Effectiveness of cognitive behavioral therapy (CBT) for child and adolescent anxiety disorders across different CBT modalities and comparisons: A systematic review and meta-analysis

Anna Lilja Sigurvinsdóttir

Lokaverkefni til MS gráðu í klínískri sálfræði
Sálfræðideild
Heilbriðsvísindasvið
2018

UNIVERSITY OF ICELAND

Effectiveness of cognitive behavioral therapy (CBT) for child and adolescent anxiety disorders across different CBT modalities and comparisons: A systematic review and meta-analysis

Anna Lilja Sigurvinsdóttir

Lokaverkefni til MS gráðu í klínískri sálfræði
Leiðbeinandi: Guðmundur Skarphéðinsson

Sálfræðideild
Heilbrigðisvísindasvið Háskóla Íslands
Júní 2018

Prentun: Háskólaprent

Reykjavík, Ísland, 2018

Þakkir

Ég vil þakka leiðbeinanda mínum, Guðmundi Skarphéðinssyni fyrir alla hans hjálp, stuðning og þolinmæði. Þekking þín og fagleg leiðsögn var ómetanleg á meðan á rannsókninni stóð.

Ég vil einnig þakka Kolbrúnu Björk Jensínudóttur og Karen Dögg Baldvinsdóttur fyrir þeirra þátt í úrvinnslu gagna. Þá á Orri Smárason, sálfræðingur þakkir skilið fyrir sitt framlag.

Þakkir fær maðurinn minn, Pétur Maack, fyrir að styðja mig, hvetja og trúa á mig. Takk fyrir að gera þetta allt að veruleika, þú ert einstakur. Ég vil einnig þakka fjölskyldu minni, sérstaklega börnunum mínum, Daníel Bent, Þorsteini og Védísi. Þið eruð mér hvatning til að gera betur.

Abstract

Cognitive behavioral therapy (CBT) is a first-line treatment of anxiety disorders in children and adolescents. This study conducts a systematic review and meta-analysis of the literature to assess the efficacy of CBT modalities in comparison to control contingencies for pediatric anxiety disorders. Studies were selected if they were randomized controlled trials, if CBT was manualized or modular, alone or in combination with medication. CBT was required to include behavioral treatment, exposure treatment, or cognitive elements. Eligible studies included participants aged 18 years or younger. Seventy-five studies were included, with 3132 CBT participants and 2307 control participants. The overall results indicated that CBT is an effective treatment for childhood anxiety disorders. The results showed that individual-based CBT is superior to wait-list and attention control. Group-based CBT is superior to wait-list control and treatment as usual. Remote-based CBT is superior to attention control and wait-list control. Family-based CBT is superior to treatment as usual, wait-list control, and attention control. Selective serotonin reuptake inhibitors are no more effective than individual-based CBT. Combination treatment is, however, more effective than individual-based CBT. To our best knowledge, no meta-analysis has thus far disentangled the effects of CBT modalities across various comparisons. This meta-analysis hence provides an important update to the literature on the efficacy of CBT for treating anxiety disorders in young people.

Keywords: CBT, anxiety, children, adolescents, meta-analysis, systematic review

Table of contents

Table of Figures

Anxiety disorders are the most common mental disorders in childhood with a lifetime prevalence of 15–20% (Beesdo, Knappe, & Pine, 2009; Costello, Egger, & Angold, 2005; Ezpeleta, Keeler, Erkanli, Costello, & Angold, 2001; Kessler et al., 2005). They are often associated with significant impairment in personal, social, and academic functioning (Pine, Helfinstein, Bar-Haim, Nelson, & Fox, 2008). Children and adolescents with anxiety disorders are at risk of developing new anxiety disorders, suffering depression, and falling into substance abuse (Connolly & Bernstein, 2007). Despite the high prevalence of childhood anxiety, up to 80% of children with anxiety disorders do not receive diagnosis or treatment (Essau, Conradt, & Petermann, 2002; Hansen, Oerbeck, Skirbekk, & Kristensen, 2016). Treatment guidelines recommend cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) as first-line treatments (Connolly & Bernstein, 2007; Socialstyrelsen, 2017). In 1994, Kendall published the first controlled study of the effects of CBT in children with an anxiety disorder (Kendall, 1994). Since then, a growing literature supports the use of individual (e.g. Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008; Kendall et al., 1997; Pina, Silverman, Fuentes, Kurtines, & Weems, 2003), group (Flannery-Schroeder & Kendall, 2000; Manassis et al., 2002; Shortt, Barrett, & Fox, 2001), and family-based (Barrett, Dadds, & Rapee, 1996; Bogels & Siqueland, 2006; Thienemann, Moore, & Tompkins, 2006; Wood, Piacentini, Southam-Gerow, Chu, & Sigman, 2006) CBT for treating anxiety disorders in children. Hence, accumulating evidence over the past decade indicates that CBT provides effective treatment for childhood anxiety (Cartwright-Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004; Higa-McMillan, Francis, Rith-Najarian, & Chorpita, 2016).

Indeed, CBT is a highly effective treatment for anxiety disorders in children regardless of the format and is more effective than wait-list control (WL) (James, James, Cowdrey, Soler, & Choke, 2013; Wang, Whiteside, Sim, & et al., 2017). However, WL studies include a number of potential performance biases such as the effects of expectancy and therapeutic alliance (Furukawa et al., 2014). A more robust (although more expensive) control for performance bias is a placebo control (e.g., pill placebo or psychotherapy placebo [attention control]). CBT has not been found to be a significantly more effective treatment than attention control. Thus, whether CBT and attention control are equally effective remains inconclusive, as only eight placebo-controlled studies were found by James et al. (2013).

Kazdin (2008) suggested that future treatment of childhood anxiety would involve untraditional interventions with a possible large reach, including minimal, brief, and low-cost treatments. Research conducted along these lines has focused on bibliotherapy (e.g Cobham, 2012) and the computer or Internet-based delivery of CBT (e.g Khanna & Kendall, 2010; Spence, Holmes, March, & Lipp, 2006). Many obstacles are present in treating children: family financial status, the amount of time required to access treatment, and the social stigma associated with seeking psychological help (Jorm & Wright, 2007). Remote-based CBT for anxiety disorders in children may therefore increase clients' self-efficacy by requiring them to take more responsibility for their progress in therapy.

Previous meta-analyses have examined treatment for pediatric anxiety disorders delivered by CBT, medication, or a combination of CBT and medication (see e.g Wang et al., 2017). However, none has disentangled the effects of CBT modalities such as regular, group, family, or remote CBT across various comparisons (e.g., WL and attention control). Our meta-analysis allows us to compare different effect sizes based on modes and comparisons, including attention control. This comparison is important given that patients' expectations for improvement alone can lead to significant symptom changes (Wampold, Minami, Tierney, Baskin, & Bhati, 2005). This meta-analysis also compares remote-based CBT with individual-based CBT.

Aim

The aim of this systematic review is to assess the effects of CBT for child and adolescent anxiety disorders (social anxiety, separation anxiety, generalized anxiety, panic disorders with/without agoraphobia) across CBT modalities and comparisons by conducting a meta-analysis. The review aims to address the acute outcome of individual, group, family, and/or remote CBT for anxiety disorders in children and adolescents. The differences in CBT mode are also analyzed.

Research questions

- What is the effect of different CBT treatments (individual, group, family, remote-based) across different controls?
- Is CBT effective compared with WL, attention control, treatment as usual (TAU), SSRIs, and a combined treatment of SSRIs and CBT?

- Regarding head-to-head trials, a) is standard CBT, in any application, efficacious compared with remote-based CBT? And b) what is the superior mode of CBT delivery (individually delivered, group, or family format)?

Method

Types of studies

Studies were selected if they were randomized controlled trials (RCTs). Trials with a cluster-randomized design were also eligible for inclusion. We excluded studies that solely had trauma-related disorders, specific (simple) phobias, selective mutism, and obsessive-compulsive disorder.

Population

Eligible studies included participants aged 18 years or younger at the time of treatment or considered to be "children and adolescents" as defined by the studies. Participants needed to have a primary diagnosis of anxiety disorders (social phobia, separation anxiety, generalized anxiety, panic disorders with or without agoraphobia), established by clinical assessment or standardized diagnostic interview.

Intervention

Studies were included if (i) CBT was manualized or modular, alone or in combination with medication; and (ii) if studies included behavioral treatment, exposure treatment, or cognitive elements. A description of the specific treatment at each stage of at least nine sessions provided by trained therapists under regular supervision was required. The choice of nine sessions of therapy complies with all other major published protocols on this topic. CBT could be delivered individually, with family or parental involvement, in a group, or remote-based. Family/parental CBT could include psycho-education for parents or teaching co-therapists skills.

CBT needed to be administered according to standard principles to assist the child to 1) recognize feelings of anxiety and the somatic reaction to anxiety, 2) clarify thoughts in situations that provoke anxiety, 3) develop coping skills (e.g., modifying anxiety-related thoughts), and 4) respond to behavioral training strategies with exposure *in vivo* or by imagination.

Types of comparison

The comparison conditions can be categorized as into the following four groups:

1) No treatment (WL)

The definition of no treatment is when patients do not receive any treatment or special care during the pre-and post-test intervals. A typical example is a waiting list.

2) Drug placebo

3) Non-CBT active control

Non-CBT active control can include psycho-education for family members, anxiety management/relaxation treatment, therapist support, peer support, group support, attention, or any other non-CBT-module.

4) Active treatment or a combination of two or more active treatments (e.g., CBT and SSRIs).

Active treatment can be pharmacotherapy, other forms of CBT such as brief, intensive, or group CBT, a combination of standard and remote-delivered CBT, or another module or other type of non-CBT active control.

Types of outcome measures

Primary outcomes

1) Remission

Existence or absence of child/adolescence anxiety disorder, diagnosed with valid and reliable interviews for DSM or ICD, including:

- Anxiety Disorder Interview Schedule for Parents (ADIS-P) (Silverman, 1987)
- Anxiety Disorder Interview Schedule for Children (ADIS-C) (Silverman, 1987)
- Diagnostic Interview Schedule for Children, Adolescents, and Parents (DISCAP) (Holland & Dadds, 1995)

The diagnostic interview must be executed independently by the treatment team. Non-specific rating scales such as the Clinical Global Impression scale - Severity (CGI-S) (Guy,

1976) or another measure of remission were included in the absence of a diagnostic interview at post-treatment. CGI-S is a seven-item scale (from 0 = illness to 6 = extremely severe) used to assess clinical severity. Consistent with previous studies, we used a score of 0 or 1 (no illness or mild illness) for remission.

2) Acceptability

We determined acceptability by the number of participants who showed up at follow-up (post-treatment).

Secondary outcomes

3) Response

The treatment response in our protocol published in PROSPERO was determined from the improvement item of the Clinical Global Impression scale - Improvement (CGI-I) scale (a seven-point scale ranging from 0 = very much worse to 6 = very much improved) (Guy, 1976). However, due to the lack of data among the included studies, the treatment response was not used in our meta-analysis. Only 21 studies reported a treatment response measure.

