control condition. This leads to 43 studies with 44 samples, comprising 3789 participants being included in this comparison. Functioning was measured with the GAF ($N = 16$), the SFS ($N = 5$), the SLOF ($N = 5$), the ILSS ($N = 3$), the GAS ($N = 2$),

the LSP ($N = 2$), the PSP ($N = 2$), the SOFAS ($N = 2$), the CORE ($N = 1$), the GSDS ($N = 1$), the HoNOS ($N = 1$), the RFS ($N = 1$), the SBS ($N = 1$), and the WHODAS 2.0 ($N = 1$). Compared to the control conditions, psychological treatments led to a greater improvement in participants' functioning scores ($SMD = -0.36$, CI -0.50 to -0.22), however with substantial heterogeneity according to the Cochrane Handbook for Systematic Reviews of Interventions ($Tau^2 = 0.17$; $Chi^2 = 195.83$, $df = 49$ ($p < 0.00001$); $I^2 = 75\%$) (Higgins, Thomas et al., 2019, p. 259).

3.6.1.1 Psychological Treatment Versus Control: Sensitivity Analyses

Excluding 11 open label studies did not substantially change the results of the analysis ($SMD = -0.33$, CI -0.48 to -0.18). Heterogeneity remained similar to the original analysis ($Tau^2 = 0.17$; $Chi^2 = 160.61$, $df = 39$ ($p < 0.00001$); $I^2 = 76\%$).

Excluding 27 studies with high researcher allegiance, the confidence interval includes the possibility of no difference between the psychological interventions and the control conditions ($SMD = -0.20$, CI -0.43 to 0.03). Heterogeneity remained similar to the original analysis ($Tau^2 = 0.18$; $Chi^2 = 72.02$, $df = 18$ ($p < 0.00001$); $I^2 = 75\%$).

Excluding 21 studies with high overall risk of bias did not change the results of the analysis substantially ($SMD = -0.37$, CI -0.56 to -0.18). Heterogeneity remained similar ($Tau^2 = 0.19$; $Chi^2 = 125.09$, $df = 26$ ($p < 0.00001$); $I^2 = 79\%$).

Excluding 10 studies with treatment resistant patients led to a slight increase of effect size ($SMD = -0.43$, CI -0.59 to -0.26). Heterogeneity remained similar ($Tau^2 = 0.19$; $Chi^2 = 170.57$, $df = 38$ ($p < 0.00001$); $I^2 = 78\%$).

3.6.1.2 Psychological Treatment Versus Control: Subgroup Analyses

3.6.1.2.1 Psychological Treatment Versus Control: Subgroup Analysis Regarding Treatment Setting

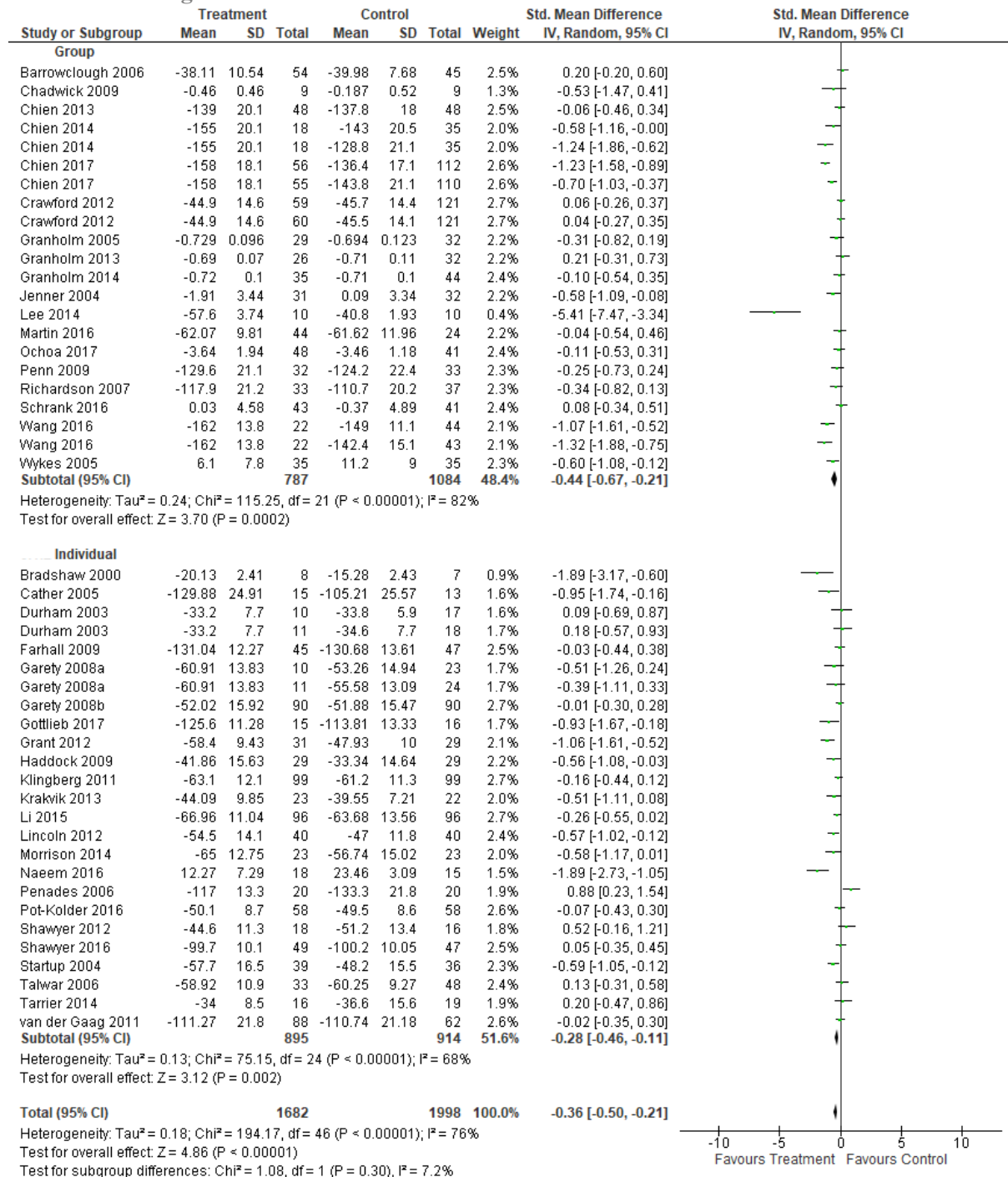


Figure 5. Forest plot of the comparison of psychological treatment versus control. Subgroup analysis regarding treatment setting.

The subgroup of psychological interventions conducted with a group setting included 18 studies with in total 1871 participants. Functioning was measured with the GAF ($N = 5$), the SLOF ($N = 4$), the ILSS ($N = 3$), the SFS ($N = 2$), the CORE ($N = 1$), the GSDS ($N = 1$), the

HoNOS ($N = 1$) and the SBS ($N = 1$). A greater improvement in functioning was found in the therapy group ($SMD = -0.44$, CI -0.67 to -0.21), with considerable heterogeneity ($Tau^2 = 0.24$; $Chi^2 = 115.25$, $df = 21$ ($p < 0.00001$); $I^2 = 82\%$) (Higgins, Thomas et al., 2019, p. 259).

The subgroup with an individual setting included 22 studies with a total of 1809 participants. The functioning scales used here were the GAF ($N = 8$), the GAS ($N = 2$), the PSP ($N = 2$), the SFS ($N = 3$), the SOFAS ($N = 2$), the LSP ($N = 2$), the RFS ($N = 1$), the SLOF ($N = 1$) and the WHODAS 2.0 ($N = 1$). Also in this subgroup, a group difference favoring therapy was found ($SMD = -0.28$, CI -0.46 to -0.11). There was moderate heterogeneity ($Tau^2 = 0.13$; $Chi^2 = 75.15$, $df = 24$ ($p < 0.00001$); $I^2 = 68\%$) (Higgins, Thomas et al., 2019, p. 259).

The test for subgroup differences did not reveal a subgroup difference between group and individual setting: $Chi^2 = 1.08$, $df = 1$ ($p = 0.30$), $I^2 = 7.2\%$.

3.6.1.2.2 Psychological Treatment Versus Control: Subgroup Analysis Regarding Therapist Expertise

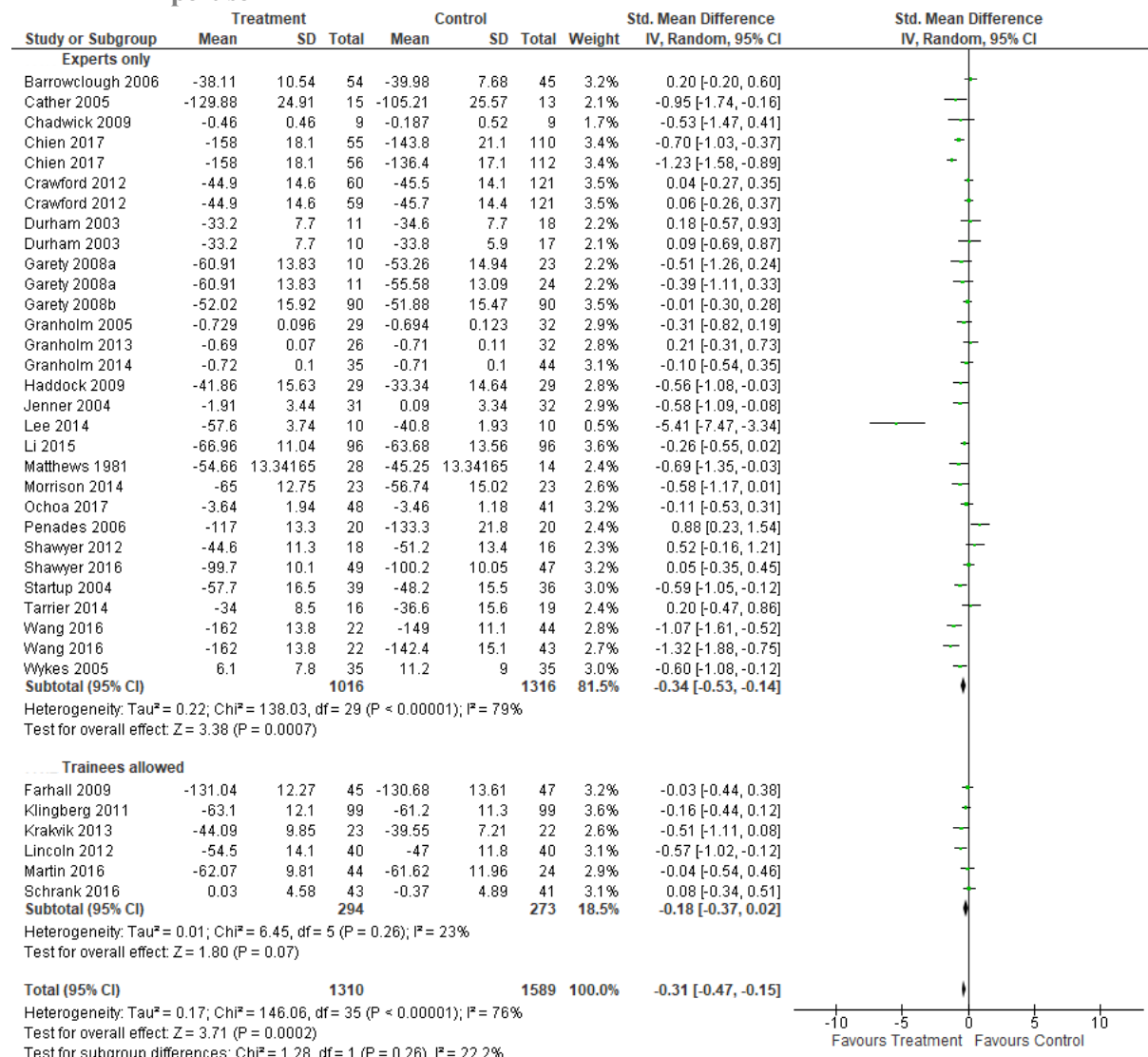


Figure 6. Forest plot of the comparison of psychological treatment versus control. Subgroup analysis regarding therapist expertise.

In the subgroup where only expert therapists conducted therapy, 24 studies comprising 2332 participants met inclusion criteria. Functioning was assessed using the GAF ($N = 9$), the ILSS ($N = 3$), the PSP ($N = 2$), the SFS ($N = 2$), the SLOF ($N = 2$), the CORE ($N = 1$), the GAS ($N = 1$), the GSDS ($N = 1$), the LSP ($N = 1$), the SBS ($N = 1$) and the SOFAS ($N = 1$). Treatments performed by expert therapists improved functioning more than control conditions ($SMD = -0.34$, CI -0.53 to -0.14), with considerable heterogeneity ($Tau^2 = 0.22$; $Chi^2 = 138.03$, $df = 29$ ($p < 0.00001$); $I^2 = 79\%$) (Higgins, Thomas et al., 2019, p. 259).

In the subgroup where therapists in training conducted treatment as well, six studies with 567 participants were included. The scales used were the GAF ($N = 4$), the HoNOS ($N = 1$) and the

LSP ($N = 1$). For studies in which the treatments could be performed by therapists in training the confidence interval includes the possibility of no difference with the control condition in improving functioning ($SMD = -0.18$, CI -0.37 to 0.02). Heterogeneity “might not be important” in this subgroup ($Tau^2 = 0.01$; $Chi^2 = 6.45$, $df = 5$ ($p = 0.26$); $I^2 = 23\%$) (Higgins, Thomas et al., 2019, p. 259).

The test for subgroup differences showed the following results: $Chi^2 = 1.28$, $df = 1$ ($p = 0.26$), $I^2 = 22.2\%$.

3.6.1.3 Psychological Treatment Versus Control: Meta-Regression Analyses

Meta-Regression Regarding Number of Sessions

The effect of psychological interventions on functioning in patients with schizophrenia was not found to be associated with number of sessions ($p = 0.1903$).

Meta-Regression Regarding Study Duration

Study duration was not found to have a role in moderating effect on functioning ($p = 0.2084$).

Meta-Regression Regarding Age

Effect on functioning was found to be associated with mean age ($p = 0.0066$).

Meta-Regression Regarding Male Ratio

Male percentage was not found to have a role in moderating effect on functioning ($p = 0.6711$).

Meta-Regression Regarding Baseline Severity

Effect on functioning was not found to be associated with baseline severity ($p = 0.2041$).

Table 7 Psychological Treatment Versus Control: Meta-Regression Analyses

Moderator	Coefficient	95% CI	Z value	p-value
Number of sessions	0.0084	-0.0042; 0.0209	1.3097	0.1903
Study duration	-0.0050	-0.0127; 0.0028	-1.2579	0.2084
Mean age	0.0269	0.0075; 0.0463	2.7161	0.0066
Male percentage	0.0036	-0.0130; 0.0202	0.4246	0.6711
Baseline severity	-0.0077	-0.0195; 0.0042	-1.2700	0.2041

3.6.2 Cognitive Behavior Therapy Versus Control

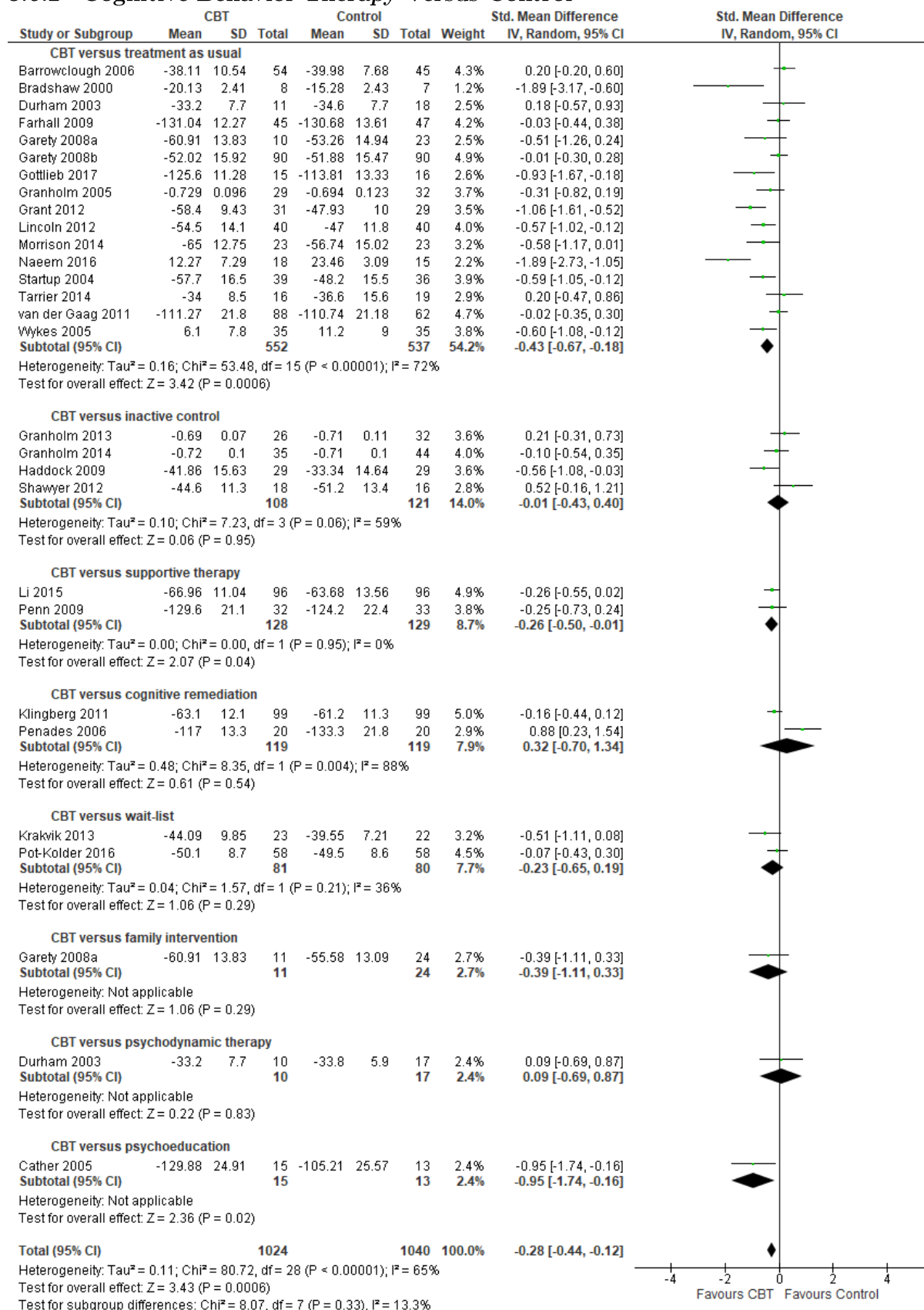


Figure 7. Forest plot of the comparison of CBT versus control. Studies with three arms appear twice.

Twenty-six studies with 2064 participants were included in this comparison. Functioning was measured with the GAF ($N = 8$), the ILSS ($N = 3$), the SFS ($N = 3$), the SOFAS ($N = 2$), the GAS ($N = 2$), the PSP ($N = 2$), the LSP ($N = 2$), the RFS ($N = 1$), the SBS ($N = 1$), the SLOF ($N = 1$) and the WHODAS 2.0 ($N = 1$). Compared to the control conditions, CBT led to a greater improvement in participants' functioning scores ($SMD = -0.28$, CI -0.44 to -0.12). There were substantial heterogeneity ($Tau^2 = 0.11$; $Chi^2 = 80.72$, $df = 28$ ($p < 0.00001$); $I^2 = 65\%$) and subgroup differences between the subgroups of studies using a different control condition ($Chi^2 = 8.07$, $df = 7$ ($p = 0.33$), $I^2 = 13.3\%$) in this sample (Higgins, Thomas et al., 2019, p. 259).

3.6.2.1 CBT Versus Control: Sensitivity Analyses

Excluding five open label studies did not substantially change the results of the analysis ($SMD = -0.24$, CI -0.42 to -0.06). Heterogeneity and subgroup differences remained similar compared to the original analysis (Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 70.99$, $df = 23$ ($p < 0.00001$); $I^2 = 68\%$; Test for subgroup differences: $Chi^2 = 9.64$, $df = 6$ ($p = 0.14$), $I^2 = 37.8\%$).

Excluding 17 studies with high researcher allegiance, the conclusion changed from the main analysis, including the possibility of no difference between CBT and control ($SMD = -0.02$, CI -0.29 to 0.24). Heterogeneity remained similar to the main analysis (Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 23.62$, $df = 9$ ($p = 0.005$); $I^2 = 62\%$; Test for subgroup differences: $Chi^2 = 8.40$, $df = 4$ ($p = 0.08$), $I^2 = 52.4\%$).

Excluding 11 studies with a high overall risk of bias, the results did not differ substantially from the original analysis ($SMD = -0.31$, CI -0.52 to -0.10). Heterogeneity remained high ($Tau^2 = 0.13$; $Chi^2 = 52.43$, $df = 16$ ($p < 0.00001$); $I^2 = 69\%$), whereas the subgroup differences decreased ($Chi^2 = 2.43$, $df = 4$ ($p = 0.66$), $I^2 = 0\%$).

Excluding eight studies that focused primarily on treatment resistant patients did not change the results substantially ($SMD = -0.34$, CI -0.54 to -0.15). Heterogeneity ($Tau^2 = 0.13$; $Chi^2 = 62.40$, $df = 19$ ($p < 0.00001$); $I^2 = 70\%$) and subgroup differences ($Chi^2 = 9.99$, $df = 5$ ($p = 0.08$), $I^2 = 50.0\%$) remained high.

3.6.2.2 CBT Versus Control: Subgroup Analyses

3.6.2.2.1 CBT Versus Control: Subgroup Analysis Regarding Treatment Setting

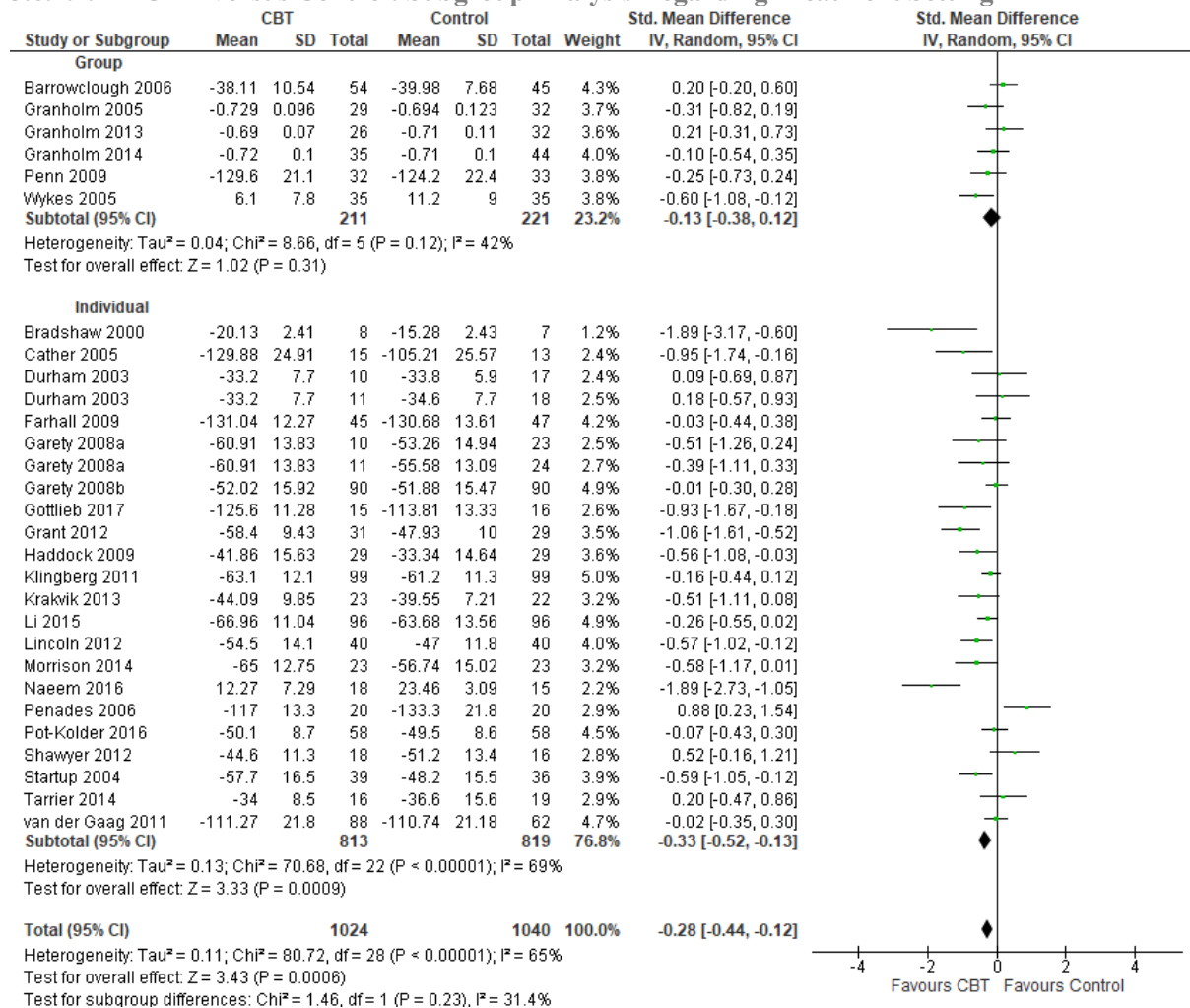


Figure 8. Forest plot of the comparison of CBT versus control. Subgroup analysis regarding treatment setting.

In the subgroup of studies where CBT was conducted in a group setting, six studies with in total 432 participants met inclusion criteria. Functioning was measured with the GAF ($N = 1$), the ILSS ($N = 3$), the SBS ($N = 1$) and the SFS ($N = 1$). The results range from a small benefit with the psychological treatments to no difference with the control conditions ($SMD = -0.13$, $CI -0.38$ to 0.12), with moderate heterogeneity ($Tau^2 = 0.04$; $Chi^2 = 8.66$, $df = 5$ ($p = 0.12$); $I^2 = 42\%$) (Higgins, Thomas et al., 2019, p. 259).

Twenty studies with a total of 1632 participants were included in the subgroup of studies where CBT was conducted in an individual setting. The functioning scales used here were the GAF ($N = 7$), the GAS ($N = 1$), the LSP ($N = 2$), the PSP ($N = 2$), the RFS ($N = 1$), the SFS

($N = 2$), the SOFAS ($N = 3$), the SLOF ($N = 1$) and the WHODAS 2.0 ($N = 1$). In this subgroup, a difference favoring CBT was found ($SMD = -0.33$, CI -0.52 to -0.13). There was moderate heterogeneity ($Tau^2 = 0.13$; $Chi^2 = 70.68$, $df = 22$ ($p < 0.00001$); $I^2 = 69%$) (Higgins, Thomas et al., 2019, p. 259).

The test for subgroup differences between the subgroup of studies with a group setting and the subgroup of studies with an individual therapy setting showed the following results: $Chi^2 = 1.46$, $df = 1$ ($p = 0.23$), $I^2 = 31.4%$.

3.6.2.2.2 CBT Versus Control: Subgroup Analysis Regarding Therapist Expertise

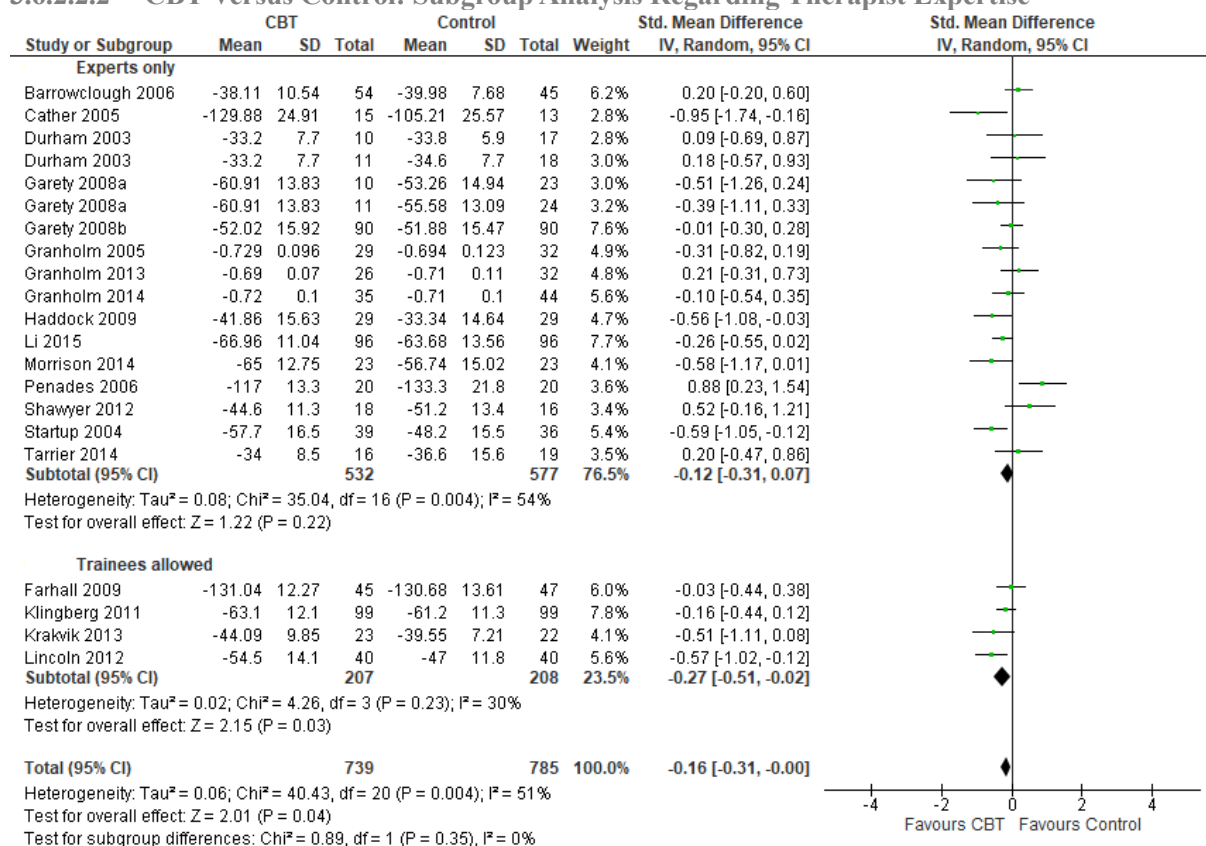


Figure 9. Forest plot of the comparison of CBT versus control. Subgroup analysis regarding therapist expertise.

In the subgroup of studies where CBT was conducted only by expert therapists, 14 studies comprising 1109 participants met inclusion criteria. Functioning was assessed using the GAF ($N = 5$), the GAS ($N = 1$), the ILSS ($N = 3$), the PSP ($N = 2$), the SFS ($N = 1$) and the SOFAS ($N = 1$), the LSP ($N = 1$). The results range from a small benefit for CBT to no difference with the control conditions ($SMD = -0.12$, CI -0.31 to 0.07), with moderate

heterogeneity ($Tau^2 = 0.08$; $Chi^2 = 35.04$, $df = 16$ ($p = 0.004$); $I^2 = 54\%$) (Higgins, Thomas et al., 2019, p. 259).

For the subgroup of studies where cognitive behavior therapy could be conducted also by therapists in training, four studies with 415 participants were included. The scales used were the GAF ($N = 3$) and the LSP ($N = 1$). A benefit of CBT was found ($SMD = -0.27$, CI -0.51 to -0.02). Heterogeneity was moderate in this subgroup ($Tau^2 = 0.02$; $Chi^2 = 4.26$, $df = 3$ ($p = 0.23$); $I^2 = 30\%$) (Higgins, Thomas et al., 2019, p. 259). The test for subgroup differences showed the following results: $Chi^2 = 0.89$, $df = 1$ ($p = 0.35$), $I^2 = 0\%$.

3.6.2.3 CBT Versus Control: Meta-Regression Analyses

Meta-Regression Regarding Number of Sessions

Effect of CBT on functioning was not found to be associated with number of sessions ($p = 0.7303$).

Meta-Regression Regarding Study Duration

Treatment duration was found to have a role in moderating effect on functioning ($p = 0.0346$).

Meta-Regression Regarding Age

Effect on functioning was not found to be associated with mean age of the patients ($p = 0.5904$).

Meta-Regression Regarding Male Ratio

Male percentage was not found to have a moderating effect on functioning ($p = 0.7975$).

Meta-Regression Regarding Baseline Severity

Effect of CBT on functioning was not found to be associated with baseline severity ($p = 0.3648$).

Table 8 CBT Versus Control: Meta-Regression Analyses

Moderator	Coefficient	95% CI	Z value	p-value
Number of sessions	0.0033	-0.0154; 0.0220	0.3448	0.7303
Study duration	-0.0090	-0.0173; -0.0007	-2.1134	0.0346
Mean age	0.0088	-0.0232; 0.0407	0.5382	0.5904
Male percentage	0.0019	-0.0127; 0.0166	0.2566	0.7975
Baseline severity	0.0076	-0.0088; 0.0239	0.9063	0.3648

3.6.2.4 CBT Versus Treatment as Usual

In this subgroup, 15 studies with in total 1089 participants met the inclusion criteria (*Figure 7*). The patients' functioning was measured with GAF ($N = 4$), GAS ($N = 2$), SOFAS ($N = 1$), ILSS ($N = 1$), LSP ($N = 1$), PSP ($N = 1$), RFS ($N = 1$), SFS ($N = 1$), SBS ($N = 1$), SLOF ($N = 1$), WHODAS 2.0 ($N = 1$). The pairwise meta-analysis showed a benefit for CBT compared with treatment as usual in improving the patients' functioning scores ($SMD = -0.43$, $CI -0.67$ to -0.18). The tests for heterogeneity showed statistically significant results that may represent substantial heterogeneity ($Tau^2 = 0.16$; $Chi^2 = 53.48$, $df = 15$ ($p < 0.00001$); $I^2 = 72\%$) (Higgins, Thomas et al., 2019, p. 259).

Sensitivity Analyses

Excluding four open label studies did not change the results substantially ($SMD = -0.44$, $CI -0.77$ to -0.12). Heterogeneity in this subgroup remained high ($Tau^2 = 0.23$; $Chi^2 = 46.69$, $df = 11$ ($p < 0.00001$); $I^2 = 76\%$).

Excluding 11 studies with high researcher allegiance, the results did not show a benefit for CBT anymore ($SMD = -0.07$, $CI -0.42$ to 0.27). As expected with the smaller number of studies, heterogeneity decreased ($Tau^2 = 0.07$; $Chi^2 = 7.02$, $df = 3$ ($p = 0.07$); $I^2 = 57\%$).

Excluding seven studies with a high overall risk of bias, the results did not change substantially ($SMD = -0.49$, $CI -0.87$ to -0.10). Heterogeneity increased despite the smaller number of studies ($Tau^2 = 0.26$; $Chi^2 = 37.22$, $df = 8$ ($p < 0.0001$); $I^2 = 79\%$).

Excluding three studies focused on treatment resistant patients, the results showed an even greater benefit for CBT ($SMD = -0.57$, $CI -0.84$ to -0.29). Heterogeneity remained high ($Tau^2 = 0.17$; $Chi^2 = 40.36$, $df = 12$ ($p < 0.0001$); $I^2 = 70\%$).

3.6.2.5 CBT Versus Inactive Control

Four studies with 229 participants met the inclusion criteria in this subgroup. For measuring the patients' functioning, the GAF ($N = 2$) and the ILSS ($N = 2$) were used in the studies. The results of the meta-analysis did not show a difference between CBT and the inactive control conditions. ($SMD = -0.01$, $CI -0.43$ to 0.40). The heterogeneity tests showed the following

results: $Tau^2 = 0.10$; $Chi^2 = 7.23$, $df = 3$ ($p = 0.06$); $I^2 = 59\%$), indicating substantial heterogeneity (Higgins, Thomas et al., 2019, p. 259).

3.6.2.6 CBT Versus Supportive Therapy

In this subgroup, two studies with a total of 257 participants were included. The patients' functioning was measured with the PSP ($N = 1$) and the SFS ($N = 1$). The pairwise meta-analysis showed a difference between CBT and supportive therapy ($SMD = -0.26$, CI -0.50 to -0.01). The results of the tests for heterogeneity did not reveal the presence of heterogeneity ($Tau^2 = 0.00$; $Chi^2 = 0.00$, $df = 1$ ($p = 0.95$); $I^2 = 0\%$).

3.6.2.7 CBT Versus Cognitive Remediation

There were two trials with 238 participants among this subgroup. The GAF ($N = 1$) and the LSP ($N = 1$) were used for assessing the patients' functioning. Compared with cognitive remediation, no benefit was found for CBT concerning functioning ($SMD = 0.32$, CI -0.70 to 1.34). There was considerable heterogeneity in this subgroup (Heterogeneity: $Tau^2 = 0.48$; $Chi^2 = 8.35$, $df = 1$ ($p = 0.004$); $I^2 = 88\%$) (Higgins, Thomas et al., 2019, p. 259).

3.6.2.8 CBT Versus Wait-List

There were two trials with 161 participants among this subgroup. The GAF ($N = 1$) and the SOFAS ($N = 1$) were used for assessing the patients' functioning. No difference was found between CBT and the wait-list condition ($SMD = -0.23$ CI -0.65 to 0.19). The inconsistency in this subgroup "might not be important" (Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 1.57$, $df = 1$ ($p = 0.21$); $I^2 = 36\%$) (Higgins, Thomas et al., 2019, p. 259).

3.6.2.9 CBT Versus Family Intervention

One study with 35 participants was included in this subgroup. The SOFAS was used to measure functioning. No difference was found between CBT and family intervention ($SMD = -0.39$, CI -1.11 to 0.33). As there is only one trial among this subgroup, tests for heterogeneity and sensitivity analyses are not applicable.

3.6.2.10 CBT Versus Psychodynamic Therapy

In this subgroup, one study with 27 participants was included. Functioning was assessed with the GAS. No difference was found between CBT and psychodynamic therapy ($SMD = 0.09$, CI -0.69 to 0.87). Heterogeneity test were not applicable with only one study in this subgroup.

3.6.2.11 CBT Versus Psychoeducation

There was only one study with 28 participants in this subgroup. Functioning was assessed with the SFS. Compared with psychoeducation, CBT provides benefit for patients' functioning ($SMD = -0.95$, CI -1.74 to -0.16). Heterogeneity tests were not applicable because there is only one study included in this subgroup.

3.6.3 Third Wave Cognitive Behavior Therapy Versus Control

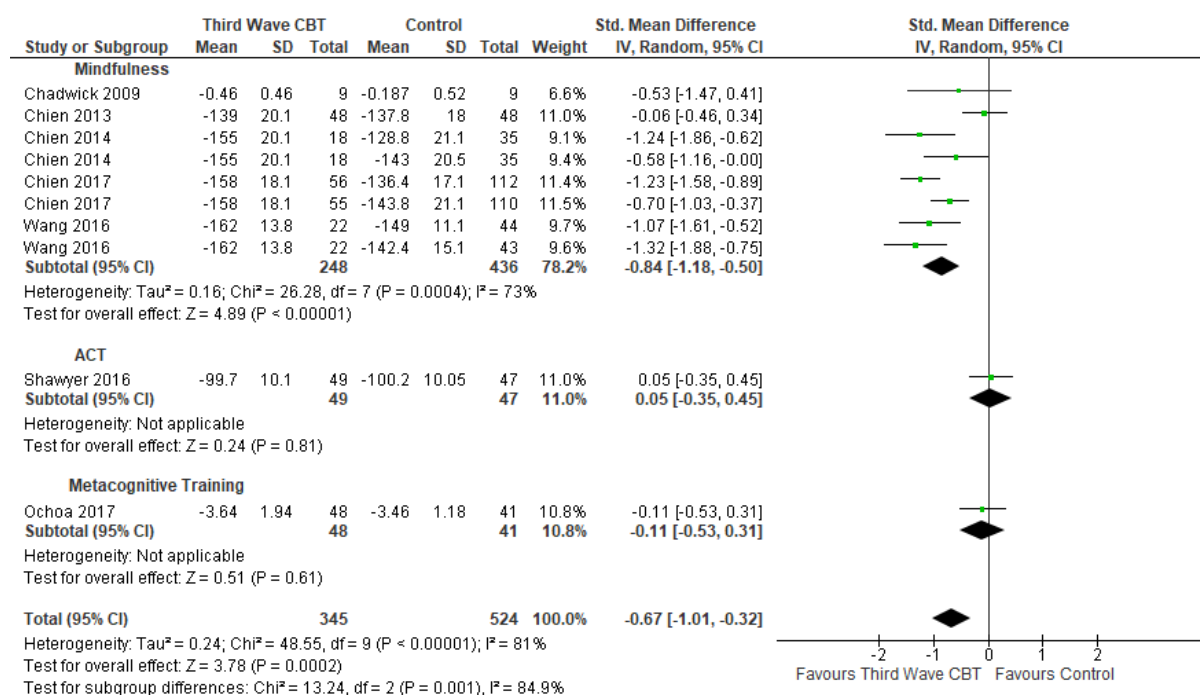


Figure 10. Forest plot of the comparison of third wave CBT versus control. Studies with three arms appear twice.

For this comparison, seven studies with 869 participants met the inclusion criteria. Functioning was assessed with the SLOF ($N = 4$), the CORE ($N = 1$), the GAF ($N = 1$) and the SFS ($N = 1$). A difference indicating a benefit of third wave CBT for the patients' functioning was found ($SMD = -0.67$, $CI -1.01$ to -0.32). There was a substantial amount of heterogeneity in this sample ($Tau^2 = 0.24$; $Chi^2 = 48.55$, $df = 9$ ($p < 0.00001$); $I^2 = 81\%$) and considerable subgroup differences ($Chi^2 = 13.24$, $df = 2$ ($p = 0.001$), $I^2 = 84.9\%$) (Higgins, Thomas et al., 2019, p. 259).

Sensitivity Analyses

One study was excluded because of an open label design which nearly did not change the results ($SMD = -0.68$, $CI -1.04$ to -0.31). Heterogeneity ($Tau^2 = 0.25$; $Chi^2 = 48.50$, $df = 8$ ($p < 0.00001$); $I^2 = 84\%$) and subgroup differences ($Chi^2 = 13.04$, $df = 2$ ($p = 0.001$), $I^2 = 84.7\%$) remained high.

Excluding six studies with high researcher allegiance did not change the results substantially ($SMD = -0.90$, CI -1.55 to -0.25). Heterogeneity decreased ($Tau^2 = 0.13$; $Chi^2 = 2.34$, $df = 1$ ($p = 0.13$); $I^2 = 57\%$) and tests for subgroup differences were not applicable.

Excluding three studies because of a high overall risk of bias did not change the results substantially ($SMD = -0.71$, CI -1.18 to -0.24). Heterogeneity ($Tau^2 = 0.30$; $Chi^2 = 38.49$, $df = 5$ ($p < 0.00001$); $I^2 = 87\%$) and subgroup differences ($Chi^2 = 8.64$, $df = 1$ ($p = 0.003$), $I^2 = 88.4\%$) remained high.

One study focused on treatment resistant patients and was therefore excluded, which did not change the results substantially ($SMD = -0.75$, 95% -1.09 to -0.41). Heterogeneity and subgroup differences remained high (Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 35.99$, $df = 8$ ($p < 0.0001$); $I^2 = 78\%$; Test for subgroup differences: $Chi^2 = 7.18$, $df = 1$ ($p = 0.007$), $I^2 = 86.1\%$).

3.6.3.1 Mindfulness Versus Control

Five studies with 684 participants met the inclusion criteria for this subgroup. The patients' functioning was measured with the CORE ($N = 1$) and the SLOF ($N = 4$) scales. The pairwise meta-analysis showed a superiority of mindfulness compared to the control condition ($SMD = -0.84$, CI -1.18 to -0.50). There was substantial heterogeneity in this sample ($Tau^2 = 0.16$; $Chi^2 = 26.28$, $df = 7$ ($p = 0.0004$); $I^2 = 73\%$) (Higgins, Thomas et al., 2019, p. 259). Possible sources of heterogeneity have been explored using sensitivity analyses.

Sensitivity Analyses

One study was excluded because of an open label design. This did not change the results substantially ($SMD = -0.87$, CI -1.23 to -0.51) and heterogeneity also remained high ($Tau^2 = 0.18$; $Chi^2 = 25.90$, $df = 6$ ($p = 0.0002$); $I^2 = 77\%$).

Excluding four studies because of high researcher allegiance did not change the results substantially ($SMD = -0.90$, CI -1.55 to -0.25) with now moderate heterogeneity ($Tau^2 = 0.13$; $Chi^2 = 2.34$, $df = 1$ ($p = 0.13$); $I^2 = 57\%$) (Higgins, Thomas et al., 2019, p. 259).

Two studies were excluded for a high overall risk of bias. This did not change the results substantially ($SMD = -0.86$, CI -1.32 to -0.40), heterogeneity stayed high ($Tau^2 = 0.22$; $Chi^2 = 23.47$, $df = 4$ ($p = 0.0001$); $I^2 = 83\%$).

No study was excluded for focusing on treatment resistant patients, so the results remained the same.

3.6.3.2 ACT Versus Control

One study with 96 participants was included in this subgroup. The SFS was used for the functioning assessment. No difference between the compared groups was found ($SMD = 0.05$, CI -0.35 to 0.45). With only one study in this subgroup, heterogeneity tests and sensitivity analyses were not applicable.

3.6.3.3 Metacognitive Training Versus Control

One study with 89 participants met inclusion criteria for this subgroup. Functioning was measured with the GAF. No difference was found between metacognitive training and the control condition. ($SMD = -0.11$, CI -0.53 to 0.31). As only one study was included in this subgroup, heterogeneity tests and sensitivity analyses were not applied.

3.6.4 Creative Therapy Versus Control

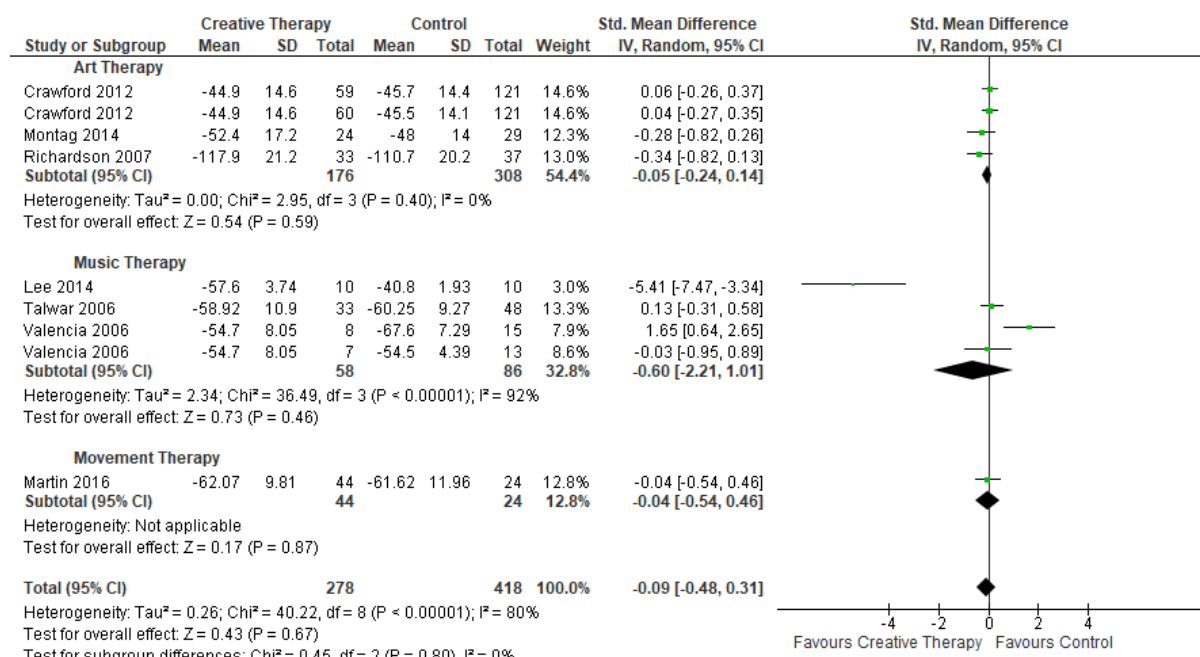


Figure 11. Forest plot of the comparison of creative therapy versus control. Studies with three arms appear twice.