4) Continuous measure

The reduction in anxiety symptoms can be measured by using psychometrically robust measures of anxiety symptoms that yield symptom scores on continuous scales. These scales are self-reported or completed by a parent/guardian or an independent evaluator. In this study, measurement by an independent evaluator was preferred followed by the child/adolescent report and parent report. The most validated, best recognized, or most frequently used measure was included in the review. The following scales were used to measure anxiety symptoms:

- The Pediatric Anxiety Rating Scale (PARS) (The Research Units On Pediatric Psychopharmacology Anxiety Study, 2002)
- Revised Children's Manifest Anxiety Scale (RCMAS) (Reynolds & Richmond, 1985)
- Social Anxiety Scale for Adolescents (SAS-A) (La Greca, 1998)
- Fear Survey for Children Revised (FSSC-R) (Ollendick & King, 1998)
- Social Phobia and Anxiety Inventory for Children (SPAI-C) (Beidel, Turner, & Morris, 1995)

- SCAS (Spence Child Anxiety Scale, Child and Parent Versions) (Spence, 1997)
- Child Behavior Checklist (CBCL) (Achenbach, 1991)
- State-Trait Anxiety Inventory for Children (STAI-C) (Spielberger, Edwards, Montuori, & Lushene, 1973)
- Screen for Child Anxiety Related Emotional Disorders (SCARED) (Birmaher, 1999)
- Revised Children´s Anxiety and Depression Scale (Chorpita, Moffitt, & Gray, 2005).

The critical issue is the extent to which these measures discriminate between clinical and non-clinical levels of anxiety. Seligman and Ollendick (2011) found a large effect size for CBCL, RCMAS, and STAI-C in discriminating children and adolescents with anxiety disorders from controls and assessing those with externalizing disorders, but not affective disorders. These scales are also moderately sensitive to treatment gains. The outcome was measured by the change between pre-treatment and post-treatment assessment. Where change data for these were not available, the endpoint difference was used.

Time

We include immediate (acute) outcome studies with a time period of 9 to 16 weeks.

Search method for identification of studies

As we used the meta-analysis by James et al. (2013) and Rooksby, Elouafkaoui, Humphris, Clarkson, and Freeman (2015), the search for research before 2013 was not necessary for our meta-analysis. We identified all studies that might describe the RCTs of CBT for anxiety disorders in children and adolescents from the Cochrane Central Register of Controlled Trials (CENTRAL) and PubMed (2013-present) via electronic search. No limits were applied for language. The search strategies were adapted to each database.

We inspected the reference lists of all selected studies for more published reports and citations of unpublished research. The authors of registered trials and other experts in the field were asked for their knowledge of other studies, unpublished as well as published. Where appropriate, the first author of the included studies was contacted for clarification or additional information. We included unpublished, raw datasets from completed trials if available.

Selection of studies

By using inclusion criteria and the whole reports of studies, three reviewers (ALS [Anna Lilja Sigurvinsdóttir], KBJ [Kolbrún Björk Jensínudóttir], and KDB [Karen Dögg Baldvinsdóttir]) reviewed each study and independently selected trials eligible for inclusion

(all abstracts and full reports were scanned by a minimum of two reviewers). All articles that met our inclusion criteria were obtained and the full text was independently assessed. Disagreements were resolved through discussion or using a fourth reviewer (GS [Guðmundur Skarphéðinsson]).

Data extraction and management

Five reviewers (ALS, KBJ [Kolbrún Björk Jensínudótir], KDB [Karen Dögg Baldvinsdóttir], OS [Orri Smárason], and GS [Gudmundur Skarphedinsson]) performed the data extraction by using a data extraction form. This included the verification of study eligibility, sample size, age (mean, standard deviation [SD], and range), age of the onset of the anxiety disorder (mean and SD), comorbidity (as a whole and individual disorders), exclusion criteria, comorbid disorders (e.g., major depressive disorder, autism spectrum disorder [ASD]), anxiety treatment, diagnostic criteria used, diagnostic interview used, length of treatment, active agent and dose, control condition, outcome, reported statistics, length of follow-up, and number of participants lost and excluded. GS checked any discrepancies in the data.

Assessment of risk of bias in included studies

Three reviewers (ALS, OS, and GS) independently applied the Cochrane Collaboration's "Risk of bias" tool to each trial.

Data analysis

We used a random effects model, which is usually more conservative than a model with fixed effects. In a random effects model, the true effect can vary from individual studies depending on various factors such as slight variations in the intervention, the characteristics of the participants, and the reliability of measurement.

Assessment of heterogeneity

Heterogeneity between studies, providing data on the same comparison, was examined formally by using I-squared (I^2). When evidence of marked heterogeneity ($I^2 > 50\%$) existed, data were not pooled. When there was moderate heterogeneity and a sufficient number of studies, data pooling was carried out by using a random effects model. If marked heterogeneity was evident and there were sufficient studies in each group, we presented subgroup results to examine if these differences could be explained through study differences.

Assessment of reporting biases

If sufficient studies were available for inclusion in the review, we tested for publication bias by using scatterplots of the treatment effects estimated against the sample size of each study (funnel plots).

Data synthesis

RCTs

The primary outcome comprised dichotomous outcome (remission vs. not remission). We used an odds ratio (OR) together with a 95% confidence interval (CI) at post-treatment. For the continuous measure, we used the standardized mean difference (SMD) (Hedge's d).

Subgroup/sensitivity analyses

We performed subgroup analyses/indirect comparisons for the following comparisons:

- Active control / Psychotherapy placebo vs. wait-list
- Active control / Psychotherapy placebo vs. pill placebo
- Active control / Psychotherapy placebo vs. SRI/SSRIs
- Pill placebo vs. wait-list

Trials including anxiety disorders (AD) and ASD vs. trials including only AD.

Results

Description of included studies

The electronic database search in addition to the systematic reviews of James et al. (2013) and Rooksby et al. (2015) returned 2051 references, 1715 of which remained after the removal of duplicates (Fig. 1). Of these, 1379 were discarded after screening abstracts and titles. Altogether, the full text of 336 studies were screened for eligibility. However, 262 studies were excluded. Exclusion reasons are listed in Fig. 1. The most frequent reason for exclusion was adult population (62 studies). In total, 74 studies were included, with 3132 CBT participants and 2307 control participants

Characteristics of included studies

The characteristics of the included studies are provided in Table S1 (supplement A). Fifty-six (75.7%) studies targeted more than one anxiety disorder, 12 (16.2%) targeted social

anxiety disorder, three (4.1%) studies targeted separation anxiety disorder, and one (1.4%) generalized anxiety disorders.

The CBT treatment form in the included studies was individual-based (68.9%), family-based (10.8%), group-based (24.3%), and remote (16.2%), including one bibliotherapy, one computer-based CBT, one online therapy without therapist assistance, and seven online therapies with therapist assistance. Forty-six studies had WL, 12 attention control, six TAU, two SSRIs, and two combinations of SSRIs and CBT. The number and length of treatment sessions were between 8 and 32 sessions and 5 and 16 weeks.

Standardized diagnostic interviews were used for all studies (100%). The most frequently used diagnostic assessment was ADIS-C (Silverman & Albano, 1996). Of the 62 studies using ADIS, 46 used both the child and the parent versions (Table S1). Fifteen studies used other standardized diagnostic interviews (Table S1). The children in these studies met the criteria in the *Diagnostic and Statistical Manual of Mental Health Disorders* (4^{th} ed.; DSM-IV) for principal anxiety disorders.

Characteristics of participants

The characteristics of participants are provided in Table S2. The age of the children included ranged from 3 to 18 years. The mean age (SD) across studies was 10.8 (1.6) years. Seven studies only included participants with AD and ASD (Chalfant, Rapee, & Carroll, 2007; Conaughton, Donovan, & March, 2017; Storch et al., 2013; Storch, Lewin, et al., 2015; White et al., 2013; Wood et al., 2009; Wood et al., 2015). Five of them showed the significant benefit of CBT over controls. One study compared CBT with remote-based CBT, where the CBT module was more efficient than WL. Forty-two studies (53.8%) did not report a comorbidity rate (see Table S2, supplement B).

Subgroup/sensitivity analyses

Sensitivity analyses were calculated to make an indirect comparison. Subgroup analyses was non-significant for individual-based CBT, indicating that the effects of treatment do not vary across subgroups. Group-based CBT had a significant subgroup analysis, indicating that the effect of CBT varies across subgroups. The subgroup analysis for family-based CBT was significant, showing that the effects of treatment vary across subgroups. Remote-based CBT had an insignificant subgroup analysis, demonstrating no variation in the effects of treatment across subgroups.