For this comparison, seven studies with 696 participants met the inclusion criteria. Functioning was assessed with the GAF ($N = 6$) and the SFS ($N = 1$). No difference was found between creative therapies and the control groups ($SMD = -0.09$, $CI -0.48$ to 0.31). There was a considerable amount of heterogeneity in this sample ($Tau^2 = 0.26$; $Chi^2 = 40.22$, $df = 8$ ($p < 0.00001$); $I^2 = 80\%$), but there were no subgroup differences between the different kinds of treatments (art therapy, music therapy and movement therapy, $Chi^2 = 0.45$, $df = 2$ ($p = 0.80$), $I^2 = 0\%$) (Higgins, Thomas et al., 2019, p. 259).

Sensitivity Analyses

Excluding one study for open label design did not change the results substantially ($SMD = -0.06$, $CI -0.50$ to 0.39). Heterogeneity remained high ($Tau^2 = 0.29$; $Chi^2 = 38.14$, $df = 7$ ($p < 0.00001$); $I^2 = 82\%$) and subgroup differences remained low ($Chi^2 = 0.55$, $df = 2$ ($p = 0.76$), $I^2 = 0\%$).

Excluding two studies because of high researcher allegiance did not change the results substantially ($SMD = -0.24$, $CI -0.69$ to 0.21). Heterogeneity did not change substantially ($Tau^2 = 0.23$;

$Chi^2 = 28.74$, $df = 5$ ($p < 0.0001$); $I^2 = 83\%$), neither did subgroup differences ($Chi^2 = 0.83$, $df = 2$ ($p = 0.66$), $I^2 = 0\%$).

Excluding five studies because of a high overall risk of bias did not substantially change the results ($SMD = 0.06$, CI -0.13 to 0.26). Heterogeneity decreased ($Tau^2 = 0.00$; $Chi^2 = 0.11$, $df = 2$ ($p = 0.94$); $I^2 = 0\%$), subgroup differences remained low ($Chi^2 = 0.11$, $df = 1$ ($p = 0.74$), $I^2 = 0\%$).

No study focused on treatment resistant patients and therefore no study was excluded for this reason.

3.6.4.1 Art Therapy Versus Control

In this subgroup, three studies with in total 484 participants met the inclusion criteria. Functioning was measured with the GAF ($N = 2$) and the SFS ($N = 1$). No difference was found between art therapy and control groups in this pairwise meta-analysis ($SMD = -0.05$, CI -0.24 to 0.14). There is no strong sign for heterogeneity (Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.95$, $df = 3$ ($p = 0.40$); $I^2 = 0\%$).

3.6.4.2 Music Therapy Versus Control

Three studies with 144 participants were included in this subgroup. The scale used for functioning assessment was the GAF in all of the studies ($N = 3$). Between music therapy and the control groups no difference was found in functioning scores ($SMD = -0.60$, CI -2.21 to 1.01). There was considerable heterogeneity in this subgroup ($Tau^2 = 2.34$; $Chi^2 = 36.49$, $df = 3$ ($p < 0.00001$); $I^2 = 92\%$) (Higgins, Thomas et al., 2019, p. 259).

3.6.4.3 Movement Therapy Versus Control

One study with 68 participants met the inclusion criteria in this subgroup. Functioning was measured with the GAF. No difference between movement therapy and the control condition was found ($SMD = -0.04$, CI -0.54 to 0.46). As there was only one study included in this subgroup, tests for heterogeneity could not be applied.

3.6.5 Multiple Therapies Versus Control

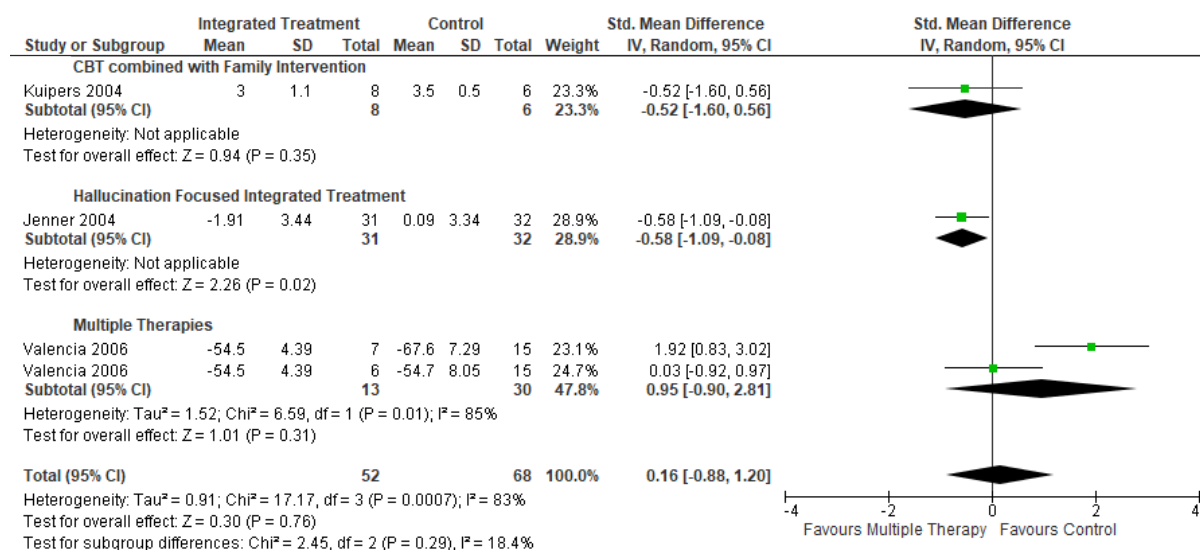


Figure 12. Forest plot of the comparison of multiple therapies versus control. Studies with three arms appear twice.

For this comparison, three studies with 120 participants fulfilled the inclusion criteria. The functioning scales used were the GAF ($N = 2$) and the GSDS ($N = 1$). No statistically significant difference between multiple therapies and the control groups was found ($SMD = -0.16$, CI -0.88 to 1.20). Heterogeneity in this comparison was considerable ($Tau^2 = 0.91$; $Chi^2 = 17.17$, $df = 3$ ($p < 0.0007$); $I^2 = 83%$), as well as the test for subgroup differences ($Chi^2 = 2.45$, $df = 2$ ($p < 0.29$), $I^2 = 18.4%$) (Higgins, Thomas et al., 2019, p. 259).

3.6.5.1 CBT Combined With Family Intervention Versus Control

One study with 14 participants was included in this subgroup. Functioning was measured with the GAF. No difference was found ($SMD = -0.52$, CI -1.60 to 0.56). Tests for heterogeneity and sensitivity analyses were not applied because this subgroup contains only one trial.

3.6.5.2 Hallucination Focused Integrated Treatment Versus Control

One study with 63 participants was included in this subgroup. Functioning was measured with the GSDS. Compared with the control group, hallucination focused integrated treatment had a benefit on the patients' functioning ($SMD = -0.58$, CI -1.09 to -0.08). Since there is only one study in this subgroup, heterogeneity tests and subgroup analyses were not applied.

3.6.5.3 Multiple Therapies Versus Control

There was one study with three arms and a total of 43 participants in this subgroup which leads to two single comparisons. Functioning was measured with the GAF. No statistically significant difference was found between multiple therapies and the control groups ($SMD = 0.95$, $CI -0.90$ to 2.81). There was a considerable amount of heterogeneity in this subgroup ($Tau^2 = 1.52$; $Chi^2 = 6.59$, $df = 1$ ($p = 0.01$); $I^2 = 85\%$) (Higgins, Thomas et al., 2019, p. 259).

3.6.6 Other Therapies Versus Control

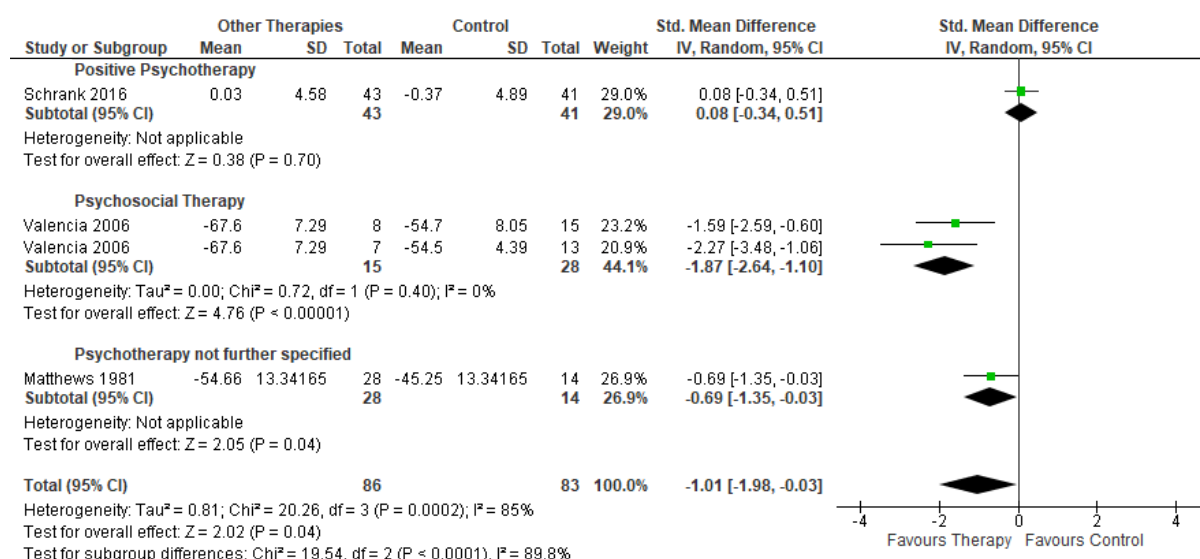


Figure 13. Forest plot of the comparison of other therapies versus control. Studies with three arms appear twice.

Three studies with 169 participants were included in this comparison. Functioning was measured with the GAF ($N = 2$) and the HoNOS ($N = 1$). A difference favoring psychotherapy was found ($SMD = -1.01$, $CI -1.98$ to -0.03). There were substantial heterogeneity ($Tau^2 = 0.81$; $Chi^2 = 20.26$, $df = 3$ ($p = 0.0002$); $I^2 = 85\%$) and subgroup differences ($Chi^2 = 19.54$, $df = 2$ ($p < 0.0001$), $I^2 = 89.8\%$) (Higgins, Thomas et al., 2019, p. 259).

3.6.6.1 Positive Psychotherapy Versus Control

One study with 84 participants was included in this subgroup. Functioning was measured with the HoNOS. No difference was found ($SMD = 0.08$, $CI -0.34$ to 0.51). Tests for heterogeneity were not applied since there is only one study in this subgroup.

3.6.6.2 Psychosocial Therapy Versus Control

One three-armed study with 43 participants was included in this subgroup. Functioning was measured with the GAF. A group difference favoring psychosocial therapy was found ($SMD = -1.87$, $CI -2.64$ to -1.10). No substantial heterogeneity was shown in the different study arms that were compared (Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.72$, $df = 1$ ($p = 0.40$); $I^2 = 0\%$).

3.6.6.3 *Psychotherapy not Further Specified Versus Control*

One study with 32 participants was included in this subgroup. Functioning was assessed with the GAF. A statistically significant group difference in favor of psychotherapy was shown ($SMD = -0.69$, CI -1.35 to -0.03). Tests for heterogeneity and sensitivity analyses were not applied as there was only one study included in the subgroup.

3.7 Publication Bias

Publication bias is investigated with funnel plots. As they are based on symmetry, it does not make sense to carry these analyses out for comparisons with only few studies. Thus, funnel plots were only generated for comparisons with more than 10 studies. (Higgins, Thomas et al., 2019, p. 365)

3.7.1 Psychological Treatment Versus Control

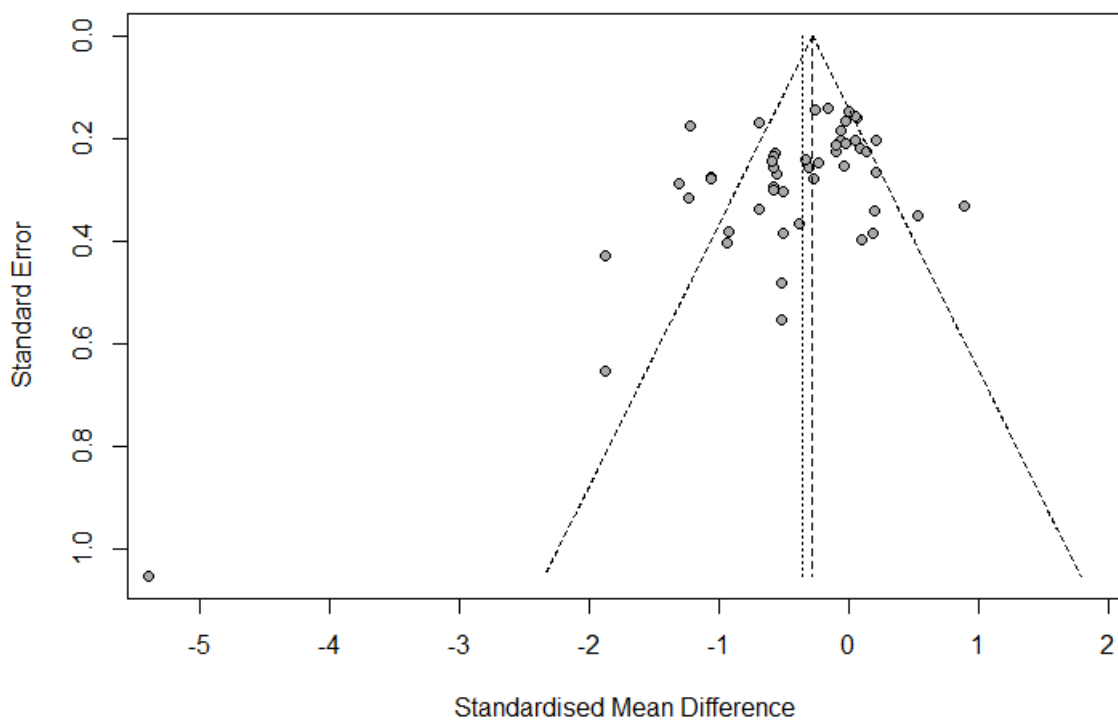


Figure 14. Funnel plot for the comparison of psychological treatment versus control.

In the comparison between psychological treatments and control conditions, there seems to be an asymmetry in the funnel plot, showing that small studies favoring the control condition might have remained unpublished (Figure 14). This was confirmed by Egger's test for funnel plot asymmetry ($p = 0.006171$) (Egger et al., 1997).

With the trim and fill method by Duval and Tweedie (2000), 13 studies were added to the funnel plot (represented as white dots in Figure 15) and the results then entailed the possibility of psychological interventions not being superior to control conditions ($SMD = -0.13$, CI -0.29 to 0.03).

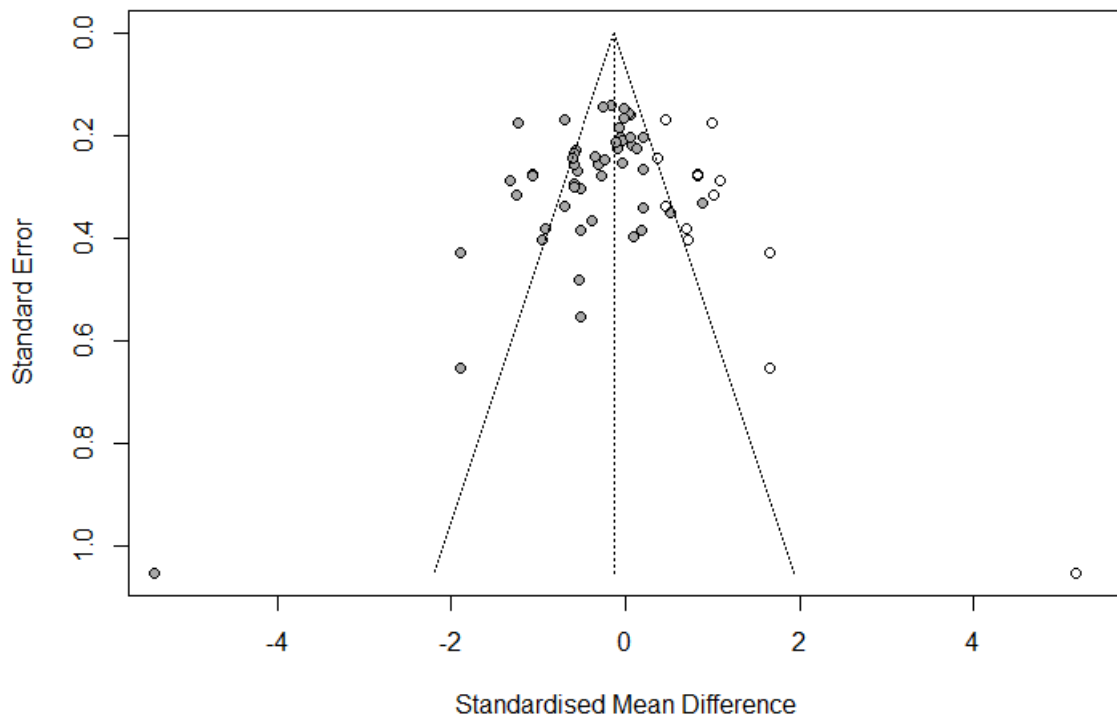


Figure 15. Funnel plot with added studies for the comparison of psychological treatment versus control.

3.7.2 Cognitive Behavior Therapy Versus Control

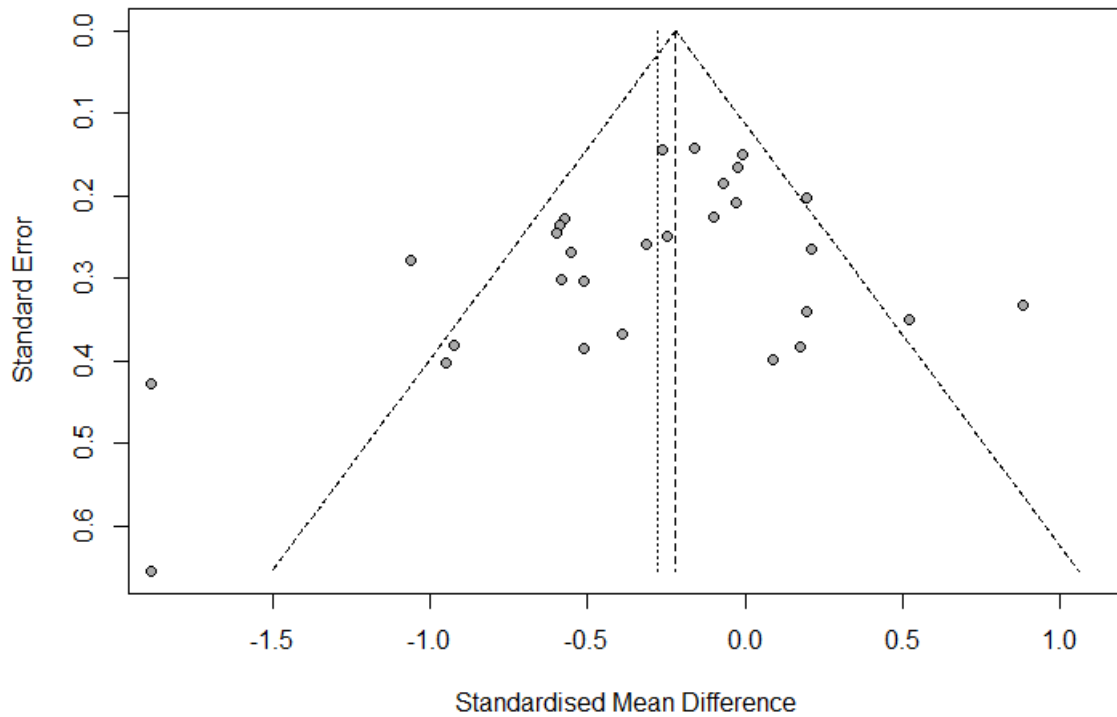


Figure 16. Funnel plot for the comparison of CBT versus control.

The visual inspection of the funnel plot does not allow a clear judgement about symmetry (Figure 16). Asymmetry might have appeared by chance, according to Egger's test for funnel plot asymmetry ($p = 0.07215$) (Egger et al., 1997).

Applying the trim and fill method, 5 studies were added to this comparison (represented as white dots in Figure 17). After adding the studies, the results included the possibility of CBT not being superior to the control conditions ($SMD = -0.15$, CI -0.32 to 0.03).

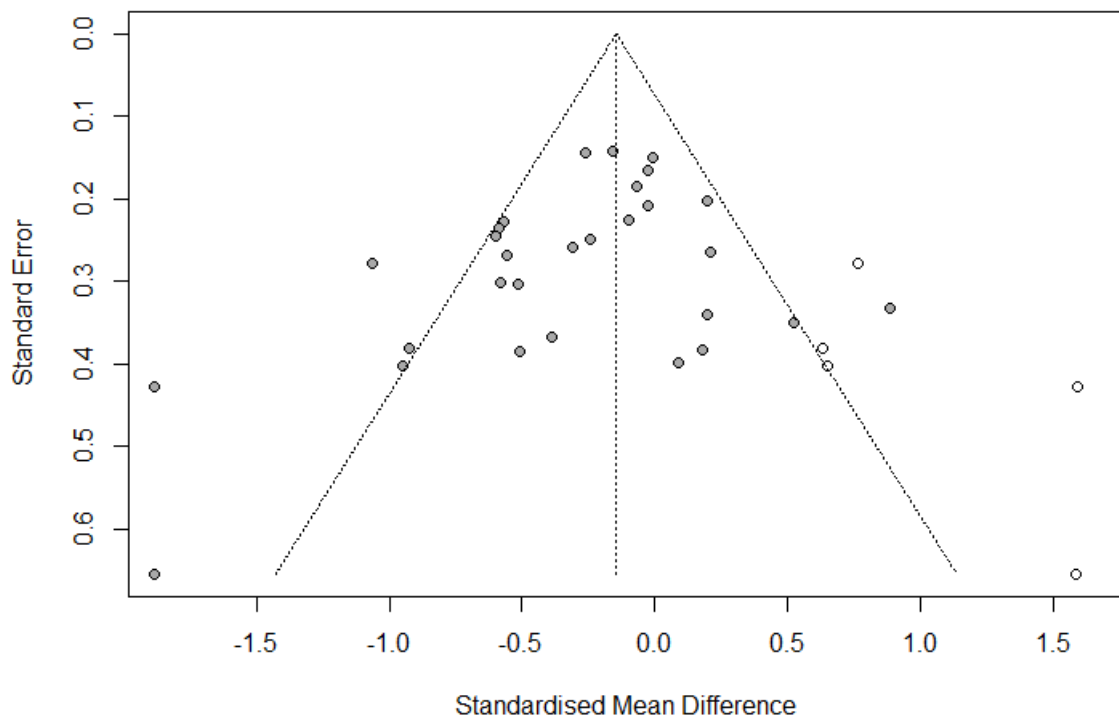


Figure 17. Funnel plot with added studies for the comparison of CBT versus control.