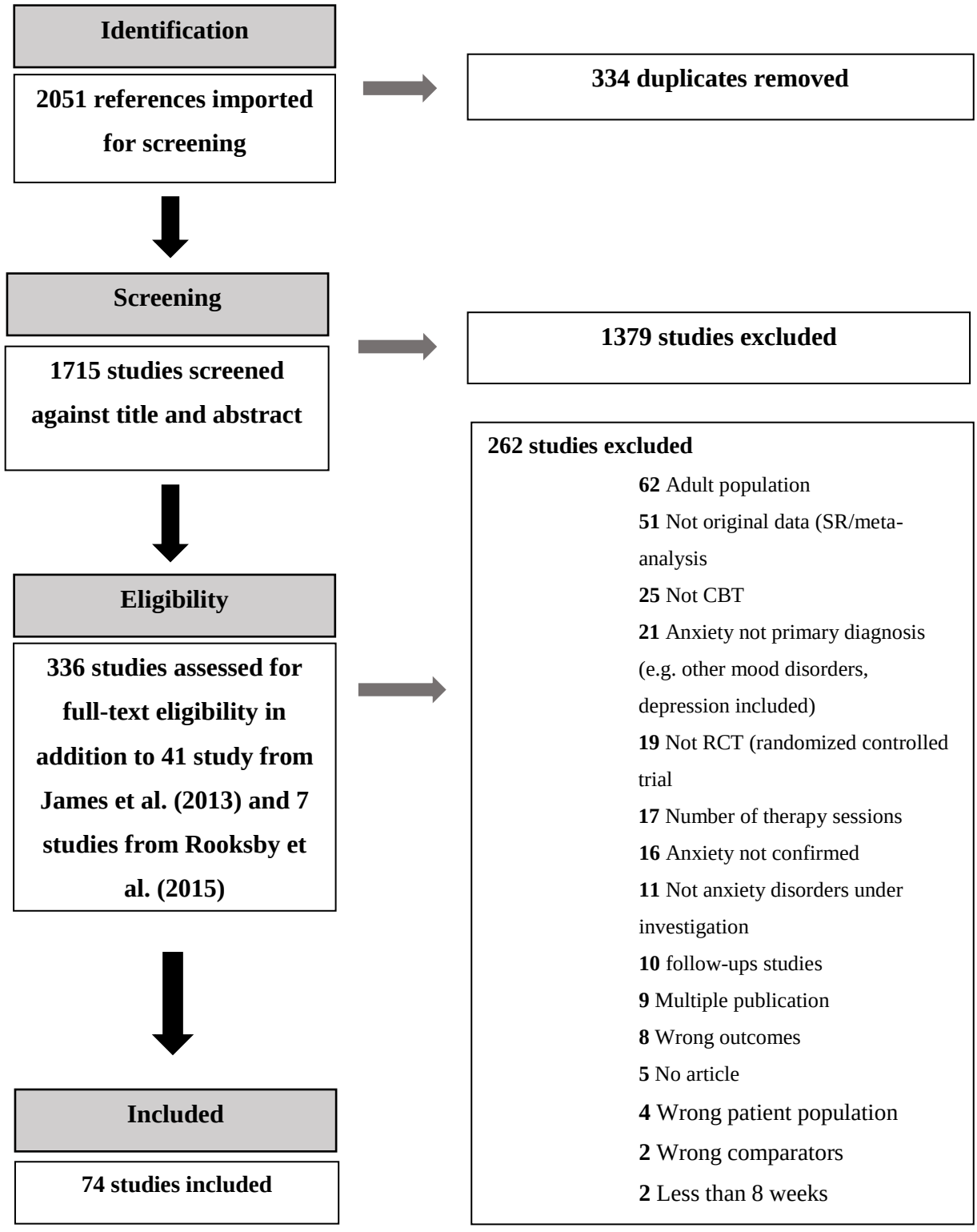


Figure 1. PRISMA flow chart

Risk of bias within studies

The risk of bias across domains was analyzed by focusing on random allocation, allocation concealment, blinding, attrition, and reporting. We did not exclude trials from the meta-analysis on the basis of the risk of a biased assessment. The results of the assessment suggested a low risk of bias in random allocation, with 64.9% of studies rated having a low risk of bias. Thirty-two percent of studies were rated as a low risk of bias in allocation concealment and 63.5% of studies in blinding of the outcome were judged to be low risk. The same shares were 64.9% in attrition and 73% in reporting. Performance bias was present in all trials due to the lack of the blinding of participants and personnel, leading to the possibility of a high degree of performance bias (Fig. 2). Seven trials had a low risk of bias in all bias assessments besides performance bias (supplement C).

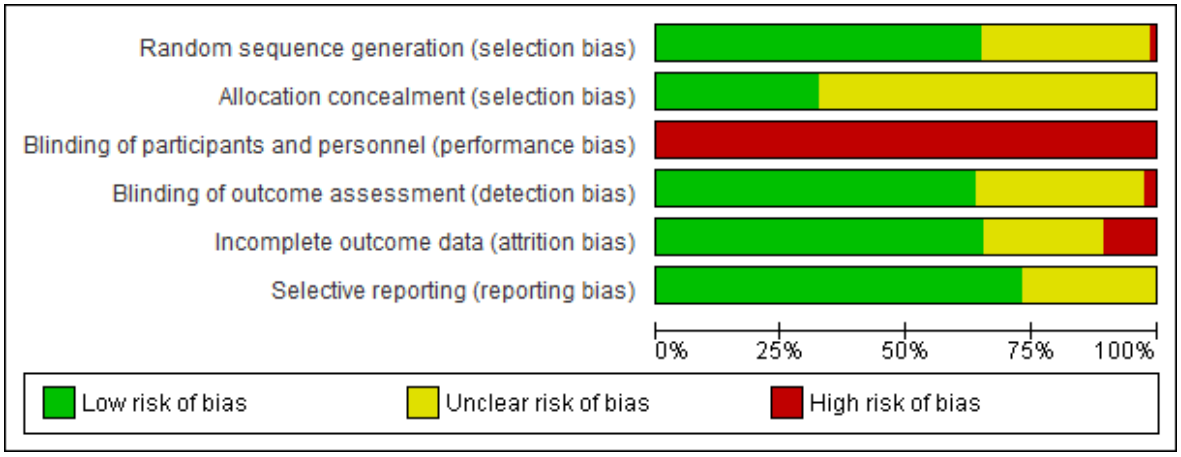


Figure 2.Risk of bias graph: Judgements about each risk of bias item presented as percentages across all included studies.

Primary outcome: Remission

Is there a difference between CBT modalities and control group?

CBT modalities versus WL

Individual-based CBT versus WL

The analysis of studies of the differences between individual-based CBT and WL favored the former, demonstrating a significant benefit compared with WL (OR = 9.53, [95% CI, 5.48 to 16.58]). There was insignificant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 3.

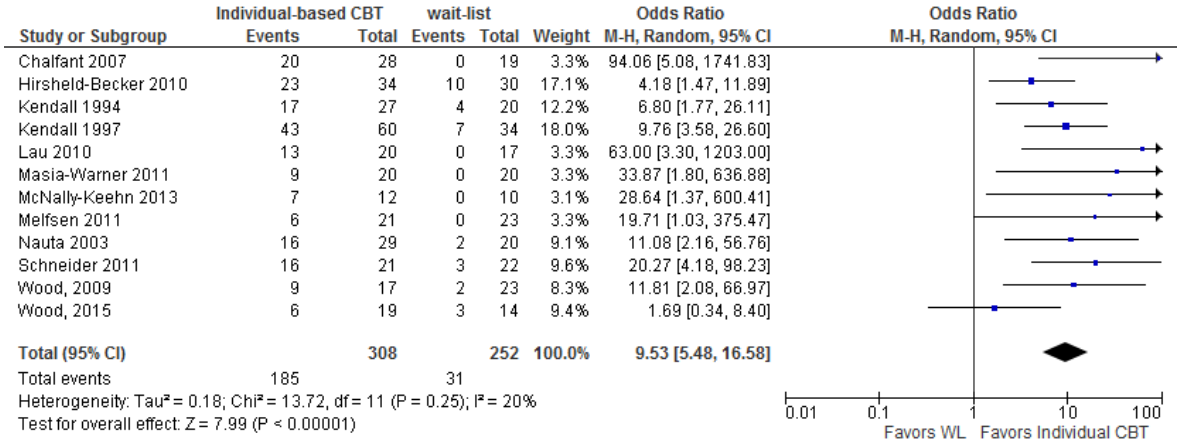


Figure 3. Forest plot: Individual-based CBT vs. wait-list control

Group-based CBT versus WL

The analysis of studies of the differences between group-based CBT and WL favored the former, demonstrating a significant benefit compared with WL (OR = 9.86, [95% CI, 3.97 to 24.48]). There was significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 4.

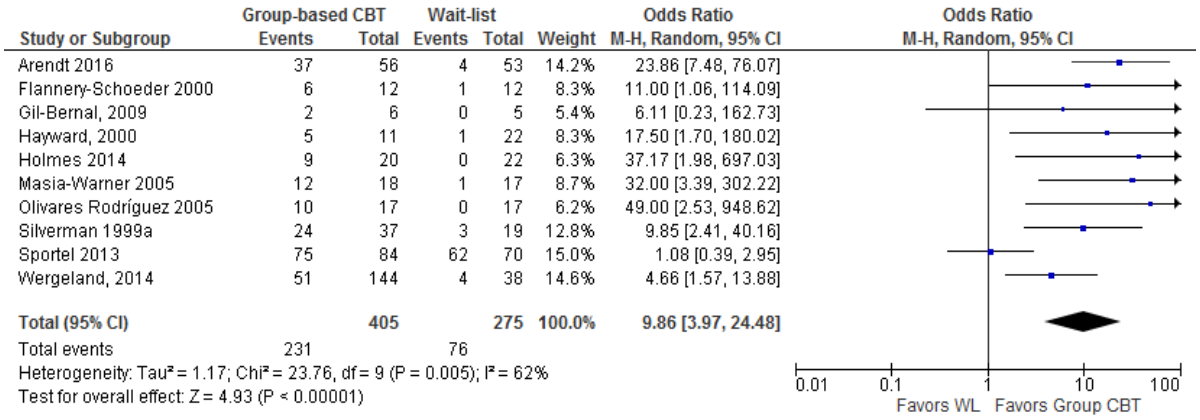


Figure 4. Forest plot: Group-based CBT vs. wait-list control

Family-based CBT versus WL

The analysis of studies of the differences between family-based CBT and WL favored the former, demonstrating a significant benefit compared with WL (OR = 26.21, [95% CI, 6.62 to 103.79]). There was insignificant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 5.

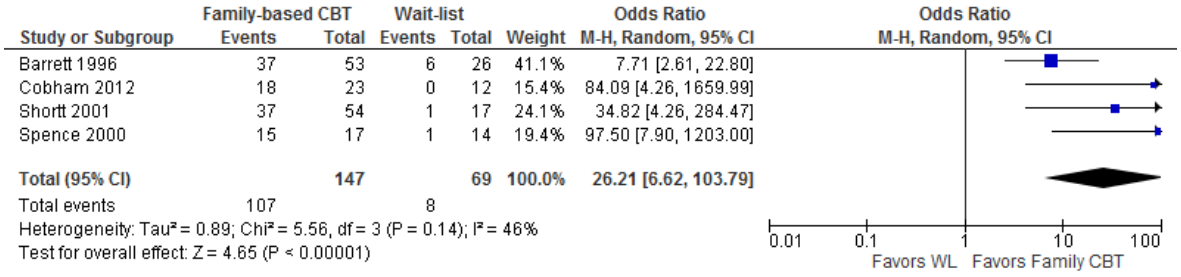


Figure 5. Forest plot: Family-based CBT vs. wait-list control

Remote-CBT versus WL

The analysis of studies of the differences between remote-based CBT and WL favored the former, demonstrating a significant benefit compared with WL (OR = 6.14, [95% CI, 2.97 to 12.71]). There was insignificant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 6.

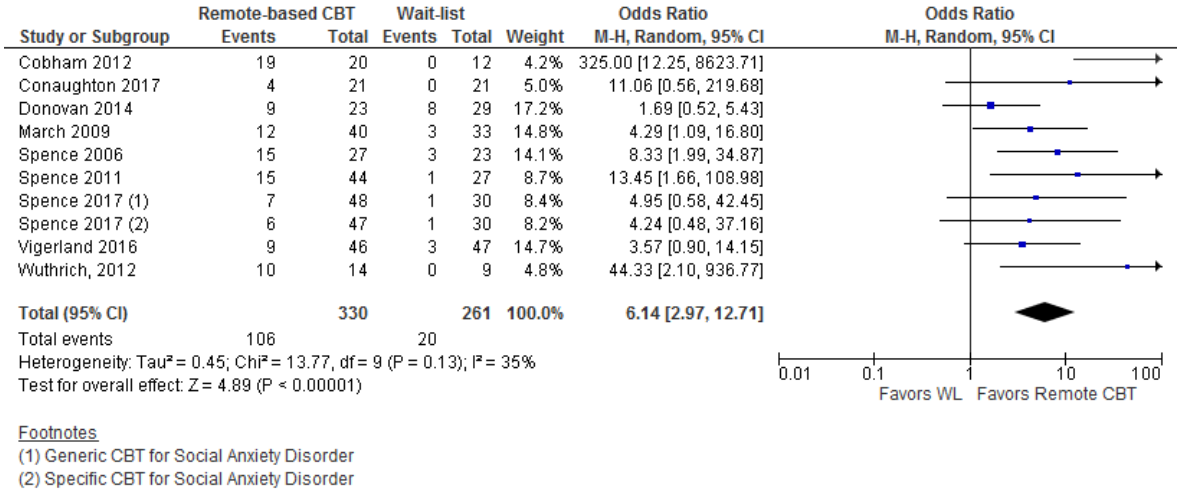


Figure 6. Forest plot: Remote-based CBT vs. wait-list control

CBT modalities versus TAU

Only two CBT modalities (group-based CBT and individual-based CBT) had TAU comparison in the meta-analysis.