4 Discussion

4.1 Summary of Main Results

This is the first systematic review and meta-analysis that focuses on the effect of different psychological interventions on functioning in people with schizophrenia. With a thorough literature search, 192 studies that met the inclusion criteria were identified, of which 44 had usable outcome data for functioning. The effect size was judged using Cohen's classification, according to which an effect size is considered small from 0.2 to 0.5, medium from 0.5 to 0.8 and large if higher than 0.8 (Cohen, 1988, pp. 25–27). Overall, psychological treatments showed a small to medium benefit for functioning in people with schizophrenia compared to the control conditions ($SMD = -0.36$, $CI -0.50$ to -0.22) (*Figure 4*). The effect size of CBT compared with any control condition was small ($SMD = -0.28$, $CI -0.44$ to -0.12) (*Figure 7*). Third wave CBT compared with any control was found to produce a moderate benefit in terms of functioning ($SMD = -0.67$, $CI -1.01$ to -0.32) (*Figure 10*). The comparison of creative therapy with any control condition did not show a benefit for these interventions ($SMD = -0.09$, $CI -0.48$ to 0.31) (*Figure 11*). No difference between multiple therapies and the control groups was found ($SMD = 0.16$, $CI -0.88$ to 1.20) (*Figure 12*). Other psychotherapies were found to produce a benefit in terms of functioning compared to any control condition ($SMD = -1.01$, $CI -1.98$ to -0.03) (*Figure 13*).

4.2 Discussion in the Light of Other Research

A network meta-analysis, to which the author of this thesis contributed as well, that investigated different psychological treatments for schizophrenia was conducted by Bighelli, Salanti, Huhn et al. (2018). However, that analysis focused on patients with positive symptoms and the outcome functioning was only considered as a secondary outcome (Bighelli, Salanti, Huhn et al., 2018, Appendix, p. 42). Thus, the effects on functioning might have been mediated, in these previous meta-analyses, by the effect of the treatments on the positive symptoms. For CBT versus treatment as usual, they found an effect size of -0.25 concerning functioning favoring CBT, whereas in the present analysis a larger effect size of -0.43 indicating a benefit of CBT was found. This could be due to the population, as positive symptoms may compromise a treatment's effect on functioning

in a special way. For CBT versus supportive therapy, family intervention, inactive control and wait-list, they found no significant difference, which goes in line with the present findings – except concerning supportive therapy. In the present analysis, CBT was superior to supportive therapy ($SMD = -0.26$, CI -0.50 to -0.01). A reason for this difference could be that the term “supportive therapy” is used in different ways. Sometimes it describes an intervention aimed at supporting the patient in dealing with current functioning goals (Penn et al., 2009, p. 54). In other cases, the term is used for a psychodynamic approach aimed at making sense of the patient’s personal narrative and working through of transference (Durham et al., 2003, p. 305) – thus in the present analysis the latter was renamed to psychodynamic therapy to highlight the difference. This leaves room for interpretation and might have led to different studies included in this comparison. It is however difficult to draw conclusions as in the present work only two studies were included in that comparison and in the work by Bighelli, Salanti, Huhn et al. (2018, Appendix, p. 42), only one study was included comparing CBT to supportive therapy investigating functioning in a pairwise comparison. For ACT versus inactive control, they found no difference, which goes in line with the present findings.

Laws et al. (2018) conducted a meta-analysis that focused on functioning, distress and quality of life, but they only looked at CBT as intervention. Another meta-analysis about the effect of CBT for psychosis on functioning was carried out by Wykes et al. (2008). Jones, Hacker, Meaden et al. conducted a Cochrane review comparing CBT with other psychosocial treatments and a Cochrane review comparing CBT to standard care (Jones, Hacker, Meaden et al., 2018; Jones, Hacker, Xia et al., 2018). The present work is the first to investigate systematically the effect of not only CBT, but many different psychological interventions on functioning in patients with schizophrenia.

Laws et al. (2018) found an effect size of 0.25 for CBT compared with any control condition, Wykes et al. (2008) found an effect size of 0.38, both favoring treatment. The effect size found in this work for CBT is closer to the effect size found by Laws et al., also favoring treatment ($SMD = -0.28$). Although the difference is minimal, some possible reasons have to be pointed out. First of all, there were some differences in the inclusion criteria. Both Laws et al. (2018) and Wykes et al. (2008) state that the majority of patients had to have a diagnosis of the schizophrenia

spectrum, but they did not use the 80% threshold that was used for the present meta-analysis. If a majority of patients had affective psychosis, the study was excluded in the present meta-analysis, but some studies that were included in those other two meta-analyses had a majority of patients with affective psychosis, or at least not 80% with non-affective psychosis or schizophrenia spectrum disorder. Second, in the present meta-analysis, first-episode patients have been excluded, which was not the case in the other two reviews on functioning. Especially Laws et al. (2018) included many trials with first-episode patients. This could have led to the slightly smaller effect size because first-episode patients might have had a better baseline functioning, so there might have been not as much room for improvement. Another point is that although Laws et al. and Wykes et al. state to not have included patients with comorbidities, they both did – studies focused on those patients were excluded in the present meta-analysis. The included studies were thus somehow different in all the three reviews. Concerning Wykes et al. (2008), not only were the inclusion criteria different, but they also included non-randomized studies and a decade has passed between their meta-analysis and the present one, leading to many new studies conducted. On top of that, to get to the standardized mean difference as effect size, Wykes et al. divided the mean by the standard deviation of the control group and not by the pooled standard deviation, which might also have contributed to the different outcome. Concerning Laws et al. (2018), for some studies it was not really understandable, why they did not include studies that were included in the present meta-analysis. They excluded one study of computerized CBT that was included here and one study of virtual reality-based CBT. They also found another study that was conducted after the last search update for the present meta-analysis in January 2018, but that study would not have met the present inclusion criteria anyway. Lastly, Wykes et al. did not allow active control conditions, which were allowed in the present meta-analysis.

Contradicting the findings of the present meta-analysis, Jones, Hacker, Meaden et al. concluded that “there is no indication that the addition of CBT to standard care has any convincing generalised effect” (Jones, Hacker, Meaden et al., 2018, p. 36) and that “functioning is seemingly unaffected by CBT” (Jones, Hacker, Xia et al., 2018, p. 37). Their different findings are however not surprising because they did not pool results from different scales and gave separate subtotals only for short, medium and long term effects which makes it not reasonable to compare their

results to the results obtained in this work. To choose one of the many comparisons analyzed in the works by Jonaes, Hacker, Meaden et al. and by Jones, Hacker, Xia et al. and to compare the numbers to the numbers obtained in the present meta-analysis would be arbitrary and not reliable.

Another type of interventions included in this meta-analysis are mindfulness-based treatments. Mindfulness was brought into western medicine in the 1980s by Kabat-Zinn (1982) as an intervention for patients with chronic pain and implemented in different psychological treatments such as mindfulness-based cognitive therapy (Williams et al., 2000) and ACT (Hayes & Wilson, 1994). In a review, Lam and Chien (2016) found six randomized controlled trials about mindfulness interventions for people with schizophrenia. These trials were also found in the search for the present thesis. Only three of those studies had usable outcome data on functioning and therefore were included in the present meta-analysis. Two additional studies were found in the search carried out for this thesis that were not included in the review by Lam and Chien. Furthermore, they did not conduct a meta-analysis, but only described the results of the single studies, whereas for this work, a meta-analysis was carried out and showed a large effect size ($SMD = -0.84$, $CI -1.18$ to -0.50). When pooled together with other third wave therapies such as ACT and metacognitive training, the results remained in favor of third wave therapies, showing a moderate effect ($SMD = -0.67$, $CI -1.01$ to -0.32). This finding is, however, limited by the still small number of studies ($N = 7$).

4.3 Discussion of Results in Detail

4.3.1 Cognitive Behavior Therapy

Cognitive behavior therapy (CBT) had a small effect size when compared to control conditions ($SMD = -0.28$, $CI -0.44$ to -0.12). Interestingly, in 15 out of 25 studies, it was compared to treatment as usual ($SMD = -0.43$, $CI -0.67$ to -0.18), whereas in 4 studies it was compared to an inactive control ($SMD = -0.01$, $CI -0.43$ to 0.40), in 2 to supportive therapy ($SMD = -0.26$, $CI -0.50$ to -0.01), in 2 to cognitive remediation ($SMD = 0.32$, $CI -0.70$ to 1.34), in 2 to a wait-list condition ($SMD = -0.23$, $CI -0.65$ to 0.19), in 1 to family intervention ($SMD = -0.39$, $CI -1.11$ to 0.33), in 1 to psychodynamic therapy ($SMD = 0.09$; $CI -0.69$ to 0.87) and in 1 to

psychoeducation ($SMD = -0.95$; CI -1.74 to -0.16). As expected, for the comparisons of CBT to control conditions other than treatment as usual, effect sizes were mostly notably smaller.

Whereas Furukawa et al. (2014) argue that wait-list could be a placebo condition and therefore lead to overestimated effect sizes, in the meta-analysis at hand, actually a smaller effect was observed for CBT when compared to wait-list than when compared to treatment as usual. This could be due to some hope that the patients get and therefore function better or maybe they want to get things done before they engage in a time and energy consuming treatment. Furukawa's findings were drawn from a network meta-analysis about the treatment response defined by a certain symptom reduction in depressive patients. So, not only is the outcome criterion different from increase in functioning scores, but also the population. These patients may react differently to being assigned to the wait-list condition than patients with schizophrenia. However, the findings in the meta-analysis at hand are limited by the small number of studies comparing CBT to a wait-list condition ($N = 2$).

A placebo effect could have led to the big effect of CBT when compared to psychoeducation, because it might be frustrating to learn about the disease without learning strategies to cope with it. However, it is difficult to draw conclusions because there was only one study comparing CBT to psychoeducation. Findings were not clear either in a review by Xia et al. (2011, p. 23) on psychoeducation compared to standard care: they reported a benefit of psychoeducation for social functioning in schizophrenia when looking at endpoint data, but no superiority when looking at change data. Referring to Carroll et al. (1999), Turkington et al. (2003, p. 98) suggested possible negative effects of psychoeducation concerning suicidal ideation.

That the effect size of CBT was smaller when compared to supportive therapy ($SMD = -0.26$, CI -0.50 to -0.01) and no significant difference was found when CBT was compared to family intervention ($SMD = -0.39$, CI -1.11 to 0.33), inactive control conditions ($SMD = -0.01$, CI -0.43 to 0.40), psychodynamic therapy ($SMD = 0.09$, CI -0.69 to 0.87) or to cognitive remediation ($SMD = 0.32$, CI -0.70 to 1.34) goes in line with Guidi et al. (2018, p. 279) that state that comparing two active treatments may lead to non-significant results and with Gold et al. (2017, p. 729) who point out that effect sizes may be smaller when compared to active

interventions. Concerning the comparison of CBT to non-specific control interventions, Turkington et al. (2003, p. 98), citing Dickerson (2000) as well as Shawyer et al. (2012, p. 119), citing Lynch et al. (2010, p. 9), mention that the effects of CBT are less evident or CBT might be no better at all. Compared to cognitive remediation, no difference could be found ($SMD = 0.32$, CI -0.70 to 1.34), also supporting the thesis that non-specific factors account for a substantial portion of the observed effects.

4.3.2 Third Wave Cognitive Behavior Therapy

Third wave cognitive behavior therapy might have a favorable effect on patients' functioning ($SMD = -0.67$, CI -1.01 to -0.32), but concerning the subgroups, this finding was clear only for mindfulness ($SMD = -0.84$, CI -1.18 to -0.50), which made the whole third wave cluster significant. Metacognitive training also favored therapy, but with a broad confidence interval including no effect ($SMD = -0.11$, CI -0.53 to 0.31). Acceptance and commitment therapy (ACT) was not found to improve functioning ($SMD = 0.05$, CI -0.35 to 0.45). This is difficult to interpret. In ACT, besides the aspect of acceptance, there is also an emphasis on commitment to goals that are set according to the patients' values (Hayes et al., 2003, p. 82). This commitment could as well lead to better functioning scores whereas in mindfulness, more emphasis is put on accepting moment-to-moment experience and not so much on formulating and working towards value-guided goals. Another possibility is that the values identified in ACT did not include domains like occupation and education and therefore maybe this therapy had a positive influence on other outcomes, but not on functioning, because it was not a target of the intervention. Any speculations have to be viewed with caution, however, as the result mentioned above for ACT stems from only one study (Shawyer et al., 2016).

4.3.3 Creative Therapy

Concerning the comparison of creative therapy versus control, there was no benefit of the intervention ($SMD = -0.09$, CI -0.48 to 0.31). Anyhow it is difficult to explain the rationale behind music therapy for functioning, whereas it seems reasonable that music and art therapy may lead to an improvement in other outcomes, for example quality of life.

4.3.4 Sensitivity Analyses

Sensitivity analyses were carried out excluding open label studies, studies with high researcher allegiance, studies with high overall risk of bias or studies focused on treatment resistant patients. Due to the small number of studies left in some sensitivity analyses, their results must be interpreted with caution.

4.3.4.1 Exclusion of Open Label Studies

For the comparison of any treatment to any control condition, the effect size in the main analysis was moderate ($SMD = -0.36$, CI -0.50 to -0.22). Excluding open label studies did not change the conclusion ($SMD = -0.33$, CI -0.48 to -0.18). It might have been expected that it would have changed the conclusion due to detection bias (Higgins, Thomas et al., 2019, p. 626). The robustness of results in hindsight of this possible bias may be thanks to the widespread use of standardized measures respectively the inclusion criteria of this meta-analysis that only allowed studies that used published scales for assessing functioning. The finding that excluding open label studies did not change the results is corroborated by a meta-epidemiological study by Moustgaard et al. (2020, p. 1) who found no “difference in estimated treatment effects between trials with and without blinded patients, healthcare providers, or outcome assessors”. In the other comparisons in which more than five studies were included and therefore this sensitivity analysis was carried out, namely CBT versus control, CBT versus treatment as usual, third wave CBT versus control, mindfulness versus control and creative therapy versus control, the conclusion did not change either.

4.3.4.2 Exclusion of Studies With High Researcher Allegiance

For the overall comparison, CBT versus control and CBT versus treatment as usual, the only sensitivity analysis that lead to a substantial change of results was the one excluding studies with high researcher allegiance. No significant difference could be found anymore ($SMD_{\text{treatment vs control}} = -0.20$, CI -0.43 to 0.03 ; $SMD_{\text{CBT vs control}} = -0.02$, CI -0.29 to 0.24 ; $SMD_{\text{CBT vs TAU}} = -0.07$, CI -0.42 to 0.27). For further comments on this topic, see also Chapters 4.4.7 and 4.6.5.

Under the assumption that researcher allegiance introduces bias in assessing, interpreting and reporting the study outcomes, the conclusion could be that the treatments do not provide a real benefit, and their results are inflated by the expectations of the authors or therapists. There is, however, also the possibility that allegiance really does change the effect and thus represents a non-specific factor enabling treatment success and therefore a treatment that is delivered half-heartedly does not work.

For the comparisons of third wave cognitive behavior therapies, mindfulness and creative therapy versus their respective control groups, excluding studies with high researcher allegiance did not change the results substantially.

4.3.4.3 Exclusion of Studies With High Overall Risk of Bias

Excluding studies with high overall risk of bias did not change the conclusion ($SMD = -0.37$, $CI -0.56$ to -0.18). This was the case for all the relevant comparisons. The opposite would have been expected as shown by Savović et al. (2018) who found in a meta-epidemiological study exaggerated effect sizes associated with high or unclear risk of bias in the domains random sequence generation and allocation concealment. However, Savović et al. looked specifically at distinct domains whereas in this particular sensitivity analysis the overall risk of bias as proposed by Furukawa et al. (2016, p. 6) was used.

Excluding studies with a high overall risk of bias did not change the conclusion in the comparison of CBT to control conditions either ($SMD = -0.31$, $CI -0.52$ to -0.10).

Concerning third wave CBT, mindfulness and creative therapy, the conclusion did not change either when excluding studies with a high overall risk of bias.

4.3.4.4 Exclusion of Studies Focused on Treatment Resistant Patients

Excluding studies on treatment resistant patients did not change the direction of results of the overall comparison, but led to a bigger effect size ($SMD = -0.43$, $CI -0.59$ to -0.26). This was expected as patients that have been treatment resistant at the beginning of the study might as well have been resistant to the study treatment or not be able to participate equally well in psychological treatment as less sick patients. The same was the case for the comparisons CBT versus control, CBT versus TAU and third wave CBT versus control. Bighelli, Salanti, Huhn et

al. (2018, Appendix, p. 73) actually found a smaller, but still significant effect concerning positive symptoms when excluding these studies (Bighelli, Salanti, Huhn et al., 2018, pp. 324–325). Concerning mindfulness versus control and creative therapy versus control, no studies were excluded for this sensitivity analysis.

4.3.5 Subgroup Analyses

Due to the small number of studies included in some subgroups, the results of subgroup analyses must be interpreted with caution.

4.3.5.1 Subgroup Analyses Regarding Treatment Setting

When analyzing the subgroup with a group setting, effect sizes ($SMD = -0.44$, $CI -0.67$ to -0.21) increased when compared to the results of the main analysis ($SMD = -0.36$, $CI -0.50$ to -0.21). When only looking at the subgroup with an individual setting, effect sizes decreased ($SMD = -0.28$, $CI -0.46$ to -0.11). The test for subgroup differences did not yield a significant result ($Chi^2 = 1.08$, $df = 1$ ($p = 0.30$), $I^2 = 7.2\%$). Contrasting these findings, Bighelli, Salanti, Huhn et al. (2018, p. 326) did not find treatment setting to play a role in moderating treatment effects on positive symptoms. A possible reason for the increase in functioning scores in the subgroup with a group setting might be that there is always some kind of social interaction in a group that can serve as example for learning by watching and as feedback respectively corrective for dysfunctional behavior – even if it is not the main objective of the intervention. This question is interesting to be further explored because applying therapy in a group setting is more resource preserving so treatment can be offered to more patients with less waiting time. This social learning effect is possibly not as important concerning positive symptoms that were investigated with subgroup analyses in the meta-analysis mentioned above.

For CBT compared to any control condition, the effect of therapy in an individual setting was bigger ($SMD = -0.33$, $CI -0.52$ to -0.13) than in group ($SMD = -0.13$, $CI -0.38$ to 0.12), which was not significant. The test for subgroup differences did not yield significant results ($Chi^2 = 1.46$, $df = 1$ ($p = 0.23$), $I^2 = 31.4\%$). This goes in line with the findings of Bighelli, Salanti, Huhn et al. (2018, p. 326) concerning the role of treatment setting for the treatment of positive symptoms.

The conflicting results of the subgroup analyses of the different comparisons cannot lead to a clear conclusion. But they should be investigated in further research as a group setting would preserve the scarce personnel and financial resources and lead to earlier treatment for more patients.

4.3.5.2 Subgroup Analyses Regarding Therapist Expertise

In the subgroup where therapists in training were allowed, the effect of psychological treatments on functioning was nonsignificant and smaller ($SMD = -0.18$, CI -0.37 to 0.02) than in the experts subgroup ($SMD = -0.34$, CI -0.53 to -0.14). The test for subgroup differences did not yield significant results ($Chi^2 = 1.28$, $df = 1$ ($p = 0.26$), $I^2 = 22.2\%$). This goes analogue to the findings of Bighelli, Salanti, Huhn et al. (2018, p. 326) who did not find that therapist expertise was a moderator for the effect on positive symptoms.

When administered by trainees, CBT seemed actually to work better ($SMD = -0.27$, CI -0.51 to -0.02) than when administered by experts ($SMD = -0.12$, CI -0.31 to 0.07). The test for subgroup differences was, however, not significant ($Chi^2 = 0.89$, $df = 1$ ($p = 0.35$), $I^2 = 0\%$). Tuma et al. (1978, p. 1123) did not find an association between therapist experience and patient outcomes in different psychological treatments for schizophrenia either. In a more recent review and meta-analysis, Webb et al. (2010, p. 207) did not find such an association for psychological interventions either. However, no studies about patients with schizophrenia were included in that work.

4.3.6 Meta-Regression Analyses

First, it has to be stated that the meta-regression analyses applied a linear regression model, so if no association was found, it could still have been a non-linear kind of association and not completely random. This is important for any of the moderators that were investigated.

4.3.6.1 Number of Sessions

Number of sessions was not found to have a moderating effect for the treatments' effects on functioning in the general comparison ($p = 0.1903$, CI -0.0042 to 0.0209) and neither in the comparison of CBT to any control condition ($p = 0.7303$, CI -0.0154 to 0.0220). This finding partially corroborates the findings of a recent systematic review, where Robinson et al. (2020,

pp. 15–16) concluded that after crossing a threshold of a minimum number of sessions, higher numbers of sessions did not lead to better outcome in routinely delivered psychological therapies across different diagnoses. It has to be noted, however, that they looked at trials with any population of mentally ill patients and did not focus on schizophrenia. On top of that, most of the primary trials used in that review investigated the dose-response relationship concerning symptomatic outcomes and not functional outcomes. Molenaar et al. (2011, p. 278) did not find a difference in social functioning in a randomized controlled trial comparing 8 and 16 sessions of psychotherapy for depression. The population of depressive patients is different from patients with schizophrenia. Lincoln et al. (2016, pp. 35–36) investigated the minimum and optimal dose of CBT for psychosis in a longitudinal study and found 15 sessions to be a minimal dose and 25 to be optimal, albeit some changes took 45 sessions. Their findings suggest a non-linear association which is not necessarily contrary to the present findings as here, a linear association was investigated.

4.3.6.2 Study Duration

Study duration measured in weeks was not found to moderate the treatment effect either in the overall comparison ($p = 0.2084$, CI -0.0127 to 0.0028). Regarding the comparison of CBT to any control condition, treatment duration could have a role in moderating effect on functioning ($p = 0.0346$, CI -0.0173 ; -0.0007) but the moderating effect would be very small (coefficient: -0.0090). In trials of antipsychotic medication for schizophrenia, shorter trial duration was found to be associated with a higher placebo response (Agid et al., 2013, p. 1338). One could argue that the placebo effect is a psychological phenomenon and therefore the effect of psychological interventions could have been influenced by the same moderator as the placebo response in drug trials. This was not the case in an eminent manner in the present analysis.

4.3.6.3 Mean Age

Mean age might have a moderating effect in the overall comparison ($p = 0.0066$, CI 0.0075 to 0.0463). This was not the case in the comparison of CBT to any control condition ($p = 0.5904$, CI -0.0232 ; 0.0407). Turner et al. (2020, pp. 8–9) found in a sensitivity analysis including only studies with low risk of bias that age could be a moderator of the effect of CBT for psychosis on positive symptoms. However, they did not judge that finding as robust.

4.3.6.4 Male Ratio

The meta-regression analysis concerning male ratio carried out for the comparison between any treatment and any control condition did not produce significant results ($p = 0.6711$, CI -0.0130 to 0.0202). Regarding the comparison of CBT to any control condition, no association could be found either ($p = 0.7975$, CI -0.0127 ; 0.0166). Savill et al. (2017, p. 75) found that women had a greater reduction in negative symptoms with body psychotherapy than men. So it would be interesting to further explore the role of gender as a moderator in other psychological treatments.