Individual-based CBT versus TAU

The analysis of studies of the differences between individual-based CBT and TAU demonstrated no significant benefit of individual-based CBT compared with TAU (OR = 3.70, [95% CI, 0.84 to 16.40]). There was significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 7.

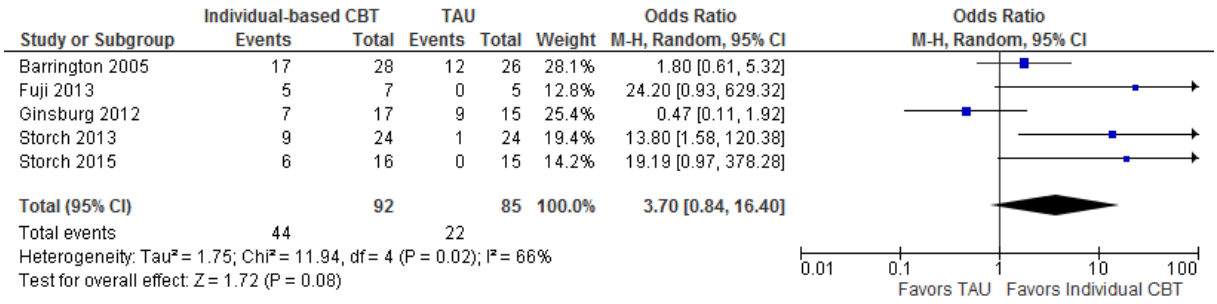


Figure 7. Forest plot: Individual-based CBT vs. TAU

Group-based CBT versus TAU

The analysis of studies of the differences between group-based CBT and TAU favored the former, demonstrating a significant benefit compared with TAU (OR = 5.73, [95% CI, 2.30 to 14.28] Z= 3.74). However, only one study (Storch, Lewin, et al., 2015) compared group-based CBT with TAU. Therefore, the estimated effect size and heterogeneity could not be calculated.

CBT modalities versus attention control

Individual-based CBT versus attention control

The analysis of studies of the differences between individual-based CBT and attention control favored the former, demonstrating a significant benefit compared with attention control (OR = 2.55, [95% CI, 1.35 to 4.93]). There was no evidence of significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 8.

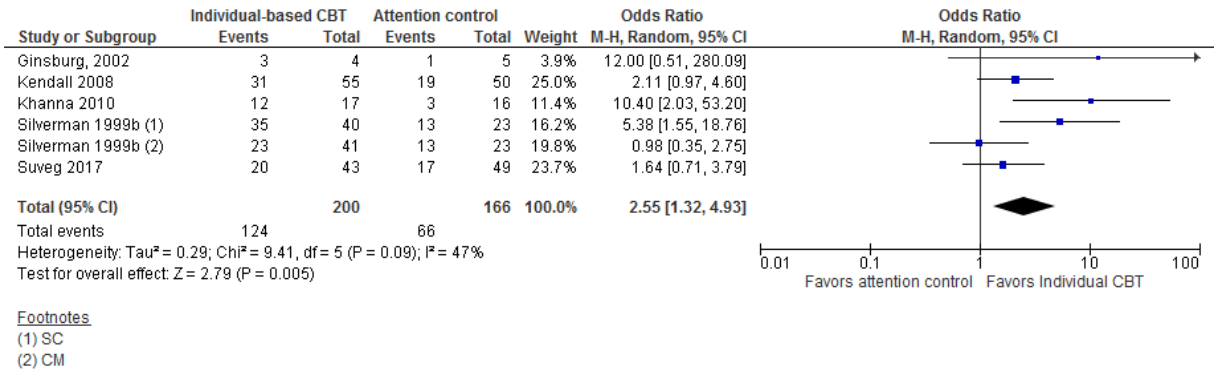


Figure 8. Forest plot: Individual-based CBT vs. attention control

Group-based CBT versus attention control

The analysis of studies of the differences between group-based CBT and attention control demonstrated no significant benefit of group-based CBT compared with attention control (OR = 0.42, [95% CI, 0.14 to 1.23]). There was no evidence of significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 9.

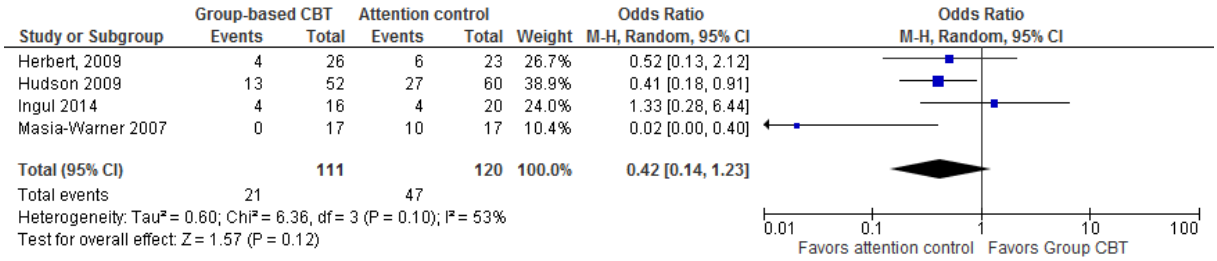


Figure 9. Forest plot: Group-based CBT vs. attention control

Family-based CBT versus attention control

The analysis of studies of the differences between family-based CBT and attention control favored the former but demonstrated no significant difference in efficacy (OR = 1.88, [95% CI, 0.87 to 4.09]). Only one study (Kendall et al., 2008) compared family-based CBT with attention control. Therefore, the estimated effect size and heterogeneity could not be calculated.

Remote CBT versus attention control

The analysis of studies of the differences between remote-based CBT and attention control favored the former, demonstrating a significant benefit compared with attention control (OR = 18.78, [95% CI, 3.18 to 110.84]). However, only one study (Khanna & Kendall, 2010) compared remote-based CBT with attention control. Therefore, the estimated effect size and heterogeneity could not be calculated.

CBT modalities versus SSRIs

Only one CBT modality (individual-based CBT) had an SSRI comparison in the meta-analysis. The analysis of studies of the differences between individual-based CBT and SSRIs demonstrated no significant benefit of one group over the other (OR = 1.01, [95% CI, 1.11 to 2.19]). However, as only one study (Walkup et al., 2008) compared individual-based CBT with SSRIs, the estimated effect size and heterogeneity could not be calculated.

CBT modalities versus combination of CBT and SSRIs

Only one CBT modality (individual-based CBT) had a combination comparison in the meta-analysis. The analysis of studies of the differences between individual-based CBT and combination favored the combination, demonstrating its significant benefit compared with individual-based CBT (OR = 0.39, [95% CI, 0.24 to 0.64]). However, as only one study (Walkup et al., 2008) compared individual-based CBT with SSRIs, the estimated effect size and heterogeneity could not be calculated.

What is the superior mode of CBT delivery (head-to-head comparison)?

Only individual-based CBT was compared with group-based CBT, family-based CBT, and remote-based CBT in the meta-analysis.

Individual-based CBT versus group-based CBT

The analysis of four trials demonstrated no significant benefit of individual-based CBT compared with group-based CBT (OR = 2.73 [95% CI, 0.98 to 7.61]). There was no evidence of significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 10.

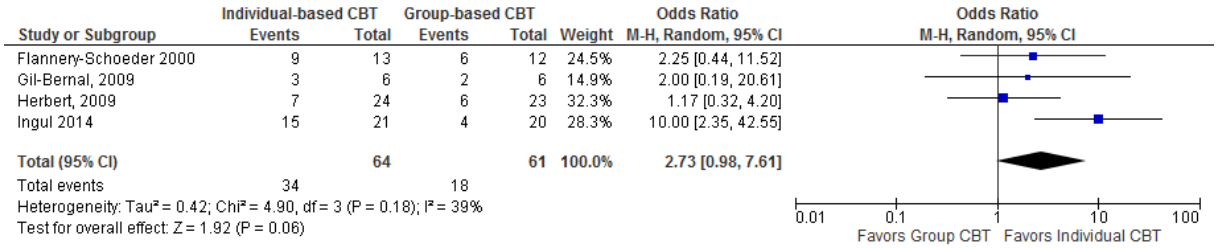


Figure 10. Forest plot: Individual-based CBT vs. Group-based CBT

Individual-based CBT versus family-based CBT

The analysis of four trials demonstrated no significant benefit of one treatment over the other (OR = 0.75 [95% CI, 0.44 to 1.26]). There was no evidence of significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 11.

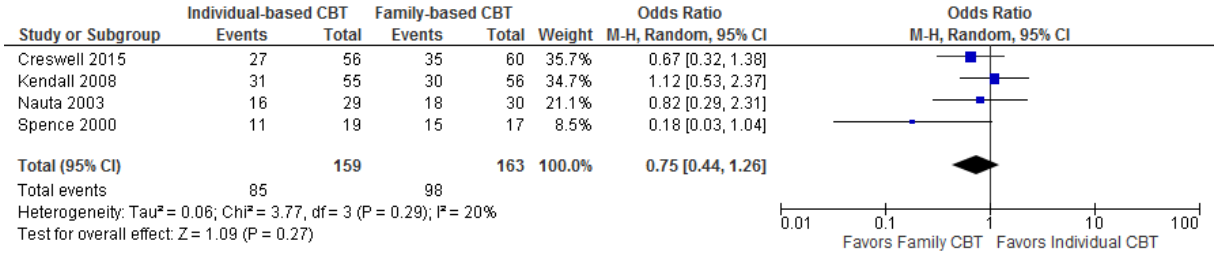


Figure 11. Forest plot: Individual-based CBT vs. Family-based CBT

Individual-based CBT versus remote-based CBT

The analysis of three trials demonstrated no significant benefit of one treatment over the other (OR = 0.91 [95% CI, 0.47 to 1.74]). There was no evidence of significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 12.

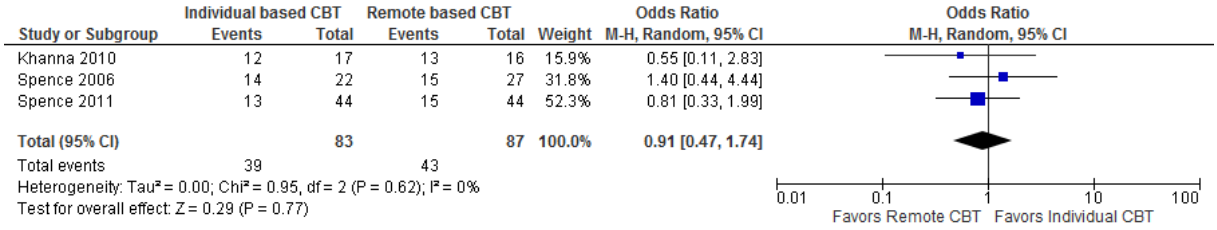


Figure 12. Forest plot: Individual-based CBT vs. Remote-based CBT

Studies of children/ adolescents with ASD

Seven studies of children/adolescents with ASD were included in the meta-analysis to examine remission from anxiety disorders. One study did not report data for remission post-treatment (White et al., 2013).

The analyses comparing individual-based CBT with WL demonstrated the significant benefit of the former (OR = 9.54 [95% CI, 1.14 to 79.71]). There was significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 13.