4.3.6.5 Baseline Severity

Baseline severity was not found to moderate treatment effect on functioning neither in the overall comparison ($p = 0.2041$, CI -0.0195 to 0.0042) nor in the comparison between CBT and control conditions ($p = 0.3648$, -0.0088 to 0.0239). In a recent individual patient data meta-analysis, Turner et al. (2020, pp. 8–9) did not find baseline symptom severity to be a moderator of the effect of CBT on symptoms either. This supports the recommendation that CBT may be sensible to be offered to patients independent of their illness severity.

4.4 Study Quality

4.4.1 What is Bias and Which Domains Were Assessed?

The methodological quality of the included studies was assessed with the Cochrane Collaboration's risk of bias tool (Higgins et al., 2017, pp. 8:10–8:26). Munder and Barth (2017) provided the following definition of bias: *Bias is defined as a systematic error in the estimation and interpretation of an observed effect, including (a) its size, (b) its causal interpretation, and (c) its attribution to intended categories (e.g., the interventions used, the outcome domains assessed)*. The Cochrane tool contains seven predefined domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, selective outcome reporting, incomplete outcome data and other bias. In this study an assessment of researchers' allegiance was added to account for the possibility that "a researcher's therapy

allegiance might unfairly influence the effect sizes of the therapies compared” (Luborsky et al., 1999, p. 102).

4.4.2 Random Sequence Generation and Allocation Concealment

By inclusion criteria, none of the studies had high risk of bias concerning random sequence generation (Bighelli, Salanti, Reitmeir et al., 2018, p. 2); 65.9% of the studies had low risk of bias and the remaining 34.1% had unclear risk of bias. In a review about the effect of antipsychotics on functioning, a similar number of 71% of the studies having low risk of bias was found (Rabaioli, 2018, p. 54). Concerning allocation concealment, 68.2% had an unclear risk of bias and 31.8% a low risk of bias. In the review by Rabaioli (2018, p. 54), almost twice as much studies (62%) had a low risk of bias in this area. In a review investigating risk of bias judgements in systematic reviews, even higher percentages judged as unclear for randomization procedure and allocation concealment were found (Savović et al., 2018, p. 1121). The authors trace this back to insufficient reporting in the studies of especially those two key design features. So, the unclear judgements might be more due to reporting than due to really insufficient implementation of randomization and allocation concealment. However, both explanations rest assumptions which is why those trials have to be judged as unclear if one applies a conservative approach and bases the judgement on facts rather than assumptions. Future research should make sure to use remote and computerized randomization and allocation procedures and report those procedures in sufficient detail.

4.4.3 Blinding of Participants and Personnel

The next criterion, blinding of participants and personnel, cannot be obtained in psychotherapy studies since the therapist cannot deliver a treatment without knowing which one. Patients could theoretically be blind to treatment condition, if they do not know anything about psychotherapy and have never received treatment before. But practically, especially in times of internet, it is not possible to find participants that do not know and will not find out which treatment they receive or that they are receiving a treatment. Especially when the comparator is their usual care, they will notice a difference. Therefore, 100% of the studies had a high risk of bias in this category.

Munder and Barth (2017, p. 5) suggest addressing the resulting risk of bias by “evaluating patients’ treatment expectations and therapists’ enthusiasm for treatment”, referring to Falkenström et al. (2013) and Laird et al. (2017).

Therapists’ enthusiasm for treatment can be evaluated with allegiance measures. One such measure is the Falkenström Allegiance Control measure for Therapists (Falkenström et al., 2013). This is a simple instrument measuring risk for allegiance bias in four degrees from 0 to 3, with 3 being the highest quality, depending on how allegiance is addressed in the article, i.e. if the problem is mentioned at all, if there is an attempt to control for allegiance effects and if measures and statistical controls for such measures are applied.

Criteria to measure allegiance based on the reprint were also already introduced by Gaffan et al. (1995, p. 968). For each treatment modality separately, the reprints are checked. They suggest checking the introduction or in rare cases the methods section for each treatment modality separately in hindsight of certain criteria defining if allegiance might be strong, moderate, weak or non-existent. The criteria include especially to what kind of previous evidence is referred, that is, if the authors refer to evidence supporting the treatment compared to another treatment or just in general or doubting it respectively not mentioning previous evidence. Another point is how detailed the treatment is described and if the authors might even have a role in developing it or give concrete evidence in their report about what they believe themselves about the treatment. The overall rating is obtained based on the general impression of the rater and how many criteria for strong, moderate, weak or no allegiance are fulfilled. A strict procedure on how to calculate the overall score is not given – so the rater’s expertise obtains more importance.

Luborsky et al. (1999) suggest judging allegiance additionally to the reprint based on two other sources: judgement by colleagues and self-rating, using a 5-point Likert scale. An overall quality measure they used in previous works includes that the patients value both treatments equally.

How the patients judge the treatment also found entrance to the implementation of the risk of bias domain “blinding of participants and personnel” proposed in a psychotherapy review by Laird et al. (2017). Following Lackner et al. (2004) and Ostelo et al. (2005), patients’ expectancies and credibility are used as “an indicator for risk of bias arising from lack of blinding” (Laird et al.,

2017, Appendix, p. 4). Unclear or low risk were only considered for studies with active comparators as defined by them. It has to be mentioned that contrarily to the present review Laird et al. also considered treatment as usual or “sham” interventions as active control. If the patients were blinded, because of the possibility of the therapists giving them unconscious cues about their assignment, risk of bias was judged as unclear. If patients were not blind but credibility measures for the patients’ expectations were used, risk of bias was also judged as unclear. A judgement as low was given only if credibility was assessed before treatment or after the first session and the result was that the treatment group had similar or lower credibility scores than the control. (Laird et al., 2017)

As pointed out by Munder and Barth (2017), the new version of the Cochrane “Risk of bias” tool, the RoB 2.0 (Higgins et al., 2016, pp. 29–31; Higgins, Savović et al., 2019, pp. 214–217) combines the previous domain “blinding of participants and personnel” and the topic of treatment integrity to a new domain called “Bias due to deviation from intended interventions”. As blinding is so difficult to obtain in psychotherapy, adequate treatment implementation should be made sure by not only measuring therapist allegiance, but also using adherence checks and training therapists to minimize bias in this domain (Munder & Barth, 2017).

4.4.4 Blinding of Outcome Assessment

Although blinding of outcome assessment is easily possible in psychotherapy trials, only 40.9% of the studies had a low risk of bias in this area, whereas 36.4% had an unclear risk and 22.7% had high risk of bias. In a review comparing the study quality of studies investigating drug treatment and studies investigating psychological interventions for schizophrenia, Bighelli et al. (2020, pp. 499–500) found that in drug studies all studies were assessor-blind and none had high risk of bias regarding outcome assessment whereas in their sample of psychotherapy studies, 25.9% had a high risk of bias which is similar to the percentage found in the present review.

4.4.5 Incomplete Outcome Data

Another area in which there is a large amount of methodological insufficiency in the included trials is “incomplete outcome data”. This means for example that no intention-to-treat-analysis was

carried out (Higgins et al., 2017, p. 8:12). A big majority of 70.4% of the studies had a high risk of bias in this area, whereas in a meta-analysis on the effect of antipsychotic medication on functioning in patients with schizophrenia, a high risk was found only for 16% of the there included studies (Rabaioli, 2018, p. 55). For 18.2%, the risk of bias was judged as low. In the remaining 11.4%, it was not clear. In the review mentioned above comparing drug and psychotherapy trials, 64% of the included psychotherapy studies had a high risk of bias in this domain whereas only 6.5% of the drug trials (Bighelli et al., 2020, p. 500).

4.4.6 Selective Reporting

In the category “selective reporting”, more than half of the studies (52.3%) had an unclear risk of bias, 29.5% had a high risk of bias, 18.2% had a low risk of bias. In other reviews, the risk of bias in this domain was high in 35.2% of psychotherapy studies and only in 12.5% (Bighelli et al., 2020, p. 500) respectively 16% (Rabaioli, 2018, p. 55) of drug studies about schizophrenia. The high percentage of studies with a high risk of bias in this domain is problematic, as selective outcome reporting was found to lead to overestimation of effect sizes and after adjusting for this bias, a review investigating this bias domain found that 20% of the included studies did not have significant results anymore (Kirkham et al., 2010, p. 7). Kirkham et al. suggest addressing the resulting risk of bias by making sure that also unpublished data is used by contacting the study authors, which was done for the present review.

4.4.7 Researcher Allegiance

Researcher allegiance was common in studies included in this meta-analysis: 63.6% of studies had high risk of bias, 22.7% had unclear risk of bias and only 13.6% had a low risk of bias. Often, the authors were involved in development or modification of therapy manuals. In the sensitivity analyses, excluding studies with high researcher allegiance almost always led to a decrease in effect sizes.

The effect size was almost cut in half when comparing psychological treatment to any control condition, now including the possibility of no difference between groups ($SMD_{\text{main analysis}} = -0.36$, CI -0.50 to -0.22 ; $SMD_{\text{excluding studies with high researcher allegiance}} = -0.20$, CI -0.43 to 0.03). For the

comparison of CBT with any control condition, results of the sensitivity analysis excluding studies with high researcher allegiance were not significant anymore ($SMD = -0.02$, CI -0.29 to 0.24). When comparing creative therapies with controls, excluding studies with high researcher allegiance also led to results including the possibility of no difference between the treatments: $SMD = -0.24$, CI -0.69 to 0.21 . Third wave therapies compared to the control conditions actually showed a higher effect size after excluding studies with high researcher allegiance ($SMD = -0.90$, CI -1.55 to -0.25), but there was only one study left.

It is plausible that researchers who developed a treatment conduct trials to investigate its efficacy and would not carry out studies for treatments they do not support. Luborsky and Singer (1975, p. 1003) summarized it as follows: “Who else but a partisan would take the time and energy to do a comparative treatment study?”

There are different ways in which allegiance may influence results. It may lead to conscious or unconscious methodological impairment as well as to actual differences in effect. Luborsky et al. (1999, pp. 101–102) suggest that an influenced choice of control groups, Rosenthal’s (1979) “file drawer problem”, the therapists’ competence and improved therapist performance in answer to researchers’ expectations amongst others are factors contributing to allegiance effects.

To deal with allegiance effects, Hollon (1999) suggests using active comparators with experts and partisans for each therapy so that allegiance is balanced in both groups.

4.4.8 Publication Bias

In the main comparison of psychological interventions versus control conditions, funnel plot asymmetry was found (Figure 14), and confirmed by Egger’s test for funnel plot asymmetry ($p = 0.006171$) (Egger et al., 1997). After imputing 13 studies with the trim and fill method by Duval and Tweedie (2000), the possibility of psychological interventions not being superior was shown ($SMD = -0.13$, CI -0.29 to 0.03) (Figure 15). For the comparison of CBT to control conditions, visual inspection of the funnel plot did not allow a clear judgement about symmetry (Egger’s test: $p = 0.07215$), but, also here, imputing possibly missing studies led to a confidence interval including the possibility of no superiority ($SMD = -0.15$, CI -0.32 to 0.03).

An asymmetrical funnel plot means that there is an association of standard error, as a measure for study size, and effect size. Funnel plot asymmetry, indicating small-study effects, is often equated with publication bias. There are, however, other possible reasons, starting with other kinds of reporting bias, like selective outcome or analysis reporting. In smaller studies, methodology might not have been as rigorous as in bigger trials, possibly leading to inflated effect sizes. There might also be true differences in effect size being moderated by sample size. (Sterne et al., 2011, p. 3) Especially in psychotherapy studies, less changing study staff as a consequence of smaller sample sizes might allow participants to feel less anonymous and better cared for, which might have a positive impact on functioning. Finally, the presence of possible bias and a broadened confidence interval does not prove that there is no beneficial effect of psychotherapy on functioning in people with schizophrenia, but highlights the need for further research – with bigger sample sizes and a continued focus on best possible methodology and transparent reporting.

4.4.9 Summary of Study Quality

In summary, the risk of bias in the included studies was rather high. This is quite understandable for some problematic domains like blinding of participants and personnel as well as researcher allegiance, although even for these problems, numerous solutions have been suggested that are explained later in this chapter. Concerning other domains like selective reporting and incomplete outcome data, there already are a wide range of known methods to reduce risk of bias that just would have had to be implemented. These findings are in line with those of Bighelli et al. (2020) who found that psychotherapy studies had a higher risk of bias than trials comparing different types of antipsychotic medication in schizophrenia.

4.5 Limitations and Strengths

4.5.1 Limitations

There are some limitations of this work that have to be mentioned. First of all, functioning was measured with many different scales – a problem that Rabaioli was confronted with as well in a meta-analysis investigating the effect of antipsychotic medication on functioning (Rabaioli, 2018, p. 103). Laws et al. simply included any functioning measure in their review and did not address

the problem of multiple different scales because they apparently did not even consider the possibility that the variety of scales could be problematic. In the present review, however, that problem is acknowledged. For the reviewer, the question arises which scales to include in the meta-analysis and which not to include. Either choice that is made could be criticized. It is difficult to obtain a balance to not leave out any study that reports on functioning as defined by the study authors but to also put the same outcome in comparable scales together in a meta-analysis. To account for this difficulty, only data obtained with published scales were included and every scale was carefully looked at to make sure that the included scales measure functioning in a comparable way that justifies pooling the results. As effect size measures, standardized mean differences were used to also address this problem in a statistical way. This creates a good generalizability of the results and therefore external validity because even though it would be better if there was an agreement on which scale to use to assess functioning, there is – in practice – no such agreement so far. Also, if one scale would have been left out, some other should be left out as well and then the new question would be where to draw the line on which scales to include and which not to include. Therefore, all published scales measuring functioning, living skills or disability were used. Still, some scales, such as the GAS, included psychopathology and some did not, for example the SOFAS. There is a need for agreement on one functioning measure to be better able to compare research results. Currently, in the Diagnostic and Statistical Manual 5, the American Psychiatric Association (2013) suggests using the WHODAS 2.0.

Analogue to the problem of analyzing many different functioning scales together, there is a problem when pooling psychological treatments. Psychological interventions are very complex and heterogenic by nature. Thus, every decision to analyze a group of studies together may introduce selection bias in a meta-analysis. Thus, for every included study it was very carefully checked which treatment was carried out, not only by the name of treatment the study authors used, but following the description they gave. Every effort was made to put studies together in a treatment group that were actually comparable and the reasoning was discussed with a senior reviewer to reduce subjective influence. It is however not possible to completely eliminate remaining subjectivity from those decisions. To account for that problem, descriptions were given for the included treatments (see Table 4) and track was kept of the decisions which studies to analyze together, especially when

they were put in a treatment group or comparator subgroup different from the term originally used by the study authors.

Another limitation that does not depend on the design of this meta-analysis but is caused by the primary data is the scarcity of evidence on treatments other than CBT. Treatments like art or music therapy or mindfulness are already part of daily routine care in many clinics, thus it is surprising that their impact on functioning has not yet often been investigated. As a result, the broad focus of this meta-analysis did not provide robust results for many comparisons and sensitivity, subgroup or meta-regression analyses were only reasonable for the comparisons of treatment versus control and CBT versus control.

A further limitation is that this meta-analysis only looked at one outcome. It would be very interesting to compare the functioning outcome to other outcomes such as quality of life as these two outcomes can be seen as the objective and subjective domain of recovery (Roe et al., 2011, p. 133).

The pooling of treatments and structure of comparisons has to be discussed as well. Treatments like art, music and movement therapy were grouped although they are quite different in nature. The decision to analyze them together was still reasonable in the light of their common focus on non-verbal self-expression which differentiates them from the other treatments and they were also analyzed separately to account for the differences between them.

4.5.2 Strengths

This work has also important strengths. First, one noteworthy feature of this meta-analysis is the strong methodology, following Cochrane standards. Study selection and data extraction were always carried out in double by independent reviewers and when in doubt discussed with a third, senior, reviewer. This was also the case for the risk of bias assessment. This double check procedure and resolution of disagreement with the help of an expert researcher is an essential necessity in the field of systematic reviews and meta-analyses as it ensures consistent decisions and high quality of study selection, data extraction and risk of bias assessment. A priori specified sensitivity and subgroup analyses were carried out to investigate sources of heterogeneity and bias. The study

selection process was laid out clearly in a flow chart based on the PRISMA statement (*Figure 1*) (Moher et al., 2009, pp. 2–3).

Second, the broad overview of this study. This is the first meta-analysis investigating the effect of different psychological treatments on functioning. Other reviews, for example those by Jones, Hacker, Meaden et al. (2018), by Laws et al. (2018) and by Wykes et al. (2008), only focused on studies including CBT. A network-meta-analysis carried out by Bighelli, Salanti, Huhn et al. (2018) compared all psychological treatments but considered functioning only as secondary outcome and focused on a population with prominent positive symptoms as opposed to the general schizophrenia population considered for this meta-analysis. Here, an overview over the different treatments for schizophrenia is given, also about newer and not yet thoroughly investigated ones, and they are described. So, not only the effects of the different psychological treatments are compared, but it is also shown which treatments are better researched and for which treatments evidence is still lacking and to be obtained.

Third, the comparison and overview of different scales for assessing functioning. Also here, the need for agreement on using the same scale is shown.

Finally, what this study also showed is the relevance of adequate control group design. Risk of bias was assessed carefully and is illustrated and possible sources investigated as well as suggestions made to minimize bias. The importance of a strict methodology in psychotherapy research is shown and ways to address common problems are suggested.

4.6 Implications for Future Research and Practice

The present findings about the effect of psychological interventions on functioning in people with schizophrenia highlight the need for further research in this field. Suggestions for future research and practice are laid out below.

4.6.1 Identification of Active Ingredients

The present data suggests that adding psychological treatment to pharmacological treatment may be of benefit for functioning in patients with schizophrenia. CBT was the most investigated

treatment. While significantly favorable in general ($SMD = -0.28$, CI -0.44 to -0.12) and when compared to psychoeducation ($SMD = -0.95$; CI -1.74 to -0.16) or treatment as usual ($SMD = -0.43$, CI -0.67 to -0.18), no significant difference could be observed when CBT was compared to inactive control conditions ($SMD = -0.01$, CI -0.43 to 0.40). This might suggest that it is not the exact concept of CBT for psychosis which helps improve the patients' functioning, but rather unspecific factors such as the accepting and empathic attention of a therapist. Concerning positive symptoms, Bighelli, Salanti, Huhn et al. (2018) found that CBT was superior to supportive therapy concerning positive symptoms ($SMD = -0.47$, CI -0.91 to -0.03). Specific cognitive behavioral techniques might be more decisive in that domain than for functioning. Future schizophrenia research should try and identify the active ingredients of helpful treatments, especially of CBT as efficacy has already been shown and now it is important to understand how it works. For identifying active ingredients, control group design plays an important role (see 4.6.6).

4.6.2 Investigation of Treatments Other Than Cognitive Behavior Therapy

Psychological treatments other than cognitive behavior therapy have not yet been intensely investigated in hindsight of their effect on functioning in schizophrenia. Art or movement therapy are in many inpatient settings part of routine care for psychiatric inpatients with schizophrenia and other diagnoses and also recommended in the German schizophrenia guideline (Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde, 2019, pp. 51–52). There is no comprehensive evidence on efficacy of such treatments or integrated treatment forms yet. Future research should put more emphasis on investigating creative and integrated treatments to either support the present clinical practice or help make adjustments.

4.6.3 Importance of Measuring Functioning

The Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde defines as treatment goal in schizophrenia, amongst other aspects, that the patient is able to lead a self-determined life (Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde, 2019, p. 22). Functioning is explicitly mentioned as part of the definition of treatment resistance – when it is impaired (Deutsche

Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde, 2019, p. 35). This was already the case in the 2006 version of the guideline, so the relevance of this outcome is not quite new. Still, only 44 of the 192 found studies reported data on functioning. The fraction is way higher than in trials on pharmacotherapy, as Rabaioli (2018, p. 18) reported that 45 of 1066 studies measured functioning. So, compared with trials on pharmacotherapy, in psychotherapy research functioning is already measured 10 times as often. But as functioning is so important for individuals and society and thus even part of guideline recommendations, it should be measured and reported even more often in future research.

4.6.4 Usage of Published and Recommended Functioning Scales

During this work, questions of comparability arose caused by the use of numerous different functioning assessment scales: 14 different scales in the 44 included studies. This variety of available and used scales does not only show differences in form and methodology such as self-report, like the Clinical Outcomes in Routine Evaluation (Evans et al., 2000), versus observer-rated formats, like the GAF (American Psychiatric Association., 1987). It also reflects a lack of agreement on how the outcome functioning itself is defined (Burns & Patrick, 2007, p. 414; Rabaioli, 2018, p. 103): in the GAF (American Psychiatric Association., 1987), psychopathological symptoms are a defining, not separated part of the functioning assessment, whereas in the SFS (Birchwood et al., 1990), they are not considered. Another problem is the lack of data on the scales' psychometric properties when used in patients with schizophrenia (Burns & Patrick, 2007, p. 414; Rabaioli, 2018, p. 103). In the Diagnostic and Statistical Manual of Mental Disorders 5 (American Psychiatric Association., 2013), the World Health Organization Disability Assessment Schedule 2.0 (Üstün et al., 2010) is recommended, so in future research, this instrument that was developed and recommended by these two renowned organizations should be used to obtain better comparable results.

4.6.5 Minimization of Risk of Bias

More than a decade ago, Cochrane presented comprehensive recommendations for the assessment of bias risk in studies included in systematic reviews (Higgins & Altman, 2008). The different risk

of bias domains are common knowledge in research circles. Still, half of the included studies (50%) had a high overall risk of bias. In future research, attention should be paid to minimize every possible source of bias to get more valid results which will also lead to a better reputation and acceptance of psychotherapy research.

Especially simple requirements like allocation concealment and randomization can easily be met using digital technology. Assessments should be blind, as there already is a natural lack of blinding in psychotherapy research because therapists and patients cannot really be blind (Munder & Barth, 2017, p. 351). Breakings of assessor blinding should be reported in a standardized way as recommended by Baethge et al. (2013, p. 153).

It has to be admitted that there are some limitations in psychotherapy studies that cannot be undone or can only be tackled when compromising other domains. These include blinding of participants and therapists and oftentimes therapist allegiance. Allegiance effects can and should be addressed in different ways. One is to balance allegiances by comparing two active interventions each delivered by partisans (Munder & Barth, 2017, p. 8). The other approach is to assess and report researcher allegiance (Falkenström et al., 2013). For example, choosing active comparators instead of inactive controls to balance allegiances leads to a loss in specificity because two active treatments might have the same unspecific therapeutic ingredients. Other sources of bias, however, can be ruled out rather easily, for example randomization and allocation concealment. Every effort should be made to at least adequately implement these design features. For the more difficult domains of risk of bias, such as allegiance or blinding, measures should be applied and reported and breakings of blinding should be reported as well.

To address reporting bias, intention-to-treat analyses should be carried out. This was found to be common practice in trials on antipsychotic medication (Rabaioli, 2018, p. 55), but not in the majority of studies about psychotherapy for schizophrenia (Bighelli et al., 2020, p. 500). Researchers should predefine the primary and secondary outcome parameters in published trial protocols and stick to those predefined parameters when reporting their results.

Small-study effects were evident in this work, as 13 studies had to be imputed and added to the included 43 studies in the general comparison with the trim and fill method by Duval and Tweedie

(2000) (see Chapter 3.7.1). Although there might be other reasons for small-study effects (see Chapter 4.4.8), these findings highlight the problematic consequences of possible publication bias.

Therefore, investigators should publish their data regardless of direction and significance of results and trials should be registered a priori. Researchers conducting meta-analyses should search for published and unpublished data, describe the possible publication bias and apply data imputing methods to address it, even though they are flawed because of assumptions about missing data. Although most submitted works get published and the reasons for non-publication are on the side of investigators, editors should put emphasis on the relevance of the research question and methodology and not so much on the results. (Easterbrook et al., 1991, pp. 871–872) For this work, a thorough search was carried out, not only on journals but also on grey literature such as conference abstracts and trial registrations and protocols.

4.6.6 Reasonable Choice of Control Groups

A reasonable choice of control groups in trials about psychological interventions for schizophrenia can help address different issues that became evident in the present meta-analysis.

In the present meta-analysis, in the comparison of CBT to different control conditions it was shown that effect sizes strongly depended on the choice of control groups. Treatment effects were highest when CBT was compared to psychoeducation ($SMD = -0.95$, CI $-1.74, -0.16$) or treatment as usual ($SMD = -0.43$, CI -0.67 to -0.18) and changed direction when compared to cognitive remediation ($SMD = 0.32$, CI -0.70 to 1.34), an active comparator. A similar variation in effect sizes with different control groups was found in a meta-analysis of psychological interventions for depression (Mohr et al., 2014, p. 411). Considering effect size variability as well as disease severity, quality of available care and stage of treatment development, Gold et al. (2017, p. 728) illustrated a decision framework to help researchers design adequate control groups.

Furthermore, the sensitivity analyses in the present work showed that researcher allegiance possibly had an impact on the effect of psychological interventions on functioning in schizophrenia. Well-chosen control groups might reduce bias due to allegiance effects. A possible source of allegiance effects might be a lack of interest or competence when delivering the control treatment

(Hollon, 1999, p. 107). This could be solved by comparing interventions each delivered by an expert and supporter of that intervention (Hollon, 1999, p. 107).

To identify the active ingredients of a psychological treatment, inactive control groups can be helpful (Baskin et al., 2003, p. 977). Inactive control conditions have to be designed carefully and handled with attention as they may lead to “resentful demoralization” of control group participants and thus create ethical problems (Schwartz et al., 1997, p. 363). Furthermore, attention has to be paid to the aim of the study. If the main aim is to judge the efficacy of a treatment, treatment as usual or an established active treatment may serve better as control group (Baskin et al., 2003, p. 977).

Treatment as usual was used frequently ($N = 30$) as a control condition in the included studies that measured the effect of psychological interventions on functioning in schizophrenia. However, treatment as usual is often not described in sufficient detail and different study authors might have a different understanding of what is “usual”, ranging from using the term as a synonym for “no treatment” at all to regular visits with a general practitioner, or even psychotherapy (Watts et al., 2015, pp. 158–161). It also depends on the health care system in which the study is carried out (Watts et al., 2015, p. 161). Furthermore, it has been suggested that treatment as usual is not an optimal control group as it does not necessarily control for unspecific factors such as “attention and opportunity to disclosure” (Guidi et al., 2018, p. 278).

Treatment as well as control conditions should be described in sufficient detail, even or especially when they appear to be self-explaining, for example when treatment as usual is mentioned (Watts et al., 2015, p. 163). The description of treatment as usual should inform about the treatment provider and content, number and frequency of sessions and if referrals were allowed (Watts et al., 2015, p. 161).

Using control conditions appropriate to the particular research question that is investigated and describing them in a detailed way will further improve psychotherapy research on schizophrenia and in general.

4.6.7 Considerations on the Direct Comparison of Psycho- and Pharmacotherapy

Recently, there is a growing debate about whether psychotherapy could be a stand-alone treatment in schizophrenia. Laws and Gournay (2018, pp. 200–201) recommend omitting CBT altogether for patients with schizophrenia whereas Morrison (2019, pp. 94–97) supports the idea of shared decision making including the option of stand-alone CBT with no concomitant antipsychotic medication under certain circumstances, especially no risk of harm to self or others. The German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) takes a middle position in this discussion. They suggest in their S3 guideline for the treatment of schizophrenia an integrated treatment concept including both pharmacotherapy and CBT among other interventions (Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde [DGPPN], 2019, p. 24). Furthermore, in first-episode patients, they recommend beginning pharmacotherapy as early as possible (DGPPN, 2019, p. 33), and offering CBT also to patients that refuse antipsychotic medication (DGPPN, 2019, p. 47). These recommendations are, however, according to the guideline, to be discussed with and explained to the patient in a shared decision-making process (DGPPN, 2019, p. 24).

In almost all trials included in the present meta-analysis, antipsychotic drug therapy was applied in both treatment and control groups. To investigate stand-alone CBT, Morrison et al. (2014, pp. 1395–1403) carried out a randomized controlled trial including only patients that had chosen not to take antipsychotic medication. That trial is also included in the present meta-analysis, but both arms were without antipsychotic medication and the comparison was between psychotherapy and treatment as usual. Antipsychotic medication has a range of burdensome side-effects. Furthermore, most patients generally prefer psychotherapy over pharmacotherapy (McHugh et al., 2013, p. 595). Thus, delivering psychotherapy as stand-alone treatment could be of great benefit for the patients – under the premise that its efficacy is equal to that of antipsychotic medication. To investigate if psychotherapy alone might be equally efficacious as pharmacotherapy, from a theoretical point of view, trials directly comparing both of them should be carried out in which in each of the groups only one treatment form is delivered and psychotherapy is not only delivered as an add-on.

This interesting research question is however difficult when seen from an ethical point of view. Beauchamp and Childress (2013, p. 13) advocate four principles for biomedical ethics: respect for autonomy, non-maleficence, beneficence and justice. Randomized controlled trials per se and specifically trials comparing antipsychotic medication to psychotherapy in schizophrenia pose ethical problems in hindsight of these principles. The patients' autonomy can be respected by informing him in detail about the study design and potential risks and benefits of each of the possible treatments in a shared decision-making process and then only including patients in the study who have given informed consent. The other three principles of non-maleficence, beneficence and justice are potentially problematic when comparing antipsychotics to psychotherapy for schizophrenia.

To help patients and do no harm, there has to be equipoise between the two treatment possibilities (Stines & Feeny, 2008, p. 240).

Equipoise can be interpreted differently. Its strict interpretation demands that the individual researcher conducting the trial must be in serious doubt about which treatment is the best, so that before the trial both treatments are in an equal position concerning potential benefits, as judged by the investigator. This can be referred to as theoretical equipoise. A more practical definition of equipoise that is also how the term is understood in research to date is that of a serious discussion and disagreement in the clinical community and not the individual researcher, which can be referred to as clinical equipoise. (Freedman, 1987, pp. 141–144)

In order to ethically justify a direct comparison of psychotherapy and pharmacotherapy in schizophrenia, the question if there is clinical equipoise has to be answered. As described above, there is an honest disagreement among experts in the field. Whereas Morrison (2019, pp. 94–97) argues for the benefits of CBT in patients with schizophrenia, Laws and Gournay (2018, pp. 200–201) are not convinced of its efficacy. Currently available meta-analyses are showing differing results for CBT in schizophrenia, even when antipsychotic medication was applied concomitantly (McKenna et al., 2019, pp. 235–236). Taking a look at the rates of response to antipsychotic medication, an individual patient data meta-analysis found that, depending on the response criteria, up to two thirds of patients did not respond to antipsychotic medication in a clinically

meaningful way (Samara et al., 2019, p. 642). Concerning effect sizes, however, antipsychotics have been shown superior to placebo with moderate effect sizes for most substances and a large effect ($SMD = -0.88$, CI 0.73 to 1.03) for Clozapine (Leucht, Cipriani et al., 2013, p. 951). Thus, it would not seem ethical to withhold pharmacological treatment from patients in an acute phase of schizophrenia. This problem could be addressed by including only less severely ill patients, as effects of antipsychotics are usually higher in sicker patients (Furukawa et al., 2015, p. 14) – respectively the harm of not applying them. Study design for the direct comparison of psychotherapy to pharmacotherapy in schizophrenia should be dynamic and a priori criteria should be defined as to when patients might get medication even when they are in the psychotherapy group, so that it is ensured that the principle of non-harming is followed. Although informed patient consent is crucial for autonomy, this ethical requirement is not fully met by written consent because the patients' decision cannot only be biased by a lack of information – which can be resolved by talking to the researcher – but also by other circumstances in the patients' life, for example of financial nature. It is widely agreed upon that antipsychotic medication has a range of severe potential side effects. Thus, risks might not be balanced when directly comparing psychotherapy to pharmacotherapy. It has to be noted, however, that while side effects are seldom reported in psychotherapy trials, this does not mean that psychotherapy does not produce any side-effects. Linden and Schermuly-Haupt (2014, p. 307) made suggestions which side effects should be reported in psychotherapy trials. Morrison et al. (2018, pp. 411–423) actually conducted a pilot study comparing antipsychotics to cognitive behavior therapy to a combination of both. Most of their sample were recruited from an early intervention service, implying that patients might not have been as sick as in pharmacotherapy trials. They found that a head-to-head comparison is feasible and safe in a first-episode sample. Unfortunately, they did not give details about the ethical justification of their study. The study has been criticized because of CBT not being in clinical equipoise with antipsychotic medication (Mustafa, 2018, p. 540).

Besides the ambiguous data currently available, the disagreement about the justification of psychotherapy for schizophrenia might stem from a deeper ideological conflict in psychiatry in general.

This ideological conflict is fueled by the belief that psychotherapy is a psychosocial treatment and pharmacological therapy is a biological treatment and therefore more scientifically valid. That separation can be exposed as a myth when considering the current state of neuroscience and its free-energy principle. In this framework, the brain's function is to minimize the difference between its model of reality and the actual environmental input. Cognitive processes like beliefs and goals can influence neuroplasticity and in this way the brain's model of reality in a top-down process. Thus, rather than as fundamentally different treatments, pharmacological and psychosocial therapy should be appreciated as two routes leading to the same goal – improved neural functioning – and even enhancing each other on the way there. (Prosser et al., 2016, pp. 309–310)

5 Summary

Schizophrenia is a disorder that lays a heavy burden on society as well as on the affected individual. Diagnosis and treatment are complex with an emphasis put on pharmacological treatment in the past. In the last decades, psychological interventions for schizophrenia have become more and more often used in clinical settings and the object of research and meta-analyses. Functioning is an important outcome as an improvement can reduce the burden on society and contribute to the individual's quality of life. This systematic review and meta-analysis is the first to investigate the effect of many different psychosocial interventions, regardless of their comparator, on functioning in people with schizophrenia.

Randomized controlled trials that investigated the effect of psychological interventions on functioning in schizophrenia were included. There was no restriction concerning language and year of publication. Eligible articles were identified through title-abstract and full-text screening of the search results as well as a hand-search of existing reviews on the topic. Data extraction was performed using a MS Access database. Risk of bias was assessed with the Cochrane risk of bias tool. All of this was done in double to ensure correct data collection and assessment. Outcome data on functioning was of continuous nature, the effect sizes expressed using standardized mean differences. Heterogeneity was estimated and possible reasons explored with sensitivity, subgroup and meta-regression analyses. Results were presented with forest plots and publication bias was investigated with funnel plots.

21772 records were identified in the search, of which after title-abstract and full-text screening 462 articles remained corresponding to 192 studies of which 44 had usable data. The following treatment groups were investigated: cognitive behavior therapy, third wave cognitive behavior therapies, creative therapies, combinations of therapies and other therapies. Overall, psychotherapy was superior to the control conditions ($SMD = -0.36$). CBT was also superior ($SMD = -0.28$). For third wave therapies, a difference was found as well ($SMD = -0.67$). For creative therapies, no significant difference was found. Multiple treatments did not show a benefit either. The other therapies were also superior to the control groups ($SMD = -1.01$).

The proportion of studies rated as high risk of bias was rather high in most domains, except – by inclusion criteria – for randomization and allocation concealment: 22.7% concerning blinding of outcome assessment, 70.4% for incomplete outcome data, 29.5% for selective outcome reporting, 63.6% for researcher allegiance and 4.5% for other bias. There was allusion to publication bias. The present results are in the same range as the results of comparable meta-analyses, albeit not exactly the same.

An interesting finding is that excluding studies with high researcher allegiance almost always led to a decrease in effect size, sometimes rendering the result not significant. Excluding studies with a high overall risk of bias did not change the conclusion in most of the cases. Excluding open label studies led to a decrease in effect size.

For CBT, the nature of the control groups had a non-negligible influence on the results. The effect size decreased with increasing activity of the control group. This might lead to the assumption that next to its specific therapeutic ingredients, unspecific factors play a considerable role in treatment efficacy of CBT.

The meta-regression analyses concerning study duration, baseline severity, number of sessions, mean age and male ratio did not yield clinically relevant results. Mean age and study duration might have a moderating effect with younger age and longer study duration being positively associated with treatment efficacy, but it would be very small in both cases.

Blinding of participants and personnel is a problematic domain in psychotherapy research, but other authors have made several suggestions to address this problem. By comparing two active interventions, each with therapists alleged to the intervention they provide, allegiance effects can be balanced. Patients' and therapists' treatment expectations can be measured and their influence investigated. Unfortunately, active comparators have only been used in less than half of the included studies, and measures for allegiance and treatment expectations in none.

There are several limitations to this study. The outcome was assessed with different scales that all measured functioning, but each in their unique way. Study quality was overall limited, leading to a general mistrust in the results of the meta-analysis as well. Several analyses were carried out,

possibly leading to bias from multiple testing. Treatments and controls were described in the primary studies with differing levels of detail. So possibly, treatments were lumped together that were rather different.

There are however also important strengths. For this review, a strict methodology was used applying Cochrane standards. Screening, data extraction and risk of bias assessment were always carried out in duplicate. The study selection process is depicted with a flow chart following the PRISMA guidelines. Heterogeneity and sources of bias were investigated with sensitivity, subgroup and meta-regression analyses as well as funnel plots. Implications for future research and practice were worked out to improve research and treatment quality in the future. The debate about psychotherapy and pharmacotherapy was described which showed the complexity of the field. To overcome the ideological myth of psychosocial treatment being inherently different and inferior to biological treatment, improving quality of psychotherapy research is essential. This work was carried out to help patients, caregivers and researchers, always keeping in mind two aims: creating and advocating dependable, transparent research and an open debate in the scientific community, and providing evidence-based and suitable treatment to individuals affected by schizophrenia so that the burden to carry is kept as light as possible.

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10 Search Strategy

The literature search followed the strategy used by Bighelli, Salanti, Huhn et al. (2018, Appendix, pp. 3-23):

Ovid MEDLINE(R) in-process & other non-indexed citations and Ovid MEDLINE(R) <1946 to present> searched 10th January 2018

- 1 exp Schizophrenia/ (104582)
- 2 exp Psychotic Disorders/ (51539)
- 3 schizo\$.mp. (166486)
- 4 or/1-3 (201032)
- 5 exp Psychotherapy/ or exp Behavior Therapy/ or exp Cognitive Therapy/ or exp Complementary Therapies/ or exp Psychoanalysis/ or exp Counseling/ or exp Hypnosis/ or Association/ or Association learning/ (424755)
- 6 (abreaction or "acceptance and commitment therapy" or acting out or adlerian or analytical psychotherap\$ or anger control or anger management or animal therap\$ or art therap\$ or assertive\$ training or attention training technique or autogenic training or autosuggestion or aversion therap\$ or balint group or befriending or behavio?r contracting or behavio?r modification or behavio?r regulation or behavio?r therap\$ or bibliotherap\$ or biofeedback or body psychotherap\$ or brief psychotherap\$ or caregiver support or cbt or client cent\$ or cognitive behavio?r\$ or cognitive intervention\$ or cognitive rehabilit\$ or cognitive remediation or cognitive technique\$ or cognitive therap\$ or cognitive treatment\$ or colo?r therap\$ or compassionate mind training or conjoint therap\$ or contingency management or conversational therap\$ or conversion therap\$ or coping skills or counsel?ing or countertransference or couples therap\$ or covert sensitization or crisis intervention or dance therap\$ or dialectic\$ or eclectic or emotion\$ focus\$ or emotional freedom technique or encounter group therap\$ or existential therap\$ or experiential psychotherap\$ or exposure therap\$ or expressive psychotherap\$ or eye movement desensiti?ation or family intervention\$ or family therap\$ or feminist therap\$ or free association or freudian or geriatric psychotherap\$ or gestalt therap\$ or griefwork or group intervention\$ or group psychotherap\$ or group therap\$ or guided image\$ or holistic psychotherap\$ or humanistic psychotherap\$ or hypnosis or hypnotherap\$ or hypnoti?zability or imagery or implosive therap\$ or individual psychotherap\$ or insight therap\$ or integrated psychological therapy or integrative psychotherap\$ or integrative therap\$ or interpersonal or jungian or kleinian or logotherap\$ or marathon group therap\$ or marital therap\$ or meditation or mental healing or metacognitive therap\$ or metacognitive training or milieu therap\$ or mindfulness or morita therap\$ or multimodal or music therap\$ or narrative therap\$ or nondirective therap\$ or object relations or person cent\$ therap\$ or personal construct therap\$ or persuasion therap\$ or pet therap\$ or play therap\$ or primal therap\$ or problem solving or psychoanaly\$ or psychodrama or psychodynamic or psychoeducat\$ or psychologic\$ or psychological therap\$ or psychosocial treatment or psychotherap\$ or psychotherapeutic counsel\$ or psychotherapeutic processes or psychotherapeutic training or psychotherapeutic treatment\$ or rational emotive or reality therap\$ or reciprocal inhibition or rehabilitat\$ or relationship

therap\$ or relaxation or reminiscence therap\$ or rogerian or role play\$ or self analys\$ or self esteem or sensitivity training or sex therap\$ or sleep phase chronotherap\$ or social skills education or social skills training or socioenvironmental therap\$ or sociotherap\$ or solution focused or stress management or support group\$ or supportive therap\$ or systematic desensiti?ation or systemic therap\$ or therapeutic communit\$ or transactional analysis or transference or transtheoretical or validation therap\$ or (dream\$ adj3 analys\$) or (support adj3 psycho\$).mp. (1197308)

7 or/5-6 (1380129)

8 exp clinical trial/ (888265)

9 exp randomized controlled trials/ (130594)

10 exp double-blind method/ (162383)

11 exp single-blind method/ (27740)

12 exp cross-over studies/ (46911)

13 randomized controlled trial.pt. (515252)

14 clinical trial.pt. (561480)

15 controlled clinical trial.pt. (101720)

16 (clinic\$ adj2 trial).mp. (737165)

17 (random\$ adj5 control\$ adj5 trial\$).mp. (706490)

18 (crossover or cross-over).mp. (92834)

19 ((singl\$ or double\$ or trebl\$ or tripl\$) adj (blind\$ or mask\$)).mp. (236226)

20 randomi\$.mp. (844744)

21 (random\$ adj5 (assign\$ or allocat\$ or assort\$ or reciev\$)).mp. (233688)

22 or/8-21 (1388053)

23 4 and 7 and 22 (3485)

Embase <1974 to 2018 week 02> searched 10-01-18

1 exp schizophrenia/ (168146)

2 exp psychosis/ (259209)

3 schizo\$.mp. (211911)

4 or/1-3 (298021)

5 exp Psychotherapy/ or exp Behavior Therapy/ or exp Cognitive Therapy/ or exp Psychoanalysis/ or exp Counseling/ or exp Hypnosis/ or Association/ (419285)

6 (abreaction or "acceptance and commitment therapy" or acting out or adlerian or analytical psychotherap\$ or anger control or anger management or animal therap\$ or art therap\$ or assertive\$ training or attention training technique or autogenic training or autosuggestion or aversion therap\$ or balint group or befriending or behavio?r contracting or behavio?r modification or behavio?r regulation or behavio?r therap\$ or bibliotherap\$ or biofeedback or body psychotherap\$ or brief psychotherap\$ or caregiver support or cbt or client cent\$ or cognitive behavio?r\$ or cognitive intervention\$ or cognitive rehabilit\$ or cognitive remediation or cognitive technique\$ or cognitive therap\$ or cognitive treatment\$ or colo?r therap\$ or compassionate mind training or conjoint therap\$ or contingency management or conversational therap\$ or conversion therap\$ or coping skills or counsel?ing or

countertransference or couples therap\$ or covert sensitization or crisis intervention or dance therap\$ or dialectic\$ or eclectic or emotion\$ focus\$ or emotional freedom technique or encounter group therap\$ or existential therap\$ or experiential psychotherap\$ or exposure therap\$ or expressive psychotherap\$ or eye movement desensiti?ation or family intervention\$ or family therap\$ or feminist therap\$ or free association or freudian or geriatric psychotherap\$ or gestalt therap\$ or griefwork or group intervention\$ or group psychotherap\$ or group therap\$ or guided image\$ or holistic psychotherap\$ or humanistic psychotherap\$ or hypnosis or hypnotherap\$ or hypnoti?zability or imagery or implosive therap\$ or individual psychotherap\$ or insight therap\$ or integrated psychological therapy or integrative psychotherap\$ or integrative therap\$ or interpersonal or jungian or kleinian or logotherap\$ or marathon group therap\$ or marital therap\$ or meditation or mental healing or metacognitive therap\$ or metacognitive training or milieu therap\$ or mindfulness or morita therap\$ or multimodal or music therap\$ or narrative therap\$ or nondirective therap\$ or object relations or person cent\$ therap\$ or personal construct therap\$ or persuasion therap\$ or pet therap\$ or play therap\$ or primal therap\$ or problem solving or psychoanaly\$ or psychodrama or psychodynamic or psychoeducat\$ or psychologic\$ or psychological therap\$ or psychosocial treatment or psychotherap\$ or psychotherapeutic counsel\$ or psychotherapeutic processes or psychotherapeutic training or psychotherapeutic treatment\$ or rational emotive or reality therap\$ or reciprocal inhibition or rehabilitat\$ or relationship therap\$ or relaxation or reminiscence therap\$ or rogerian or role play\$ or self analys\$ or self esteem or sensitivity training or sex therap\$ or sleep phase chronotherap\$ or social skills education or social skills training or socioenvironmental therap\$ or sociotherap\$ or solution focused or stress management or support group\$ or supportive therap\$ or systematic desensiti?ation or systemic therap\$ or therapeutic communit\$ or transactional analysis or transference or transtheoretical or validation therap\$ or (dream\$ adj3 analys\$) or (support adj3 psycho\$)).mp. (1816360)

7 or/5-6 (1846489)

8 (clin\$ adj2 trial).mp. (1407667)

9 ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj (blind\$ or mask\$)).mp. (266326)

10 (random\$ adj5 (assign\$ or allocat\$)).mp. (159013)

11 randomi\$.mp. (1005968)

12 crossover.mp. (85226)

13 exp randomized-controlled-trial/ (481956)

14 exp double-blind-procedure/ (144978)

15 exp crossover-procedure/ (53823)

16 exp single-blind-procedure/ (30078)

17 exp randomization/ (76684)

18 or/8-17 (1980276)

19 4 and 7 and 18 (7787)

20 limit 19 to exclude medline journals (787)