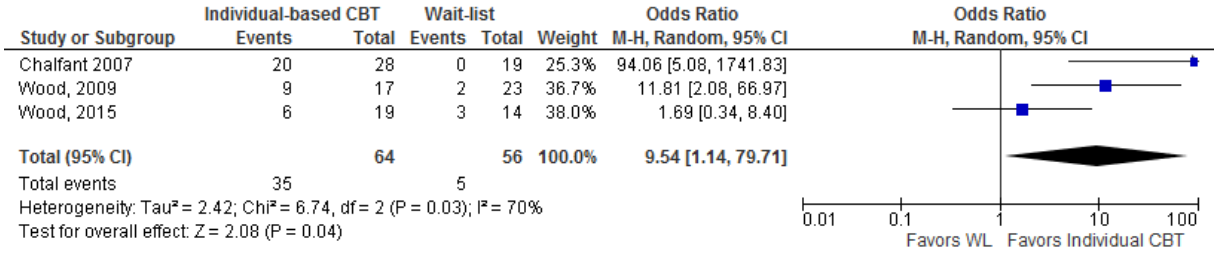


Figure 13. Forest plot. ASD: Individual-based CBT vs. WL

The analyses comparing individual-based CBT with TAU demonstrated the significant benefit of the former (OR = 15.47 [95% CI, 2.68 to 89.20]). There was no evidence of significant heterogeneity between trials. The effect size estimates and forest plots of the individual studies can be seen in Fig. 14.

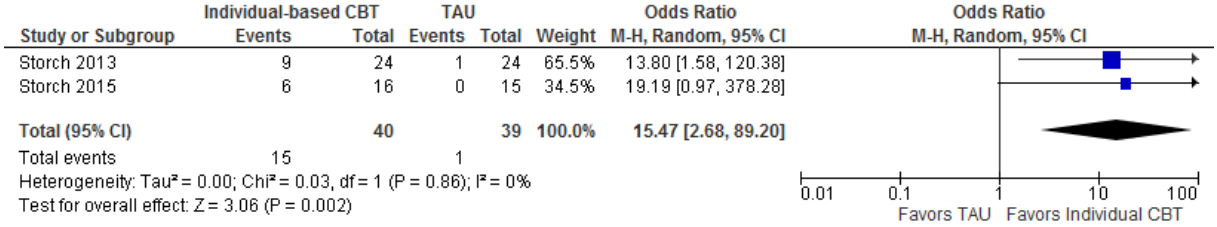


Figure 14. Forest plot. ASD: Individual-based CBT vs. TAU

The analysis of studies of the differences between remote-based CBT and WL demonstrated no significant benefit (OR = 11.06, [95% CI, 0.56 to 219.68]). However, only one study (Conaughton et al., 2017) compared remote-based CBT with WL. Therefore, the estimated effect size and heterogeneity could not be calculated.

Attrition was not greater in the control groups in comparison to CBT modalities, except in the comparison between SSRIs and individual-based CBT. The meta-analysis of one trial demonstrated an increased risk of drop-out with SSRIs compared with individual-based CBT (OR = 0.14 [95% CI, 0.05 to 0.42]). The results of attrition (supplement D) show that attrition is greater in group-based CBT in comparison to TAU and in remote-based CBT in comparison to WL.

The meta-analysis of the continuous measure was in line with the results of the primary outcome, except in group-based CBT vs. attention control (SMD of 1.30 [95% CI, -0.28 to 2.88]) and in individual-based CBT vs. TAU (SMD of 0.59 [95% CI, -0.10 to 1.28]), vs. attention control (SMD of 0.19 [95% CI, -0.14 to 0.52]), and vs. SSRIs (SMD of -0.16 [95% CI, -0.40 to 0.07]). The results of the continuous measure are shown in supplement E.

Discussion

In the past two decades, there has been rapid growth in RCTs for CBT for anxiety disorders in children and adolescents. To our best knowledge, no meta-analysis has disentangled the effects of CBT modalities (including remote CBT) across various comparisons. This meta-analysis provides an important update to the literature of the efficacy of CBT for treating anxiety disorders in children and adolescents. Building on the systematic search in the previous meta-analyses by James et al. (2013) and Rooksby et al. (2015), we reviewed the full text of 386 studies and included 75 RCT studies with 5633 participants in the meta-analysis.

Our findings showed that CBT has mixed beneficial effects based on different control conditions. The ORs for individual-based CBT demonstrated significant beneficial outcomes in remission for childhood anxiety compared with WL and attention control. Individual-based CBT is not superior to TAU. Compared with attention control, children receiving individual-based CBT were 2.6 times more likely to be free from their anxiety. James et al. (2013) and Wang et al. (2017) did not show more benefit of individual-based CBT over attention control in their meta-analyses. The reason may be the inclusion of studies with no confirmed anxiety disorders (e.g Dadds, Spence, Holland, Barrett, & Laurens, 1997; Sung et al., 2011). Individual-based CBT appears to be as effective as SSRIs, but the combination therapy is more effective than either treatment alone.

As evidence of comparative efficacy is limited to one study (Walkup et al., 2008) in this meta-analysis, further research is essential to guide practice in treating pediatric anxiety disorders. It is crucial for several studies to compare CBT with SSRIs and CBT with the combination therapy to investigate the comparative efficacy of these treatment forms as well as estimate what treatment is suitable for the patient based on his or her unique characteristics.

Group-based CBT was also significantly beneficial compared with WL and TAU but showed no benefits over attention control. Family-based CBT was 21.6 times more effective than WL. This is especially compelling given that the analysis was only based on three studies. Family-based CBT showed a significant benefit over attention control in the reduction of anxiety among children and adolescents. Remote CBT was also beneficial compared with WL and attention control in terms of remission at post-treatment. Children receiving remote CBT were almost seven times more likely to be free from anxiety disorders

than WL children and 18.7 times more likely to be free from anxiety disorders than children in the attention control group. The meta-analysis of the continuous measure is in line with the primary outcome, except in the comparisons of group-based CBT vs. attention control and individual-based CBT vs. attention control and SSRIs.

Our results indicate that individual-based CBT is neither more nor less beneficial for treating childhood anxiety disorders than remote-based CBT. However, only three studies were included, so the question on the superiority or equivalence remains inconclusive. Individual-based CBT was not superior to family-based CBT. In comparison to group-based CBT, our results show that individual-based CBT is not a superior treatment form than group-based CBT. These results are in line with previous meta-analyses showing no differences between individual-based CBT and group-based CBT (In-Albon & Schneider, 2007; Kodal et al., 2018; Silverman, Pina, & Viswesvaran, 2008).

As with most psychotherapy outcome studies, the lack of the blinding of participants and personnel causes an elevated risk of performance bias. The overall risk of bias in the meta-analysis was judged to be moderate to high for this reason.

Strengths and limitations

The present meta-analysis extends the work of James et al. (2013), Rooksby et al. (2015), and other previous meta-analysis (e.gWang et al., 2017) in several important ways. First, the present study compared CBT modalities with attention control. Second, this meta-analysis compared remote-based CBT with individual-based CBT. Third, the current results expand on earlier research by providing evidence that CBT and variants of CBT can be effective (e.g James et al., 2013).

One of the limitations of this review was the lack of studies that compared SSRIs with combination therapy. Only one study was included (Walkup et al., 2008) in this regard. The CBT used (Coping Cat) was shortened from 16 weeks to 12 weeks. A more enhanced CBT might have been more beneficial. Furthermore, we did not conduct a meta-regression, which might be appropriate to analyze which factor influences CBT efficacy.

Conclusion

The overall results indicated that CBT is an effective treatment for childhood anxiety disorders both against the weak WL comparison and the stronger TAU and attention control.

Reference

Achenbach, T. M. (1991). *Program Manual for the Child Behavior Checklist 4-18 profile. .* Berlington, VT: University Associates in Psychiatry. .

Afshari, A., Neshat-Doost, H. T., Maracy, M. R., Ahmady, M. K., & Amiri, S. (2014). The effective comparison between emotion-focused cognitive behavioral group therapy and cognitive behavioral group therapy in children with separation anxiety disorder. *Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences, 19*(3), 221-227.

Arendt, K., Thastum, M., & Hougaard, E. (2016). Efficacy of a Danish version of the Cool Kids program: a randomized wait-list controlled trial. *Acta Psychiatrica Scandinavica, 133*(2), 109-121. doi:doi:10.1111/acps.12448

Barrett, P. M., Dadds, M. R., & Rapee, R. M. (1996). Family treatment of childhood anxiety: a controlled trial. *J Consult Clin Psychol, 64*(2), 333-342.

Barrington, J., Prior, M., Richardson, M., & Allen, K. (2005). Effectiveness of CBT versus standard treatment for childhood anxiety disorders in a community clinic setting. *Behaviour Change, 22*(1), 29-43.

Beesdo, K., Knappe, S., & Pine, D. S. (2009). Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. *Psychiatry Clin North Am, 32*(3), 483-524. doi:10.1016/j.psc.2009.06.002

Beidel, D. C., Turner, S. M., & Morris, T. L. (1995). A new inventory to assess childhood social anxiety and phobia: The Social and Anxiety Inventory for Children. . *Psychological Assessment, 7*(1), 73-79. doi:http://dx.doi.org/10.1037/1040-3590.7.1.73

Birmaher, B. (1999). *Screen for Child Anxiety Related Emotional Disorders (SCARED). .* Pittsburgh, PA.: Western Psychiatric Institute and Clinic.

Bogels, S. M., & Siqueland, L. (2006). Family cognitive behavioral therapy for children and adolescents with clinical anxiety disorders. *J Am Acad Child Adolesc Psychiatry, 45*(2), 134-141. doi:10.1097/01.chi.0000190467.01072.ee

Britton, J. C., Bar-Haim, Y., Clementi, M. A., Sankin, L. S., Chen, G., Shechner, T., . . . Pine, D. S. (2013). Training-associated changes and stability of attention bias in youth: Implications for Attention Bias Modification Treatment for pediatric anxiety. *Developmental Cognitive Neuroscience, 4*, 52-64. doi:https://doi.org/10.1016/j.dcn.2012.11.001

Cartwright-Hatton, S., Roberts, C., Chitsabesan, P., Fothergill, C., & Harrington, R. (2004). Systematic review of the efficacy of cognitive behaviour therapies for childhood and adolescent anxiety disorders. *Br J Clin Psychol, 43*(Pt 4), 421-436. doi:10.1348/0144665042388928

Chalfant, A. M., Rapee, R., & Carroll, L. (2007). Treating Anxiety Disorders in Children with High Functioning Autism Spectrum Disorders: A Controlled Trial. *Journal of Autism and Developmental Disorders, 37*(10), 1842-1857. doi:10.1007/s10803-006-0318-4

Chavira, D. A., Drahota, A., Garland, A. F., Roesch, S., Garcia, M., & Stein, M. B. (2014). Feasibility of two modes of treatment delivery for child anxiety in primary care. *Behav Res Ther, 60*, 60-66. doi:https://doi.org/10.1016/j.brat.2014.06.010