PsycINFO <1806 to January week 1 2018> searched 10-01-18

- 1 exp Schizophrenia/ (83900)
- 2 exp psychosis/ (107318)
- 3 schizo\$.mp. (127877)
- 4 or/1-3 (146915)
- 5 exp psychotherapy/ or exp Behavior Therapy/ or exp Cognitive Therapy/ or exp PSYCHOANALYSIS/ or exp psychotherapeutic counseling/ or hypnosis/ or free association/ (218371)
- 6 (abreaction or "acceptance and commitment therapy" or acting out or adlerian or analytical psychotherap\$ or anger control or anger management or animal therap\$ or art therap\$ or assertive\$ training or attention training technique or autogenic training or autosuggestion or aversion therap\$ or balint group or befriending or behavio?r contracting or behavio?r modification or behavio?r regulation or behavio?r therap\$ or bibliotherap\$ or biofeedback or body psychotherap\$ or brief psychotherap\$ or caregiver support or cbt or client cent\$ or cognitive behavio?r\$ or cognitive intervention\$ or cognitive rehabilit\$ or cognitive remediation or cognitive technique\$ or cognitive therap\$ or cognitive treatment\$ or colo?r therap\$ or compassionate mind training or conjoint therap\$ or contingency management or conversational therap\$ or conversion therap\$ or coping skills or counsel?ing or countertransference or couples therap\$ or covert sensitization or crisis intervention or dance therap\$ or dialectic\$ or eclectic or emotion\$ focus\$ or emotional freedom technique or encounter group therap\$ or existential therap\$ or experiential psychotherap\$ or exposure therap\$ or expressive psychotherap\$ or eye movement desensiti?ation or family intervention\$ or family therap\$ or feminist therap\$ or free association or freudian or geriatric psychotherap\$ or gestalt therap\$ or griefwork or group intervention\$ or group psychotherap\$ or group therap\$ or guided image\$ or holistic psychotherap\$ or humanistic psychotherap\$ or hypnosis or hypnotherap\$ or hypnoti?zability or imagery or implosive therap\$ or individual psychotherap\$ or insight therap\$ or integrated psychological therapy or integrative psychotherap\$ or integrative therap\$ or interpersonal or jungian or kleinian or logotherap\$ or marathon group therap\$ or marital therap\$ or meditation or mental healing or metacognitive therap\$ or metacognitive training or milieu therap\$ or mindfulness or morita therap\$ or multimodal or music therap\$ or narrative therap\$ or nondirective therap\$ or object relations or person cent\$ therap\$ or personal construct therap\$ or persuasion therap\$ or pet therap\$ or play therap\$ or primal therap\$ or problem solving or psychoanaly\$ or psychodrama or psychodynamic or psychoeducat\$ or psychologic\$ or psychological therap\$ or psychosocial treatment or psychotherap\$ or psychotherapeutic counsel\$ or psychotherapeutic processes or psychotherapeutic training or psychotherapeutic treatment\$ or rational emotive or reality therap\$ or reciprocal inhibition or rehabilitat\$ or relationship therap\$ or relaxation or reminiscence therap\$ or rogerian or role play\$ or self analys\$ or self esteem or sensitivity training or sex therap\$ or sleep phase chronotherap\$ or social skills education or social skills training or socioenvironmental therap\$ or sociotherap\$ or solution focused or stress management or support group\$ or supportive therap\$ or systematic desensiti?ation or systemic therap\$ or therapeutic communit\$ or transactional analysis or transference or transtheoretical or validation therap\$ or (dream\$ adj3 analys\$) or (support adj3

psycho\$)).mp. (1068413)
 7 or/5-6 (1068614)
 8 ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj (blind\$ or mask\$)).mp. (23874)
 9 (random\$ adj5 (assign\$ or allocat\$)).mp. (39290)
 10 randomi\$.mp. (72094)
 11 crossover.mp. (6680)
 12 or/8-11 (114666)
 13 4 and 7 and 12 (1873)

Cochrane Library searched 10th January 2018

#1 MeSH descriptor: [Schizophrenia] explode all trees [5749]
 #2 MeSH descriptor: [Psychotic Disorders] explode all trees [1902]
 #3 schizo*:ti,ab,kw (Word variations have been searched) [12880]
 #4 #1 or #2 or #3 [13755]
 #5 MeSH descriptor: [Psychotherapy] explode all trees [21548]
 #6 MeSH descriptor: [Behavior Therapy] explode all trees [14721]
 #7 MeSH descriptor: [Cognitive Therapy] explode all trees [7698]
 #8 MeSH descriptor: [Complementary Therapies] explode all trees [18611]
 #9 MeSH descriptor: [Psychoanalysis] explode all trees [16]
 #10 MeSH descriptor: [Counseling] explode all trees [4818]
 #11 MeSH descriptor: [Hypnosis] explode all trees [668]
 #12 MeSH descriptor: [Association] explode all trees [475]
 #13 MeSH descriptor: [Association Learning] explode all trees [345]
 #14 (abreaction or "acceptance and commitment therapy" or acting out or adlerian or analytical psychotherap* or anger control or anger management or animal therap* or art therap* or assertive* training or attention training technique or autogenic training or autosuggestion or aversion therap* or balint group or befriending or behavio?r contracting or behavio?r modification or behavio?r regulation or behavio?r therap* or bibliotherap* or biofeedback or body psychotherap* or brief psychotherap* or caregiver support or cbt or client cent* or cognitive behavio?r* or cognitive intervention* or cognitive rehabilit* or cognitive remediation or cognitive technique* or cognitive therap* or cognitive treatment* or colo?r therap* or compassionate mind training or conjoint therap* or contingency management or conversational therap* or conversion therap* or coping skills or counsel?ing or countertransference or couples therap* or covert sensitization or crisis intervention or dance therap* or dialectic* or eclectic or emotion* focus* or emotional freedom technique or encounter group therap* or existential therap* or experiential psychotherap* or exposure therap* or expressive psychotherap* or eye movement desensiti?ation or family intervention* or family therap* or feminist therap* or free association or freudian or geriatric psychotherap* or gestalt therap* or griefwork or group intervention* or group psychotherap* or group therap* or guided image* or holistic psychotherap* or humanistic psychotherap* or hypnosis or hypnotherap* or hypnoti?zability or imagery or implosive therap* or individual psychotherap* or insight therap* or integrated psychological therapy or integrative

psychotherap* or integrative therap* or interpersonal or jungian or kleinian or logotherap* or marathon group therap* or marital therap* or meditation or mental healing or metacognitive therap* or metacognitive training or milieu therap* or mindfulness or morita therap* or multimodal or music therap* or narrative therap* or nondirective therap* or object relations or person cent* therap* or personal construct therap* or persuasion therap* or pet therap* or play therap* or primal therap* or problem solving or psychoanaly* or psychodrama or psychodynamic or psychoeducat* or psychologic* or psychological therap* or psychosocial treatment or psychotherap* or psychotherapeutic counsel* or psychotherapeutic processes or psychotherapeutic training or psychotherapeutic treatment* or rational emotive or reality therap* or reciprocal inhibition or rehabilitat* or relationship therap* or relaxation or reminiscence therap* or rogerian or role play* or self analys* or self esteem or sensitivity training or sex therap* or sleep phase chronotherap* or social skills education or social skills training or socioenvironmental therap* or sociotherap* or solution focused or stress management or support group* or supportive therap* or systematic desensiti?ation or systemic therap* or therapeutic communit* or transactional analysis or transference or transtheoretical or validation therap* or (dream* near/3 analys*) or (support near/3 psycho*)):ti,ab,kw (Word variations have been searched)[411716]
 #15 #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 [419239]
 #16 #4 and #15 in Trials [6420]

Biosis searched 10th January 2018

13 684 #12 AND #11 AND #10

Indexes=BCI Timespan=All years

12 403,516 TITLE: ((abreaction or "acceptance and commitment therapy" or "acting out" or adlerian or "analytical psychotherap*" or "anger control" or "anger management" or "animal therap*" or "art therap*" or "assertive* training" or "attention training technique" or "autogenic training" or autosuggestion or "aversion therap*" or "balint group" or befriending or "behavior contracting" or "behavior modification" or "behavior regulation" or "behavior therap*" or "behaviour contracting" or "behaviour modification" or "behaviour regulation" or "behaviour therap*" or bibliotherap* or biofeedback or "body psychotherap*" or "brief psychotherap*" or "caregiver support" or cbt or "client cent*" or "cognitive behavior*" or "cognitive behaviour*" or "cognitive intervention*" or "cognitive rehabilit*" or "cognitive remediation" or "cognitive technique*" or "cognitive therap*" or "cognitive treatment*" or "color therap*" or "colour therap*" or "compassionate mind training" or "conjoint therap*" or "contingency management" or "conversational therap*" or "conversion therap*" or "coping skills" or counseling or counselling or countertransference or "couples therap*" or "covert sensitization" or "covert sensitisation" or "crisis intervention" or "dance therap*" or dialectic* or eclectic or emotion* focus* or "emotional freedom technique" or "encounter group therap*" or "existential therap*" or "experiential psychotherap*" or "exposure therap*" or "expressive psychotherap*" or "eye movement desensitization" or "eye movement desensitisation" or "family intervention*" or "family therap*" or "feminist therap*" or "free association" or freudian or "geriatric

psychotherap*" or "gestalt therap*" or griefwork or "group intervention*" or "group psychotherap*" or "group therap*" or "guided image*" or "holistic psychotherap*" or "humanistic psychotherap*" or hypnosis or hypnotherap* or hypnotizability or hypnotisability or imagery or "implosive therap*" or "individual psychotherap*" or "insight therap*" or "integrated psychological therapy" or "integrative psychotherap*" or "integrative therap*" or interpersonal or jungian or kleinian or logotherap* or "marathon group therap*" or "marital therap*" or meditation or "mental healing" or "metacognitive therap*" or "metacognitive training" or "milieu therap*" or mindfulness or "morita therap*" or multimodal or "music therap*" or "narrative therap*" or "nondirective therap*" or "object relations" or person cent* therap* or "personal construct therap*" or "persuasion therap*" or "pet therap*" or "play therap*" or "primal therap*" or "problem solving" or psychoanaly* or psychodrama or psychodynamic or psychoeducat* or psycholog* or "psychological therap*" or "psychosocial treatment" or psychotherap* or "psychotherapeutic counsel*" or "psychotherapeutic processes" or "psychotherapeutic training" or "psychotherapeutic treatment*" or "rational emotive" or "reality therap*" or "reciprocal inhibition" or rehabilitat* or "relationship therap*" or relaxation or "reminiscence therap*" or rogerian or "role play*" or "self analys*" or "self esteem" or "sensitivity training" or "sex therap*" or "sleep phase chronotherap*" or "social skills education" or "social skills training" or "socioenvironmental therap*" or sociotherap* or "solution focused" or "stress management" or "support group*" or "supportive therap*" or "systematic desensitization" or "systematic desensitisation" or "systemic therap*" or "therapeutic communit*" or "transactional analysis" or transference or transtheoretical or "validation therap*" or (dream* Near/3 analys*) or (support Near/3 psycho*)) OR TOPIC: ((abreaction or "acceptance and commitment therapy" or "acting out" or adlerian or "analytical psychotherap*" or "anger control" or "anger management" or "animal therap*" or "art therap*" or "assertive* training" or "attention training technique" or "autogenic training" or autosuggestion or "aversion therap*" or "balint group" or befriending or "behavior contracting" or "behavior modification" or "behavior regulation" or "behavior therap*" or "behaviour contracting" or "behaviour modification" or "behaviour regulation" or "behaviour therap*" or bibliotherap* or biofeedback or "body psychotherap*" or "brief psychotherap*" or "caregiver support" or cbt or "client cent*" or "cognitive behavior*" or "cognitive behaviour*" or "cognitive intervention*" or "cognitive rehabilit*" or "cognitive remediation" or "cognitive technique*" or "cognitive therap*" or "cognitive treatment*" or "color therap*" or "colour therap*" or "compassionate mind training" or "conjoint therap*" or "contingency management" or "conversational therap*" or "conversion therap*" or "coping skills" or counseling or counselling or countertransference or "couples therap*" or "covert sensitization" or "covert sensitisation" or "crisis intervention" or "dance therap*" or dialectic* or eclectic or emotion* focus* or "emotional freedom technique" or "encounter group therap*" or "existential therap*" or "experiential psychotherap*" or "exposure therap*" or "expressive psychotherap*" or "eye movement desensitization" or "eye movement desensitisation" or "family intervention*" or "family therap*" or "feminist therap*" or "free association" or freudian or "geriatric psychotherap*" or "gestalt therap*" or griefwork or "group intervention*" or "group psychotherap*" or "group therap*" or "guided image*" or "holistic psychotherap*" or "humanistic psychotherap*" or hypnosis or hypnotherap* or hypnotizability or hypnotisability or imagery or "implosive therap*" or

"individual psychotherap*" or "insight therap*" or "integrated psychological therapy" or "integrative psychotherap*" or "integrative therap*" or interpersonal or jungian or kleinian or logotherap* or "marathon group therap*" or "marital therap*" or meditation or "mental healing" or "metacognitive therap*" or "metacognitive training" or "milieu therap*" or mindfulness or "morita therap*" or multimodal or "music therap*" or "narrative therap*" or "nondirective therap*" or "object relations" or person cent* therap* or "personal construct therap*" or "persuasion therap*" or "pet therap*" or "play therap*" or "primal therap*" or "problem solving" or psychoanaly* or psychodrama or psychodynamic or psychoeducat* or psychologic* or "psychological therap*" or "psychosocial treatment" or psychotherap* or "psychotherapeutic counsel*" or "psychotherapeutic processes" or "psychotherapeutic training" or "psychotherapeutic treatment*" or "rational emotive" or "reality therap*" or "reciprocal inhibition" or rehabilitat* or "relationship therap*" or relaxation or "reminiscence therap*" or rogerian or "role play*" or "self analys*" or "self esteem" or "sensitivity training" or "sex therap*" or "sleep phase chronotherap*" or "social skills education" or "social skills training" or "socioenvironmental therap*" or sociotherap* or "solution focused" or "stress management" or "support group*" or "supportive therap*" or "systematic desensitization" or "systematic desensitisation" or "systemic therap*" or "therapeutic communit*" or "transactional analysis" or transference or transtheoretical or "validation therap*" or (dream* Near/3 analys*) or (support Near/3 psycho*))

Indexes=BCI Timespan=All years

11 152,007 TOPIC: (schizo* or psychotic* or psychosis or psychoses) OR TITLE: (schizo* or psychotic* or psychosis or psychoses)

Indexes=BCI Timespan=All years

10 383,461 #9 OR #8 OR #7 OR #6 OR #3 OR #2

Indexes=BCI Timespan=All years

9 39,824 TS=crossover* OR TI=crossover*

Indexes=BCI Timespan=All years

8 467 TS=(randomi* Near/1 assign*) or TI=(randomi* Near/1 assign*)

Indexes=BCI Timespan=All years

7 80 TS=(randomi* Near/1 allocate*) or TI=(randomi* Near/1 allocate*)

Indexes=BCI Timespan=All years

6 122,301 #5 AND #4

Indexes=BCI Timespan=All years

5 225,151 TS=(mask* OR blind*) OR TI=(mask* OR blind*)

Indexes=BCI Timespan=All years

4 2,256,036 TS=(singl* OR Doubl* OR Tripl* OR Trebl*) OR TI=(singl* OR Doubl* OR Tripl* OR Trebl*)

Indexes=BCI Timespan=All years

3 316,443 TI=(randomi*) OR TS=(randomi*)

Indexes=BCI Timespan=All years

2 165,438 TS=(Randomized clinical trial*) OR TI=(Randomized clinical trial*)

Indexes=BCI Timespan=All years

1 10,515,925 TA=(Hominidae)
Indexes=BCI Timespan=All years

Pubmed Searched 10th January 2018

#10 Search (#4 and #8 and #9) 6852

#9 Search (((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomized[tiab]) OR (placebo[tiab]) OR (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab]))) NOT (animals[mh] NOT humans[mh])) 3607526

#8 Search (#6 or #7) 979810

#7 Search (abreaction[Title/Abstract] OR "acceptance[Title/Abstract] AND commitment therapy"[Title/Abstract] OR "acting out"[Title/Abstract] OR adlerian[Title/Abstract] OR "analytical psychotherapy"[Title/Abstract] OR "analytical psychotherapies"[Title/Abstract] OR "anger control"[Title/Abstract] OR "anger management"[Title/Abstract] OR "animal therapy"[Title/Abstract] OR "animal therapies"[Title/Abstract] OR "art therapy"[Title/Abstract] OR "art therapies"[Title/Abstract] OR "assertive training"[Title/Abstract] OR "assertiveness training"[Title/Abstract] OR "attention training technique"[Title/Abstract] OR "autogenic training"[Title/Abstract] OR autosuggestion[Title/Abstract] OR "aversion therapy"[Title/Abstract] OR "aversion therapies"[Title/Abstract] OR "balint group"[Title/Abstract] OR befriending[Title/Abstract] OR "behavior contracting"[Title/Abstract] OR "behavior modification"[Title/Abstract] OR "behavior regulation"[Title/Abstract] OR "behavior therapy"[Title/Abstract] OR "behavior therapies"[Title/Abstract] OR "behaviour contracting"[Title/Abstract] OR "behaviour modification"[Title/Abstract] OR "behaviour regulation"[Title/Abstract] OR "behaviour therapy"[Title/Abstract] OR "behaviour therapies"[Title/Abstract] OR bibliotherapy[Title/Abstract] OR bibliotherapies[Title/Abstract] OR biofeedback[Title/Abstract] OR "body psychotherapy"[Title/Abstract] OR "body psychotherapies"[Title/Abstract] OR "brief psychotherapy"[Title/Abstract] OR "brief psychotherapies"[Title/Abstract] OR "caregiver support"[Title/Abstract] OR cbt[Title/Abstract] OR "client centre"[Title/Abstract] OR "client center"[Title/Abstract] OR "cognitive behavior"[Title/Abstract] OR "cognitive behavioral"[Title/Abstract] OR "cognitive intervention"[Title/Abstract] OR "cognitive interventions"[Title/Abstract] OR "cognitive rehabilitation"[Title/Abstract] OR "cognitive remediation"[Title/Abstract] OR "cognitive technique"[Title/Abstract] OR "cognitive techniques"[Title/Abstract] OR "cognitive therapy"[Title/Abstract] OR "cognitive therapies"[Title/Abstract] OR "cognitive treatment"[Title/Abstract] OR "cognitive treatments"[Title/Abstract] OR "color therapy"[Title/Abstract] OR "color therapies"[Title/Abstract] OR "colour therapy"[Title/Abstract] OR "colour therapies"[Title/Abstract] OR "compassionate mind training"[Title/Abstract] OR "conjoint therapy"[Title/Abstract] OR "conjoint therapies"[Title/Abstract] OR "contingency management"[Title/Abstract] OR "conversational therapy"[Title/Abstract] OR "conversational therapies"[Title/Abstract] OR "conversion therapy"[Title/Abstract] OR "conversion therapies"[Title/Abstract] OR "coping skills"[Title/Abstract] OR counseling[Title/Abstract] OR counselling[Title/Abstract] OR

countertransference[Title/Abstract] OR "couples therapy"[Title/Abstract] OR "couples therapies"[Title/Abstract] OR "covert sensitization"[Title/Abstract] OR "covert sensitisation"[Title/Abstract] OR "crisis intervention"[Title/Abstract] OR "dance therapy"[Title/Abstract] OR "dance therapies"[Title/Abstract] OR dialectic[Title/Abstract] OR dialectical[Title/Abstract] OR "dream analysis"[Title/Abstract] OR eclectic[Title/Abstract] OR "emotion focused"[Title/Abstract] OR "emotionally focused"[Title/Abstract] OR "emotional freedom technique"[Title/Abstract] OR "encounter group therapy"[Title/Abstract] OR "encounter group therapies"[Title/Abstract] OR "existential therapy"[Title/Abstract] OR "existential therapies"[Title/Abstract] OR "experiential psychotherapy"[Title/Abstract] OR "experiential psychotherapies"[Title/Abstract] OR "exposure therapy"[Title/Abstract] OR "exposure therapies"[Title/Abstract] OR "expressive psychotherapy"[Title/Abstract] OR "expressive psychotherapies"[Title/Abstract] OR "eye movement desensitization"[Title/Abstract] OR "eye movement desensitisation"[Title/Abstract] OR "family intervention"[Title/Abstract] OR "family interventions"[Title/Abstract] OR "family therapy"[Title/Abstract] OR "family therapies"[Title/Abstract] OR "feminist therapy"[Title/Abstract] OR "feminist therapies"[Title/Abstract] OR "free association"[Title/Abstract] OR freudian[Title/Abstract] OR "geriatric psychotherapy"[Title/Abstract] OR "geriatric psychotherapies"[Title/Abstract] OR "gestalt therapy"[Title/Abstract] OR "gestalt therapies"[Title/Abstract] OR griefwork[Title/Abstract] OR "group intervention"[Title/Abstract] OR "group interventions"[Title/Abstract] OR "group psychotherapy"[Title/Abstract] OR "group psychotherapies"[Title/Abstract] OR "group therapy"[Title/Abstract] OR "group therapies"[Title/Abstract] OR "guided imagery"[Title/Abstract] OR "holistic psychotherapy"[Title/Abstract] OR "holistic psychotherapies"[Title/Abstract] OR "humanistic psychotherapy"[Title/Abstract] OR "humanistic psychotherapies"[Title/Abstract] OR hypnosis[Title/Abstract] OR hypnotherapy[Title/Abstract] OR hypnotherapies[Title/Abstract] OR hypnotizability[Title/Abstract] OR hypnotisability[Title/Abstract] OR imagery[Title/Abstract] OR "implosive therapy"[Title/Abstract] OR "implosive therapies"[Title/Abstract] OR "individual psychotherapy"[Title/Abstract] OR "individual psychotherapies"[Title/Abstract] OR "insight therapy"[Title/Abstract] OR "insight therapies"[Title/Abstract] OR "integrated psychological therapy"[Title/Abstract] OR "integrative psychotherapy"[Title/Abstract] OR "integrative psychotherapies"[Title/Abstract] OR "integrative therapy"[Title/Abstract] OR "integrative therapies"[Title/Abstract] OR interpersonal[Title/Abstract] OR jungian[Title/Abstract] OR kleinian[Title/Abstract] OR logotherapy[Title/Abstract] OR logotherapies[Title/Abstract] OR "marathon group therapy"[Title/Abstract] OR "marathon group therapies"[Title/Abstract] OR "marital therapy"[Title/Abstract] OR "marital therapies"[Title/Abstract] OR meditation[Title/Abstract] OR "mental healing"[Title/Abstract] OR "metacognitive therapy"[Title/Abstract] OR "metacognitive therapies"[Title/Abstract] OR "metacognitive training"[Title/Abstract] OR "milieu therapy"[Title/Abstract] OR "milieu therapies"[Title/Abstract] OR mindfulness[Title/Abstract] OR "morita therapy"[Title/Abstract] OR "morita therapies"[Title/Abstract] OR multimodal[Title/Abstract] OR "music therapy"[Title/Abstract] OR "music therapies"[Title/Abstract] OR "narrative therapy"[Title/Abstract] OR "narrative

therapies"[Title/Abstract] OR "nondirective therapy"[Title/Abstract] OR "nondirective therapies"[Title/Abstract] OR "object relations"[Title/Abstract] OR "person centred therapy"[Title/Abstract] OR "person centred therapies"[Title/Abstract] OR "person centered therapy"[Title/Abstract] OR "person centered therapies"[Title/Abstract] OR "personal construct therapy"[Title/Abstract] OR "personal construct therapies"[Title/Abstract] OR "persuasion therapy"[Title/Abstract] OR "persuasion therapies"[Title/Abstract] OR "pet therapy"[Title/Abstract] OR "pet therapies"[Title/Abstract] OR "play therapy"[Title/Abstract] OR "play therapies"[Title/Abstract] OR "primal therapy"[Title/Abstract] OR "primal therapies"[Title/Abstract] OR "problem solving"[Title/Abstract] OR psychoanalyse[Title/Abstract] OR psychoanalysed[Title/Abstract] OR psychoanalysis[Title/Abstract] OR psychoanalytic[Title/Abstract] OR psychodrama[Title/Abstract] OR psychodynamic[Title/Abstract] OR psychoeducate[Title/Abstract] OR psychoeducation[Title/Abstract] OR psychoeducating[Title/Abstract] OR psychologic[Title/Abstract] OR psychological[Title/Abstract] OR psychologically[Title/Abstract] OR "psychological therapy"[Title/Abstract] OR "psychological therapies"[Title/Abstract] OR "psychosocial treatment"[Title/Abstract] OR "psychosocial treatments"[Title/Abstract] OR psychotherapy[Title/Abstract] OR psychotherapies[Title/Abstract] OR "psychotherapeutic counsel"[Title/Abstract] OR "psychotherapeutic counseling"[Title/Abstract] OR "psychotherapeutic counselling"[Title/Abstract] OR "psychotherapeutic processes"[Title/Abstract] OR "psychotherapeutic training"[Title/Abstract] OR "psychotherapeutic treatment"[Title/Abstract] OR "psychotherapeutic treatments"[Title/Abstract] OR "rational emotive"[Title/Abstract] OR "reality therapy"[Title/Abstract] OR "reality therapies"[Title/Abstract] OR "reciprocal inhibition"[Title/Abstract] OR rehabilitation[Title/Abstract] OR rehabilitating[Title/Abstract] OR "relationship therapy"[Title/Abstract] OR "relationship therapies"[Title/Abstract] OR relaxation[Title/Abstract] OR "reminiscence therapy"[Title/Abstract] OR "reminiscence therapies"[Title/Abstract] OR rogerian[Title/Abstract] OR "role play"[Title/Abstract] OR "role plays"[Title/Abstract] OR "role playing"[Title/Abstract] OR "self analysis"[Title/Abstract] OR "self analysing"[Title/Abstract] OR "self esteem"[Title/Abstract] OR "sensitivity training"[Title/Abstract] OR "sex therapy"[Title/Abstract] OR "sex therapies"[Title/Abstract] OR "sleep phase chronotherapy"[Title/Abstract] OR "sleep phase chronotherapies"[Title/Abstract] OR "social skills education"[Title/Abstract] OR "social skills training"[Title/Abstract] OR "socioenvironmental therapy"[Title/Abstract] OR "socioenvironmental therapies"[Title/Abstract] OR sociotherapy[Title/Abstract] OR sociotherapies[Title/Abstract] OR "solution focused"[Title/Abstract] OR "stress management"[Title/Abstract] OR "support group"[Title/Abstract] OR "support groups"[Title/Abstract] OR "supportive therapy"[Title/Abstract] OR "supportive therapies"[Title/Abstract] OR "systematic desensitization"[Title/Abstract] OR "systematic desensitisation"[Title/Abstract] OR "systemic therapy"[Title/Abstract] OR "systemic therapies"[Title/Abstract] OR "therapeutic community"[Title/Abstract] OR "therapeutic communities"[Title/Abstract] OR "transactional analysis"[Title/Abstract] OR

transference[Title/Abstract] OR transtheoretical[Title/Abstract] OR "validation therapy"[Title/Abstract] OR "validation therapies"[Title/Abstract]) 710433