Chiu, A. W., Langer, D. A., McLeod, B. D., Har, K., Drahota, A., Galla, B. M., . . . Wood, J. J. (2013). Effectiveness of Modular CBT for Child Anxiety in Elementary Schools. *School psychology quarterly : the official journal of the Division of School Psychology, American Psychological Association, 28*(2), 141-153. doi:10.1037/spq0000017

Chorpita, B. F., Moffitt, C. E., & Gray, J. (2005). Psychometric properties of the Revised Child Anxiety and Depression Scale in a clinical sample. *Behav Res Ther, 43*(3), 309-322. doi:10.1016/j.brat.2004.02.004

Cobham, V. E. (2012). Do anxiety-disordered children need to come into the clinic for efficacious treatment? *Journal of Consulting and Clinical Psychology., 80*(3), 465-476. doi:http://dx.doi.org/10.1037/a0028205

Conaughton, R. J., Donovan, C. L., & March, S. (2017). Efficacy of an internet-based CBT program for children with comorbid High Functioning Autism Spectrum Disorder and anxiety: A randomised controlled trial. *Journal of Affective Disorders, 218*, 260-268. doi:10.1016/j.jad.2017.04.032

Connolly, S. D., & Bernstein, G. A. (2007). Practice Parameter for the Assessment and Treatment of Children and Adolescents With Anxiety Disorders. *Journal of the American Academy of Child & Adolescent Psychiatry, 46*(2), 267-283. doi:10.1097/01.chi.0000246070.23695.06

Costello, E. J., Egger, H., & Angold, A. (2005). 10-year research update review: the epidemiology of child and adolescent psychiatric disorders: I. Methods and public health burden. *J Am Acad Child Adolesc Psychiatry, 44*(10), 972-986. doi:10.1097/01.chi.0000172552.41596.6f

Creswell, C., Cruddace, S., Gerry, S., Gitau, R., McIntosh, E., Mollison, J., . . . Cooper, P. J. (2015). Treatment of childhood anxiety disorders in the context of maternal anxiety disorder: A randomised controlled trial and economic analysis. *Health Technology Assessment, 19*(28).

Dadds, M., Spence, S. H., Holland, D. E., Barrett, P. M., & Laurens, K. R. (1997). Prevention and early intervention for anxiety disorders: A controlled trial. *J Consult Clin Psychol, 65*(4), 627-635. doi:doi.org/10.1037/0022-006X.65.4.627

Donovan, C. L., & March, S. (2014). Online CBT for preschool anxiety disorders: A randomised control trial. *Behav Res Ther, 58*, 24-35. doi:https://doi.org/10.1016/j.brat.2014.05.001

Esbjørn, B. H., Reinholdt-Dunne, M. L., Nielsen, S. K., Smith, A. C., Breinholst, S., & Leth, I. (2015). Exploring the Effect of Case Formulation Driven CBT for Children with Anxiety Disorders: A Feasibility Study. *Behavioural and Cognitive Psychotherapy, 43*(1), 20-30. doi:10.1017/S1352465813000702

Essau, C. A., Conradt, J., & Petermann, F. (2002). Course and outcome of anxiety disorders in adolescents. *Journal of Anxiety Disorders, 16*(1), 67-81. doi:https://doi.org/10.1016/S0887-6185(01)00091-3

Ezpeleta, L., Keeler, G., Erkanli, A., Costello, E. J., & Angold, A. (2001). Epidemiology of psychiatric disability in childhood and adolescence. *J Child Psychol Psychiatry, 42*(7), 901-914.

Flannery-Schroeder, E. C., & Kendall, P. C. (2000). Group and Individual Cognitive-Behavioral Treatments for Youth with Anxiety Disorders: A Randomized Clinical Trial. *Cognitive Therapy and Research, 24*(3), 251-278. doi:10.1023/a:1005500219286

Fujii, C., Renno, P., McLeod, B. D., Lin, C. E., Decker, K., Zielinski, K., & Wood, J. J. (2013). Intensive Cognitive Behavioral Therapy for Anxiety Disorders in School-aged Children with Autism: A Preliminary Comparison with Treatment-as-Usual. *School Mental Health, 5*(1), 25-37. doi:10.1007/s12310-012-9090-0

Furukawa, T. A., Noma, H., Caldwell, D. M., Honyashiki, M., Shinohara, K., Imai, H., . . . Churchill, R. (2014). Waiting list may be a nocebo condition in psychotherapy trials: a contribution from network meta-analysis. *Acta Psychiatrica Scandinavica, 130*(3), 181-192. doi:doi:10.1111/acps.12275

Gaesser, A. H., & Karan, O. C. (2017). A Randomized Controlled Comparison of Emotional Freedom Technique and Cognitive-Behavioral Therapy to Reduce Adolescent Anxiety: A Pilot Study. *The Journal of Alternative and Complementary Medicine, 23*(2), 102-108. doi:10.1089/acm.2015.0316

Galla, B. M., Wood, J. J., Chiu, A. W., Langer, D. A., Jacobs, J., Ifekwunigwe, M., & Larkins, C. (2012). One Year Follow-up to Modular Cognitive Behavioral Therapy for the Treatment of Pediatric Anxiety Disorders in an Elementary School Setting. *Child Psychiatry & Human Development, 43*(2), 219-226. doi:10.1007/s10578-011-0258-x

Garcia-Lopez, L. J., Díaz-Castela, M. d. M., Muela-Martinez, J. A., & Espinosa-Fernandez, L. (2014). Can parent training for parents with high levels of expressed emotion have a positive effect on their child's social anxiety improvement? *Journal of Anxiety Disorders, 28*(8), 812-822. doi:https://doi.org/10.1016/j.janxdis.2014.09.001

García-López, L., Olivares, J., Turner, S. M., Beidel, D. C., Albano, A. M., & Sánchez-Meca, J. (2002). Result at long-term among three psychological treatments for adolescents with

generalized social phobia (II): Clinical significance and effect size. *Psicología Conductual, 10*(2), 371-385.
Gil-Bernal, F., & Hernández-Guzmán, L. (2009). Tratamiento cognitivo-conductual para ninos mexicanos con fobia social. *Anuario de Psicología, 40*(1), 89-104.
Ginsburg, G. S., Becker, K. D., Drazdowski, T. K., & Tein, J.-Y. (2012). Treating Anxiety Disorders in Inner City Schools: Results from a Pilot Randomized Controlled Trial Comparing CBT and Usual Care. *Child & youth care forum, 41*(1), 1-19. doi:10.1007/s10566-011-9156-4
Ginsburg, G. S., & Drake, K. L. (2002). School-Based Treatment for Anxious African-American Adolescents: A Controlled Pilot Study. *Journal of the American Academy of Child & Adolescent Psychiatry, 41*(7), 768-775. doi:10.1097/00004583-200207000-00007
Guy, W. (1976). *Clinical global impresions. ECDEU Assessment Manual for Psychopharmacology.* . Rockville: NIMH.
Hancock, K. M., Swain, J., Hainsworth, C. J., Dixon, A. L., Koo, S., & Munro, K. (2016). Acceptance and Commitment Therapy versus Cognitive Behavior Therapy for Children With Anxiety: Outcomes of a Randomized Controlled Trial. *Journal of Clinical Child and Adolescent Psychology, 47*(2), 296-311. doi:10.1080/15374416.2015.1110822
Hansen, B. H., Oerbeck, B., Skirbekk, B., & Kristensen, H. (2016). Non-obsessive–compulsive anxiety disorders in child and adolescent mental health services – Are they underdiagnosed, and how accurate is referral information? *Nordic Journal of Psychiatry, 70*(2), 133-139. doi:10.3109/08039488.2015.1061053
Hayward, C., Varady, S., Albano, A. M., Thienemann, M., Henderson, L., & Schatzberg, A. F. (2000). Cognitive-Behavioral Group Therapy for Social Phobia in Female Adolescents: Results of a Pilot Study. *Journal of the American Academy of Child & Adolescent Psychiatry, 39*(6), 721-726. doi:10.1097/00004583-200006000-00010
Herbert, J. D., Gaudiano, B. A., Rheingold, A. A., Moitra, E., Myers, V. H., Dalrymple, K. L., & Brandsma, L. L. (2009). Cognitive Behavior Therapy for Generalized Social Anxiety Disorder in Adolescents: A Randomized Controlled Trial. *Journal of Anxiety Disorders, 23*(2), 167-177. doi:10.1016/j.janxdis.2008.06.004
Higa-McMillan, C. K., Francis, S. E., Rith-Najarian, L., & Chorpita, B. F. (2016). Evidence Base Update: 50 Years of Research on Treatment for Child and Adolescent Anxiety. *J Clin Child Adolesc Psychol, 45*(2), 91-113. doi:10.1080/15374416.2015.1046177
Hirshfeld-Becker, D. R., Masek, B., Henin, A., Blakely, L. R., Pollock-Wurman, R. A., McQuade, J., . . . Biederman, J. (2010). Gognitive behavioral therapy for 4-to 7-year-old children with anxiety disorders: A randomized clinical trial. *Journal of Consulting and Clinical Psychology., 78*(4), 498-510.
Holland, D., & Dadds, M. (1995). *Diagnostic Interview Schedule for Children, Adolescents and Parents.* . Brisbane: Griffith University.
Holmes, M. C., Donovan, C. L., Farrell, L. J., & March, S. (2014). The efficacy of a group-based, disorder-specific treatment program for childhood GAD – A randomized controlled trial. *Behav Res Ther, 61*, 122-135. doi:https://doi.org/10.1016/j.brat.2014.08.002
Hudson, J. L., Newall, C., Rapee, R. M., Lyneham, H. J., Schniering, C. C., Wuthrich, V. M., . . . Gar, N. S. (2014). The Impact of Brief Parental Anxiety Management on Child Anxiety Treatment Outcomes: A Controlled Trial. *Journal of Clinical Child and Adolescent Psychology, 43*(3), 370-380. doi:10.1080/15374416.2013.807734
Hudson, J. L., Rapee, R. M., Deveney, C., Schniering, C. A., Lyneham, H. J., & Bovopoulos, N. (2009). Cognitive-behavioral treatment versus an active control for children and adolescents with anxiety disorders: a randomized trial. *J Am Acad Child Adolesc Psychiatry, 48*(5), 533-544. doi:10.1097/CHI.0b013e31819c2401
In-Albon, T., & Schneider, S. (2007). Psychotherapy of childhood anxiety disorders: A meta-analysis. *Psychother Psychosom, 76*(1), 15-24. doi:10.1159/000096361
Ingul, J. M., Aune, T., & Nordahl, H. M. (2014). A Randomized Controlled Trial of Individual Cognitive Therapy, Group Cognitive Behaviour Therapy and Attentional Placebo for Adolescent Social Phobia. *Psychother Psychosom, 83*(1), 54-61.

James, James, Cowdrey, Soler, & Choke. (2013). Cognitive behavioural therapy for anxiety disorders in children and adolescents. *Cochrane Database Syst Rev*(6), Cd004690. doi:10.1002/14651858.CD004690.pub3

Jorm, A. F., & Wright, A. (2007). Beliefs of Young People and Their Parents about the Effectiveness of Interventions for Mental Disorders. *Australian & New Zealand Journal of Psychiatry, 41*(8), 656-666. doi:10.1080/00048670701449179

Kazdin, A. E. (2008). Evidence-based treatments and delivery of psychological services: Shifting our emphases to increase impact. *Psychological Services 5*(3), 201-215.

Kendall, P. C. (1994). Treating anxiety disorders in children: Results of a randomized clinical trial. . *J Consult Clin Psychol, 62*(1), 100-110. doi:http://dx.doi.org/10.1037/0022-006X.62.1.100

Kendall, P. C., Hudson, J. L., Gosch, E., Flannery-Schroeder, E., & Suveg, C. (2008). Cognitive-behavioral therapy for anxiety disordered youth: a randomized clinical trial evaluating child and family modalities. *J Consult Clin Psychol, 76*(2), 282-297. doi:10.1037/0022-006x.76.2.282

Kendall, P. C., Philip, C., Flannery-Schroeder, E., Panichelli-Mindel, S. M., Southam-Gerow, M., Henin, A., & Warman, M. (1997). Therapy for youths with anxiety disorders: A second randomized trial. . *Journal of Consulting and Clinical Psychology., 65*(3), 366-380.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry, 62*(6), 593-602. doi:10.1001/archpsyc.62.6.593

Khanna, M. S., & Kendall, P. C. (2010). Computer-assisted cognitive behavioral therapy for child anxiety: Results of a randomized clinical trial. *Journal of Consulting and Clinical Psychology., 78*(5), 737-745. doi:http://dx.doi.org/10.1037/a0019739

Kodal, A., Fjermestad, K., Bjelland, I., Gjestad, R., Öst, L.-G., Bjaastad, J. F., . . . Wergeland, G. J. (2018). Long-term effectiveness of cognitive behavioral therapy for youth with anxiety disorders. *Journal of Anxiety Disorders, 53*, 58-67. doi:https://doi.org/10.1016/j.janxdis.2017.11.003

La Greca, A. (1998). Manual for Social Anxiety Scales for Children and Adolescents. . Coral Gables, FI.: University of Miami.

Lau, W.-y., Chan, C. K.-y., Li, J. C.-h., & Au, T. K.-f. (2010). Effectiveness of group cognitive-behavioral treatment for childhood anxiety in community clinics. *Behav Res Ther, 48*(11), 1067-1077. doi:https://doi.org/10.1016/j.brat.2010.07.007

Manassis, K., Mendlowitz, S. L., Scapillato, D., Avery, D., Fiksenbaum, L., Freire, M., . . . Owens, M. (2002). Group and individual cognitive-behavioral therapy for childhood anxiety disorders: a randomized trial. *J Am Acad Child Adolesc Psychiatry, 41*(12), 1423-1430. doi:10.1097/00004583-200212000-00013

March, S., Spence, S. H., & Donovan, C. L. (2009). The Efficacy of an Internet-Based Cognitive-Behavioral Therapy Intervention for Child Anxiety Disorders. *Journal of Pediatric Psychology, 34*(5), 474-487. doi:10.1093/jpepsy/jsn099

Masia-Warner, C., Colognori, D., Kim, R. E., Reigada, L. C., Klein, R. G., Browner-Elhanan, K. J., . . . Benkov, K. (2011). Cognitive-behavioral treatment of persistent functional somatic complaints and pediatric anxiety: an initial controlled trial. *Depression and Anxiety, 28*(7), 551-559. doi:doi:10.1002/da.20821

Masia-Warner, C., Fisher, P. H., Shrout, P. E., Rathor, S., & Klein, R. G. (2007). Treating adolescents with social anxiety disorder in school: an attention control trial. *Journal of Child Psychology and Psychiatry, 48*(7), 676-686. doi:doi:10.1111/j.1469-7610.2007.01737.x

Masia-Warner, C., Klein, R. G., Dent, H. C., Fisher, P. H., Alvir, J., Marie Albano, A., & Guardino, M. (2005). School-Based Intervention for Adolescents with Social Anxiety Disorder: Results of a Controlled Study. *J Abnorm Child Psychol, 33*(6), 707-722. doi:10.1007/s10802-005-7649-z

McNally Keehn, R. H., Lincoln, A. J., Brown, M. Z., & Chavira, D. A. (2013). The Coping Cat Program for Children with Anxiety and Autism Spectrum Disorder: A Pilot Randomized Controlled Trial. *Journal of Autism and Developmental Disorders, 43*(1), 57-67. doi:10.1007/s10803-012-1541-9

Melfsen, S., Kühnemund, M., Schwieger, J., Warnke, A., Stadler, C., Poustka, F., & Stangier, U. (2011). Cognitive behavioral therapy of socially phobic children focusing on cognition: a randomised wait-list control study. *Child and Adolescent Psychiatry and Mental Health, 5*(1), 5. doi:10.1186/1753-2000-5-5

Mendlowitz, S. L., Manassis, K., Bradley, S., Scapillato, D., Miezitis, S., & Shaw, B. E. (1999). Cognitive‐Behavioral Group Treatments in Childhood Anxiety Disorders: The Role of Parental Involvement. *Journal of the American Academy of Child & Adolescent Psychiatry, 38*(10), 1223-1229. doi:10.1097/00004583-199910000-00010

Mitchell, J. H., Newall, C., Broeren, S., & Hudson, J. L. (2013). The role of perfectionism in cognitive behaviour therapy outcomes for clinically anxious children. *Behav Res Ther, 51*(9), 547-554. doi:https://doi.org/10.1016/j.brat.2013.05.015

Muris, P., Meesters, C., & van Melick, M. (2002). Treatment of childhood anxiety disorders: a preliminary comparison between cognitive-behavioral group therapy and a psychological placebo intervention. *Journal of Behavior Therapy and Experimental Psychiatry, 33*(3), 143-158. doi:https://doi.org/10.1016/S0005-7916(02)00025-3

Nauta, M. H., Scholing, A., Emmelkamp, P. M. G., & Minderaa, R. B. (2003). Cognitive-Behavioral Therapy for Children With Anxiety Disorders in a Clinical Setting: No Additional Effect of a Cognitive Parent Training. *Journal of the American Academy of Child & Adolescent Psychiatry, 42*(11), 1270-1278. doi:10.1097/01.chi.0000085752.71002.93

Olivares, J., García-López, L., Beidel, D. C., Turner, S. M., Albano, A. M., & Hidalgo, M. D. (2002). Results at long-term among three psychological treatments for adolescents with generalized social phobia (I): Statistical significance. *Psicología Conductual Revista Internacional de Psicología Clínica de la Salud 10*(1), 147-164.

Olivares Rodríguez, J., Alcázar, A. I. R., & Piqueras Rodríguez, J. A. (2005). Detección temprana y tratamiento de adolescentes con fobia social generalizada. *Psicothema, 17*(1), 1-18.

Ollendick, T. H., & King, N. J. (1998). Empirically supported treatments for children with phobic and anxiety disorders: current status. *J Clin Child Psychol, 27*(2), 156-167. doi:10.1207/s15374424jccp2702_3

Pina, A. A., Silverman, W. K., Fuentes, R. M., Kurtines, W. M., & Weems, C. F. (2003). Exposure-based cognitive-behavioral treatment for phobic and anxiety disorders: treatment effects and maintenance for Hispanic/Latino relative to European-American youths. *J Am Acad Child Adolesc Psychiatry, 42*(10), 1179-1187. doi:10.1097/00004583-200310000-00008

Pine, D. S., Helfinstein, S. M., Bar-Haim, Y., Nelson, E., & Fox, N. A. (2008). Challenges in Developing Novel Treatments for Childhood Disorders: Lessons from Research on Anxiety. *Neuropsychopharmacology, 34*, 213. doi:10.1038/npp.2008.113

Reynolds, C. R., & Richmond, B. O. (1985). *Revised Children´s Manifest Anxiety Scale (RCAMS) Manual*. Los Angeles, CA.: Western Psychological Services.

Rooksby, M., Elouafkaoui, P., Humphris, G., Clarkson, J., & Freeman, R. (2015). Internet-assisted delivery of cognitive behavioural therapy (CBT) for childhood anxiety: systematic review and meta-analysis. *Journal of Anxiety Disorders, 29*, 83-92. doi:10.1016/j.janxdis.2014.11.006

Sánchez-García, R., & Olivares, J. (2009). Effectiveness of a program for early detection/intervention in children/adolescents with generalized social phobia. *Anales de Psicología, 25*(2), 241-249.

Schneider, S., Blatter-Meunier, J., Herren, C., Adornetto, C., In-Albon, T., & Lavallee, K. (2011). Disorder-specific cognitive-behavioral therapy for separation anxiety disorder in young children: a randomized waiting-list-controlled trial. *Psychother Psychosom, 80*(4), 206-215. doi:https://dx.doi.org/10.1159/000323444

Schneider, S., Blatter-Meunier, J., Herren, C., In-Albon, T., Adornetto, C., Meyer, A., & Lavallee, K. (2013). The efficacy of a family-based cognitive-behavioral treatment for separation anxiety disorder in children aged 8-13: a randomized comparison with a general anxiety program*81*(5), 932-940. Retrieved from http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/541/CN-01000541/frame.html doi:10.1037/a0032678

Seligman, L. D., & Ollendick, T. H. (2011). Cognitive-Behavioral Therapy for Anxiety Disorders in Youth. *Child and Adolescent Psychiatric Clinics, 20*(2), 217-238. doi:10.1016/j.chc.2011.01.003

Sevi Tok, E. S., Arkar, H., & Bildik, T. (2016). The effectiveness of cognitive bahavioral therapy, medication, or combined treatment for childhood anxiety disorders. *Turkish Journal of Psychiatry, 27*(2), 1-8.

Shechner, T., Rimon-Chakir, A., Britton, J. C., Lotan, D., Apter, A., Bliese, P. D., . . . Bar-Haim, Y. (2014). Attention Bias Modification Treatment Augmenting Effects on Cognitive Behavioral Therapy in Children With Anxiety: Randomized Controlled Trial. *J Am Acad Child Adolesc Psychiatry, 53*(1), 61-71. doi:10.1016/j.jaac.2013.09.016

Shortt, A. L., Barrett, P. M., & Fox, T. L. (2001). Evaluating the FRIENDS program: a cognitive-behavioral group treatment for anxious children and their parents. *J Clin Child Psychol, 30*(4), 525-535. doi:10.1207/s15374424jccp3004_09

Silk, J. S., Sheeber, L., Tan, P. Z., Ladouceur, C. D., Forbes, E. E., McMakin, D. L., . . . Ryan, N. D. (2013). "You can do it!": The role of parental encouragement of bravery in child anxiety treatment. *Journal of Anxiety Disorders, 27*(5), 439-446. doi:https://doi.org/10.1016/j.janxdis.2013.06.002

Silk, J. S., Tan, P. Z., Ladouceur, C. D., Meller, S., Siegle, G. J., McMakin, D. L., . . . Ryan, N. D. (2016). A Randomized Clinical Trial Comparing Individual Cognitive Behavioral Therapy and Child-Centered Therapy for Child Anxiety Disorders. *J Clin Child Adolesc Psychol*, 1-13. doi:10.1080/15374416.2016.1138408

Silverman, W. K. (1987). *Anxiety Disorder Interview for Children (ADIS).* New York, NY: Graywind Publications.