#6 Search ("Psychotherapy"[Mesh] or "Behavior Therapy"[Mesh] or "Cognitive Therapy"[Mesh] or "Complementary Therapies"[Mesh] or "Psychoanalysis"[Mesh] or "Counseling"[Mesh] or "Hypnosis"[Mesh] or "Association"[Mesh] or "Association Learning"[Mesh]) 391836

#4 Search (#1 or #2 or #3) 188523

#3 Search (schizo*[Title/Abstract] OR psychotic*[Title/Abstract] OR psychosis[Title/Abstract] OR psychoses[Title/Abstract]) 170577

#2 Search "Paranoid Disorders"[Mesh] 3942

#1 Search "Schizophrenia"[Mesh] 96307

Clinicaltrials.gov Searched 12/01/18

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schizophrenia and random and "psychotherapeutic training" = 0
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schizophrenia and random and psychoanalyse = 0
schizophrenia and random and psychoanalysed = 0
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schizophrenia and random and psychodrama = 0
schizophrenia and random and psychodynamic = 2
schizophrenia and random and psychoeducate = 0
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schizophrenia and random and psychological = 105
schizophrenia and random and psychologically = 2
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schizophrenia and random and "psychological therapies" = 8
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schizophrenia and random and "behavior modification" = 146
schizophrenia and random and "behavior regulation" = 0

schizophrenia and random and "behavior therapy" = 146
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schizophrenia and random and "behaviour contracting" = 1
schizophrenia and random and "behaviour modification" = 146
schizophrenia and random and "behaviour regulation" = 0
schizophrenia and random and "behaviour therapy" = 146
schizophrenia and random and "behaviour therapies" = 146
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schizophrenia and random and "cognitive treatments" = 7
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schizophrenia and random and "acceptance and commitment therapy" = 8
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schizophrenia and random and adlerian = 0
schizophrenia and random and "anger control" = 0
schizophrenia and random and "anger management" = 1
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schizophrenia and random and autosuggestion = 0
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schizophrenia and random and "balint group" = 0
schizophrenia and random and befriending = 5
schizophrenia and random and bibliotherapy = 6
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schizophrenia and random and biofeedback = 0
schizophrenia and random and "caregiver support" = 1
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schizophrenia and random and "couples therapies" = 0
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schizophrenia and random and "dance therapy" = 0
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schizophrenia and random and "dream analysis" = 0
schizophrenia and random and eclectic = 0
schizophrenia and random and "emotion focused" = 1
schizophrenia and random and "emotionally focused" = 0
schizophrenia and random and "emotional freedom technique" = 0
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schizophrenia and random and "eye movement desensitization" = 0
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schizophrenia and random and interpersonal = 30
schizophrenia and random and jungian = 0
schizophrenia and random and kleinian = 0
schizophrenia and random and logotherapy = 0
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schizophrenia and random and "marathon group therapy" = 0
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schizophrenia and random and meditation = 8
schizophrenia and random and "mental healing" = 0
schizophrenia and random and "metacognitive therapy" = 4
schizophrenia and random and "metacognitive therapies" = 4
schizophrenia and random and "metacognitive training" = 7
schizophrenia and random and "milieu therapy" = 1
schizophrenia and random and "milieu therapies" = 1
schizophrenia and random and mindfulness = 31
schizophrenia and random and "morita therapy" = 0
schizophrenia and random and "morita therapies" = 0
schizophrenia and random and multimodal = 15

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schizophrenia and random and "music therapies" = 2
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 schizophrenia and random and "support group" = 15
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 schizophrenia and random and transference = 0
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Psychosis and random and bibliotherapy = 27
Psychosis and random and bibliotherapies = 27
Psychosis and random and biofeedback = 84
Psychosis and random and "caregiver support" = 15
Psychosis and random and "client centre" = 0
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Psychosis and random and "color therapy" = 0
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Psychosis and random and "colour therapies" = 0
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Psychosis and random and "conversion therapies" = 0
Psychosis and random and "coping skills" = 138
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Psychosis and random and counselling = 897
Psychosis and random and countertransference = 0
Psychosis and random and "couples therapy" = 16
Psychosis and random and "couples therapies" = 16
Psychosis and random and "covert sensitization" = 0
Psychosis and random and "covert sensitisation" = 0
Psychosis and random and "crisis intervention" = 9
Psychosis and random and "dance therapy" = 0
Psychosis and random and "dance therapies" = 0
Psychosis and random and dialectic = 4
Psychosis and random and dialectical = 38
Psychosis and random and "dream analysis" = 0
Psychosis and random and eclectic = 7
Psychosis and random and "emotion focused" = 13
Psychosis and random and "emotionally focused" = 1
Psychosis and random and "emotional freedom technique" = 6
Psychosis and random and "encounter group therapy" = 0
Psychosis and random and "encounter group therapies" = 0
Psychosis and random and "existential therapy" = 0
Psychosis and random and "existential therapies" = 0
Psychosis and random and "exposure therapy" = 158

Psychosis and random and "exposure therapies" = 158
Psychosis and random and "eye movement desensitization" = 19
Psychosis and random and "eye movement desensitisation" = 19
Psychosis and random and "family intervention" = 32
Psychosis and random and "family interventions" = 32
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Psychosis and random and freudian = 0
Psychosis and random and "gestalt therapy" = 2
Psychosis and random and "gestalt therapies" = 2
Psychosis and random and griefwork = 0
Psychosis and random and "group intervention" = 123
Psychosis and random and "group interventions" = 123
Psychosis and random and "group therapy" = 257
Psychosis and random and "group therapies" = 257
Psychosis and random and "guided imagery" = 30
Psychosis and random and hypnosis = 16
Psychosis and random and hypnotherapy = 16
Psychosis and random and hypnotherapies = 16
Psychosis and random and hypnotizability = 0
Psychosis and random and hypnotisability = 0
Psychosis and random and imagery = 103
Psychosis and random and "implosive therapy" = 2
Psychosis and random and "implosive therapies" = 2
Psychosis and random and "insight therapy" = 0
Psychosis and random and "insight therapies" = 0
Psychosis and random and "integrated psychological therapy" = 3
Psychosis and random and "integrative therapy" = 1
Psychosis and random and "integrative therapies" = 1
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Psychosis and random and jungian = 0
Psychosis and random and kleinian = 0
Psychosis and random and logotherapy = 1
Psychosis and random and logotherapies = 1
Psychosis and random and "marathon group therapy" = 0
Psychosis and random and "marathon group therapies" = 0
Psychosis and random and "marital therapy" = 2
Psychosis and random and "marital therapies" = 2
Psychosis and random and meditation = 140
Psychosis and random and "mental healing" = 0
Psychosis and random and "metacognitive therapy" = 16

Psychosis and random and "metacognitive therapies" = 16
Psychosis and random and "metacognitive training" = 10
Psychosis and random and "milieu therapy" = 6
Psychosis and random and "milieu therapies" = 6
Psychosis and random and mindfulness = 246
Psychosis and random and "morita therapy" = 0
Psychosis and random and "morita therapies" = 0
Psychosis and random and multimodal = 81
Psychosis and random and "music therapy" = 31
Psychosis and random and "music therapies" = 31
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Psychosis and random and "narrative therapies" = 2
Psychosis and random and "nondirective therapy" = 13
Psychosis and random and "nondirective therapies" = 13
Psychosis and random and "object relations" = 2
Psychosis and random and "person centred therapy" = 0
Psychosis and random and "person centred therapies" = 0
Psychosis and random and "person centered therapy" = 0
Psychosis and random and "person centered therapies" = 0
Psychosis and random and "personal construct therapy" = 1
Psychosis and random and "personal construct therapies" = 1
Psychosis and random and "persuasion therapy" = 0
Psychosis and random and "persuasion therapies" = 0
Psychosis and random and "pet therapy" = 6
Psychosis and random and "pet therapies" = 6
Psychosis and random and "play therapy" = 5
Psychosis and random and "play therapies" = 5
Psychosis and random and "primal therapy" = 0
Psychosis and random and "primal therapies" = 0
Psychosis and random and "problem solving" = 339
Psychosis and random and "rational emotive" = 2
Psychosis and random and "reality therapy" = 5
Psychosis and random and "reality therapies" = 5
Psychosis and random and "reciprocal inhibition" = 0
Psychosis and random and rehabilitation = 466
Psychosis and random and rehabilitating = 1
Psychosis and random and "relationship therapy" = 0
Psychosis and random and "relationship therapies" = 0
Psychosis and random and relaxation = 307
Psychosis and random and "reminiscence therapy" = 7
Psychosis and random and "reminiscence therapies" = 7
Psychosis and random and rogerian = 3
Psychosis and random and "role play" = 27
Psychosis and random and "role plays" = 27

Psychosis and random and "role playing" = 21
 Psychosis and random and "self analysis" = 1
 Psychosis and random and "self analysing" = 0
 Psychosis and random and "self esteem" = 142
 Psychosis and random and "sensitivity training" = 0
 Psychosis and random and "sex therapy" = 6
 Psychosis and random and "sex therapies" = 6
 Psychosis and random and "sleep phase chronotherapy" = 0
 Psychosis and random and "sleep phase chronotherapies" = 0
 Psychosis and random and "social skills education" = 0
 Psychosis and random and "social skills training" = 70
 Psychosis and random and "socioenvironmental therapy" = 0
 Psychosis and random and "socioenvironmental therapies" = 0
 Psychosis and random and sociotherapy = 1
 Psychosis and random and sociotherapies = 1
 Psychosis and random and "solution focused" = 4
 Psychosis and random and "stress management" = 55
 Psychosis and random and "support group" = 103
 Psychosis and random and "support groups" = 103
 Psychosis and random and "supportive therapy" = 1553
 Psychosis and random and "supportive therapies" = 1553
 Psychosis and random and "systematic desensitization" = 3
 Psychosis and random and "systematic desensitisation" = 3
 Psychosis and random and "systemic therapy" = 2
 Psychosis and random and "systemic therapies" = 2
 Psychosis and random and "therapeutic community" = 5
 Psychosis and random and "therapeutic communities" = 5
 Psychosis and random and "transactional analysis" = 0
 Psychosis and random and transference = 2
 Psychosis and random and transtheoretical = 13
 Psychosis and random and "validation therapy" = 0
 Psychosis and random and "validation therapies" = 0

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schizo* and random* and psychotherap* = 15
 schizo* and random* and psychoanaly* = 0
 schizo* and random* and psychodrama = 24
 schizo* and random* and psychodynamic = 2
 schizo* and random* and psychoeducat* = 15
 schizo* and random* and psychologic* = 9
 schizo* and random* and abreaction = 0
 schizo* and random* and "acceptance and commitment therapy" = 2

schizo* and random* and “acting out” = 24
schizo* and random* and Adlerian = 0
schizo* and random* and “anger control” = 0
schizo* and random* and “anger management” = 0
schizo* and random* and animal therap* = 0
schizo* and random* and art therap* = 2
schizo* and random* and assertive* training = 0
schizo* and random* and “attention training technique” = 0
schizo* and random* and autogenic training = 0
schizo* and random* and autosuggestion = 0
schizo* and random* and aversion therap* = 0
schizo* and random* and balint group = 0
schizo* and random* and befriending = 4
schizo* and random* and behavior = 25
schizo* and random* and behaviour = 37
schizo* and random* and bibliotherap* = 2
schizo* and random* and biofeedback = 0
schizo* and random* and caregiver support = 1
schizo* and random* and cbt = 22
schizo* and random* and client cent* = 0
schizo* and random* and cognitive behavior = 3
schizo* and random* and cognitive behaviour = 7
schizo* and random* and cognitive intervention* = 0
schizo* and random* and cognitive rehabilit* = 3
schizo* and random* and cognitive remediation = 17
schizo* and random* and cognitive technique* = 1
schizo* and random* and cognitive therap* = 7
schizo* and random* and cognitive treatment* = 3
schizo* and random* and color therap* = 0
schizo* and random* and colour therap* = 0
schizo* and random* and compassionate mind training = 0
schizo* and random* and conjoint therap* = 0
schizo* and random* and contingency management = 1
schizo* and random* and conversational therap* = 0
schizo* and random* and conversion therap* = 0
schizo* and random* and coping skills = 1
schizo* and random* and counsel* = 6
schizo* and random* and countertransference = 0
schizo* and random* and couples therap* = 0
schizo* and random* and covert sensitization = 0
schizo* and random* and crisis intervention = 1
schizo* and random* and dance therap* = 0
schizo* and random* and dialectic* = 0
schizo* and random* and dream analysis = 0

schizo* and random* and eclectic = 0
schizo* and random* and emotion* and focus* = 3
schizo* and random* and emotional freedom technique = 0
schizo* and random* and encounter group therap* = 0
schizo* and random* and existential therap* = 0
schizo* and random* and exposure therap* = 0
schizo* and random* and eye movement desensiti* = 0
schizo* and random* and family intervention* = 2
schizo* and random* and family therap* = 0
schizo* and random* and feminist therap* = 0
schizo* and random* and free association = 0
schizo* and random* and freudian = 0
schizo* and random* and gestalt therap* = 0
schizo* and random* and griefwork = 0
schizo* and random* and group intervention* = 6
schizo* and random* and group therap* = 7
schizo* and random* and guided image* = 0
schizo* and random* and hypnosis = 0
schizo* and random* and hypnotherap* = 0
schizo* and random* and hypnoti* = 0
schizo* and random* and imagery = 1
schizo* and random* and implosive therap* = 0
schizo* and random* and insight therap* = 1
schizo* and random* and integrative therap* = 0
schizo* and random* and interpersonal = 1
schizo* and random* and jungian = 0
schizo* and random* and kleinian = 0
schizo* and random* and logotherap* = 0
schizo* and random* and marathon group therap* = 0
schizo* and random* and marital therap* = 0
schizo* and random* and meditation = 3
schizo* and random* and mental healing = 0
schizo* and random* and metacognitive therap* = 2
schizo* and random* and metacognitive training = 4
schizo* and random* and milieu therap* = 0
schizo* and random* and mindfulness = 87
schizo* and random* and morita therap* = 0
schizo* and random* and multimodal = 1
schizo* and random* and music therap* = 2
schizo* and random* and narrative therap* = 0
schizo* and random* and nondirective therap* = 0
schizo* and random* and object relations = 0
schizo* and random* and person cent* = 0
schizo* and random* and personal construct therap* = 0

schizo* and random* and persuasion therap* = 0
 schizo* and random* and pet therap* = 0
 schizo* and random* and play therap* = 0
 schizo* and random* and primal therap* = 0
 schizo* and random* and problem solving = 6
 schizo* and random* and psychosocial treatment = 2
 schizo* and random* and rational emotive = 0
 schizo* and random* and reality therap* = 0
 schizo* and random* and reciprocal inhibition = 0
 schizo* and random* and rehabilitat* = 15
 schizo* and random* and relationship therap* = 0
 schizo* and random* and relaxation = 4
 schizo* and random* and reminiscence therap* = 0
 schizo* and random* and rogerian = 0
 schizo* and random* and role play* = 2
 schizo* and random* and self analys* = 0
 schizo* and random* and self esteem = 5
 schizo* and random* and sensitivity training = 0
 schizo* and random* and sex therap* = 0
 schizo* and random* and sleep phase chronotherap* = 0
 schizo* and random* and social skills education = 0
 schizo* and random* and social skills training = 9
 schizo* and random* and socioenvironmental therap* = 0
 schizo* and random* and sociotherap* = 0
 schizo* and random* and solution focused = 0
 schizo* and random* and stress management = 3
 schizo* and random* and support group* = 4
 schizo* and random* and supportive therap* = 1
 schizo* and random* and systematic desensiti* = 0
 schizo* and random* and systemic therap* = 0
 schizo* and random* and therapeutic communit* = 0
 schizo* and random* and transactional analysis = 0
 schizo* and random* and transference = 0
 schizo* and random* and transtheoretical = 0
 schizo* and random* and validation therap* = 0
 psycho* and random* and psychotherap* = 318
 psycho* and random* and psychoanaly* = 15
 psycho* and random* and psychodrama = 12
 psycho* and random* and psychodynamic = 40
 psycho* and random* and psychoeducat* = 222
 psycho* and random* and psychologic* = 766
 psycho* and random* and abreaction = 0
 psycho* and random* and "acceptance and commitment therapy" = 34
 psycho* and random* and "acting out" = 12

psycho* and random* and Adlerian = 1
 psycho* and random* and “anger control” = 1
 psycho* and random* and “anger management” = 6
 psycho* and random* and animal therap* = 1
 psycho* and random* and art therap* = 8
 psycho* and random* and assertive* training = 0
 psycho* and random* and “attention training technique” = 0
 psycho* and random* and autogenic training = 30
 psycho* and random* and autosuggestion = 0
 psycho* and random* and aversion therap* = 0
 psycho* and random* and balint group = 0
 psycho* and random* and befriending = 10
 psycho* and random* and behavior = 408
 psycho* and random* and behaviour = 546
 psycho* and random* and bibliotherap* = 13
 psycho* and random* and biofeedback = 13
 psycho* and random* and caregiver support = 2
 psycho* and random* and cbt = 320
 psycho* and random* and client cent* = 15
 psycho* and random* and cognitive behavior = 37
 psycho* and random* and cognitive behaviour = 129
 psycho* and random* and cognitive intervention* = 10
 psycho* and random* and cognitive rehabilit* = 6
 psycho* and random* and cognitive remediation = 16
 psycho* and random* and cognitive technique* = 3
 psycho* and random* and cognitive therap* = 67
 psycho* and random* and cognitive treatment* = 3
 psycho* and random* and color therap* = 0
 psycho* and random* and colour therap* = 0
 psycho* and random* and compassionate mind training = 0
 psycho* and random* and conjoint therap* = 0
 psycho* and random* and contingency management = 9
 psycho* and random* and conversational therap* = 0
 psycho* and random* and conversion therap* = 0
 psycho* and random* and coping skills = 31
 psycho* and random* and counsel* = 177
 psycho* and random* and countertransference = 0
 psycho* and random* and couples therap* = 1
 psycho* and random* and covert sensitization = 0
 psycho* and random* and crisis intervention = 12
 psycho* and random* and dance therap* = 0
 psycho* and random* and dialectic* = 10
 psycho* and random* and dream analysis = 0
 psycho* and random* and eclectic = 5

psycho* and random* and emotion* focus* = 6
psycho* and random* and emotional freedom technique = 1
psycho* and random* and encounter group therap* = 0
psycho* and random* and existential therap* = 1
psycho* and random* and exposure therap* = 20
psycho* and random* and eye movement desensiti* = 16
psycho* and random* and family intervention* = 19
psycho* and random* and family therap* = 16
psycho* and random* and feminist therap* = 0
psycho* and random* and free association = 0
psycho* and random* and freudian = 0
psycho* and random* and gestalt therap* = 0
psycho* and random* and griefwork = 0
psycho* and random* and group intervention* = 64
psycho* and random* and group therap* = 56
psycho* and random* and guided image* = 8
psycho* and random* and hypnosis = 13
psycho* and random* and hypnotherap* = 9
psycho* and random* and hypnoti* = 2
psycho* and random* and imagery = 37
psycho* and random* and implosive therap* = 0
psycho* and random* and insight therap* = 1
psycho* and random* and integrative therap* = 0
psycho* and random* and interpersonal = 80
psycho* and random* and jungian = 0
psycho* and random* and kleinian = 0
psycho* and random* and logotherap* = 0
psycho* and random* and marathon group therap* = 0
psycho* and random* and marital therap* = 0
psycho* and random* and meditation = 49
psycho* and random* and mental healing = 0
psycho* and random* and metacognitive therap* = 11
psycho* and random* and metacognitive training = 3
psycho* and random* and milieu therap* = 0
psycho* and random* and mindfulness = 196
psycho* and random* and morita therap* = 0
psycho* and random* and multimodal = 17
psycho* and random* and music therap* = 8
psycho* and random* and narrative therap* = 3
psycho* and random* and nondirective therap* = 0
psycho* and random* and object relations = 0
psycho* and random* and person cent* = 13
psycho* and random* and personal construct therap* = 0
psycho* and random* and persuasion therap* = 0

psycho* and random* and pet therap* = 0
psycho* and random* and play therap* = 3
psycho* and random* and primal therap* = 0
psycho* and random* and problem solving = 156
psycho* and random* and psychosocial treatment = 9
psycho* and random* and rational emotive = 1
psycho* and random* and reality therap* = 0
psycho* and random* and reciprocal inhibition = 0
psycho* and random* and rehabilitat* = 140
psycho* and random* and relationship therap* = 0
psycho* and random* and relaxation = 147
psycho* and random* and reminiscence therap* = 3
psycho* and random* and rogerian = 0
psycho* and random* and role play* = 32
psycho* and random* and self analys* = 0
psycho* and random* and self esteem = 45
psycho* and random* and sensitivity training = 0
psycho* and random* and sex therap* = 1
psycho* and random* and sleep phase chronotherap* = 0
psycho* and random* and social skills education = 0
psycho* and random* and social skills training = 11
psycho* and random* and socioenvironmental therap* = 0
psycho* and random* and sociotherap* = 1
psycho* and random* and solution focused = 4
psycho* and random* and stress management = 52
psycho* and random* and support group* = 39
psycho* and random* and supportive therap* = 11
psycho* and random* and systematic desensiti* = 0
psycho* and random* and systemic therap* = 2
psycho* and random* and therapeutic communit* = 4
psycho* and random* and transactional analysis = 0
psycho* and random* and transference = 4
psycho* and random* and transtheoretical = 4
psycho* and random* and validation therap* = 0

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schizo* and random* = 38
psycho* and random* = 174