Silverman, W. K., & Albano, A. M. (1996). *The Anxiety Disorders Interview Schedule for Chilren for DSM-IV, child and parent version*. San Antonio, TX: Psychological Corporation.

Silverman, W. K., Kurtines, W. M., Ginsburg, G. S., Weems, C. F., Lumpkin, P. W., & Carmichael, D. H. (1999). Treating anxiety disorders in children with group cognitive-behaviorial therapy: a randomized clinical trial. *J Consult Clin Psychol, 67*(6), 995-1003.

Silverman, W. K., Kurtines, W. M., Ginsburg, G. S., Weems, C. F., Rabian, B., & Serafini, L. T. (1999). Contingency management, self-control, and education support in the treatment of childhood phobic disorders: a randomized clinical trial. *J Consult Clin Psychol, 67*(5), 675-687.

Silverman, W. K., Pina, A. A., & Viswesvaran, C. (2008). Evidence-Based Psychosocial Treatments for Phobic and Anxiety Disorders in Children and Adolescents. *Journal of Clinical Child & Adolescent Psychology, 37*(1), 105-130. doi:10.1080/15374410701817907

Smith, A., Flannery-Schroeder, E., Gorman, K., & Cook, N. (2014). Parent cognitive-behavioral intervention for the treatment of childhood anxiety disorders: a pilot study*61*, 156-161. Retrieved from http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/685/CN-01021685/frame.html doi:10.1016/j.brat.2014.08.010

Socialstyrelsen. (2017). *Nationella riktlinjer för vård vid depression och ångestsyndrom: Stöd för styrning och ledning [The Swedish National Clinical Guidelines for anxiety- and affective disorders: Support for management and administration]*. Stockholm: Socialstyrelsen.

Spence, S. H. (1997). Structure of anxiety symptoms among children: a confirmatory factor-analytic study. *J Abnorm Psychol, 106*(2), 280-297.

Spence, S. H., Donovan, C., & Brechman-Toussaint, M. (2000). The treatment of childhood social phobia: the effectiveness of a social skills training-based, cognitive-behavioural

intervention, with and without parental involvement. *J Child Psychol Psychiatry, 41*(6), 713-726.
Spence, S. H., Donovan, C. L., March, S., Gamble, A., Anderson, R. E., Prosser, S., & Kenardy, J. (2011). A randomized controlled trial of online versus clinic-based CBT for adolescent anxiety. *Journal of Consulting and Clinical Psychology., 79*(5), 629-642. doi:http://dx.doi.org/10.1037/a0024512
Spence, S. H., Donovan, C. L., March, S., Kenardy, J., & Hearn, C. (2017). Generic versus disorder specific cognitive behavior therapy for social anxiety disorder in youth: a randomized controlled trial using internet delivery*90*, 41-57. Retrieved from http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-01300639/frame.html doi:10.1016/j.brat.2016.12.003
Spence, S. H., Holmes, J. M., March, S., & Lipp, O. V. (2006). The feasibility and outcome of clinic plus internet delivery of cognitive-behavior therapy for childhood anxiety. *Journal of Consulting & Clinical Psychology, 74*(3), 614-621.
Spielberger, C., Edwards, C., Montuori, J., & Lushene, R. (1973). *State-Trait Anxiety Inventory for Children.* . Palto Alto, CA.: Consulting Psychologist Press.
Sportel, B., Hullu, E., Jong, P., & Nauta, M. (2013). Cognitive bias modification versus CBT in reducing adolescent social anxiety: a randomized controlled trial*8*(5), e64355. Retrieved from http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/756/CN-00963756/frame.html doi:10.1371/journal.pone.0064355
Storch, E. A., Arnold, E. B., Lewin, A. B., Nadeau, J. M., Jones, A. M., De Nadai, A. S., . . . Murphy, T. K. (2013). The Effect of Cognitive-Behavioral Therapy Versus Treatment as Usual for Anxiety in Children With Autism Spectrum Disorders: A Randomized, Controlled Trial. *Journal of the American Academy of Child & Adolescent Psychiatry, 52*(2), 132-142.e132. doi:10.1016/j.jaac.2012.11.007
Storch, E. A., Lewin, A. B., Collier, A. B., Arnold, E., Nadai, A. S. D., Dane, B. F., . . . Murphy, T. K. (2015). A RANDOMIZED CONTROLLED TRIAL OF COGNITIVE-BEHAVIORAL THERAPY VERSUS TREATMENT AS USUAL FOR ADOLESCENTS WITH AUTISM SPECTRUM DISORDERS AND COMORBID ANXIETY. *Depression and Anxiety, 32*(3), 174-181. doi:doi:10.1002/da.22332
Storch, E. A., Salloum, A., King, M. A., Crawford, E. A., Andel, R., McBride, N. M., & Lewin, A. B. (2015). A RANDOMIZED CONTROLLED TRIAL IN COMMUNITY MENTAL HEALTH CENTERS OF COMPUTER-ASSISTED COGNITIVE BEHAVIORAL THERAPY VERSUS TREATMENT AS USUAL FOR CHILDREN WITH ANXIETY. *Depression and Anxiety, 32*(11), 843-852. doi:doi:10.1002/da.22399
Sung, M., Ooi, Y. P., Goh, T. J., Pathy, P., Fung, D. S. S., Ang, R. P., . . . Lam, C. M. (2011). Effects of Cognitive-Behavioral Therapy on Anxiety in Children with Autism Spectrum Disorders: A Randomized Controlled Trial. *Child Psychiatry & Human Development, 42*(6), 634-649. doi:10.1007/s10578-011-0238-1
Suveg, C., Jones, A., Davis, M., Jacob, M. L., Morelen, D., Thomassin, K., & Whitehead, M. (2018). Emotion-Focused Cognitive-Behavioral Therapy for Youth with Anxiety Disorders: A Randomized Trial. *J Abnorm Child Psychol, 46*(3), 569-580. doi:10.1007/s10802-017-0319-0
The Research Units On Pediatric Psychopharmacology Anxiety Study, G. (2002). The Pediatric Anxiety Rating Scale (PARS): Development and Psychometric Properties. *Journal of the American Academy of Child & Adolescent Psychiatry, 41*(9), 1061-1069. doi:https://doi.org/10.1097/00004583-200209000-00006
Thienemann, M., Moore, P., & Tompkins, K. (2006). A parent-only group intervention for children with anxiety disorders: pilot study. *J Am Acad Child Adolesc Psychiatry, 45*(1), 37-46. doi:10.1097/01.chi.0000186404.90217.02
Vigerland, S., Ljótsson, B., Thulin, U., Öst, L.-G., Andersson, G., & Serlachius, E. (2016). Internet-delivered cognitive behavioural therapy for children with anxiety disorders: A randomised controlled trial. *Behav Res Ther, 76*, 47-56. doi:https://doi.org/10.1016/j.brat.2015.11.006

Walkup, J. T., Albano, A. M., Piacentini, J., Birmaher, B., Compton, S. N., Sherrill, J. T., . . . Kendall, P. C. (2008). Cognitive Behavioral Therapy, Sertraline, or a Combination in Childhood Anxiety. *The New England journal of medicine, 359*(26), 2753-2766. doi:10.1056/NEJMoa0804633

Wampold, B. E., Minami, T., Tierney, S. C., Baskin, T. W., & Bhati, K. S. (2005). The placebo is powerful: Estimating placebo effects in medicine and psychotherapy from randomized clinical trials. *Journal of Clinical Psychology, 61*(7), 835-854. doi:doi:10.1002/jclp.20129

Wang, Z., Whiteside, S. H., Sim, L., & et al. (2017). Comparative effectiveness and safety of cognitive behavioral therapy and pharmacotherapy for childhood anxiety disorders: A systematic review and meta-analysis. *JAMA Pediatrics, 171*(11), 1049-1056. doi:10.1001/jamapediatrics.2017.3036

Waters, A. M., Ford, L. A., Wharton, T. A., & Cobham, V. E. (2009). Cognitive-behavioural therapy for young children with anxiety disorders: Comparison of a Child + Parent condition versus a Parent Only condition. *Behav Res Ther, 47*(8), 654-662. doi:https://doi.org/10.1016/j.brat.2009.04.008

Wergeland, G. J. H., Fjermestad, K. W., Marin, C. E., Haugland, B. S.-M., Bjaastad, J. F., Oeding, K., . . . Heiervang, E. R. (2014). An effectiveness study of individual vs. group cognitive behavioral therapy for anxiety disorders in youth. *Behav Res Ther, 57*, 1-12. doi:https://doi.org/10.1016/j.brat.2014.03.007

White, S. W., Ollendick, T., Albano, A. M., Oswald, D., Johnson, C., Southam-Gerow, M. A., . . . Scahill, L. (2013). Randomized Controlled Trial: Multimodal Anxiety and Social Skill Intervention for Adolescents with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders, 43*(2), 382-394. doi:10.1007/s10803-012-1577-x

Wood, J. J., Drahota, A., Sze, K., Har, K., Chiu, A., & Langer, D. A. (2009). Cognitive behavioral therapy for anxiety in children with autism spectrum disorders: a randomized, controlled trial. *Journal of Child Psychology and Psychiatry, 50*(3), 224-234. doi:doi:10.1111/j.1469-7610.2008.01948.x

Wood, J. J., Ehrenreich-May, J., Alessandri, M., Fujii, C., Renno, P., Laugeson, E., . . . Storch, E. A. (2015). Cognitive Behavioral Therapy for Early Adolescents With Autism Spectrum Disorders and Clinical Anxiety: A Randomized, Controlled Trial. *Behavior Therapy, 46*(1), 7-19. doi:https://doi.org/10.1016/j.beth.2014.01.002

Wood, J. J., Piacentini, J. C., Southam-Gerow, M., Chu, B. C., & Sigman, M. (2006). Family cognitive behavioral therapy for child anxiety disorders. *J Am Acad Child Adolesc Psychiatry, 45*(3), 314-321. doi:10.1097/01.chi.0000196425.88341.b0

Wuthrich, V. M., Rapee, R. M., Cunningham, M. J., Lyneham, H. J., Hudson, J. L., & Schniering, C. A. (2012). A Randomized Controlled Trial of the Cool Teens CD-ROM Computerized Program for Adolescent Anxiety. *Journal of the American Academy of Child & Adolescent Psychiatry, 51*(3), 261-270. doi:10.1016/j.jaac.2011.12.002

Supplement A: Information about characteristics of included studies

Table 1. Characteristics of included studies

Study	n (CBT group)	n (control group)	Type of control	Diagnostic assessment	CBT treatment			
					Setting	Treatment form	Treatment target	Treatment duration (sessions/weeks)
Afshari, Neshat-Doost, Maracy, Ahmady, and Amiri (2014)	CBT: 12; ECBT: 12	10	No treatment	ADIS C-P	Clinical	Individual	Separation anxiety	CBT: 10/10; ECBT: 12/12
Arendt, Thastum, and Hougaard (2016)	56	53	Wait-list	ADIS C-P	Clinical	Group	General	10/10
Barrett et al. (1996)	53	26	Wait-list	ADIS C-P	Clinical	Individual/ family	General	12/12
Barrington, Prior, Richardson, and Allen (2005)	28	26	TAU	ADIS C	Clinical	Individual	General	12/12-52
Britton et al. (2013)	17	CBT+ABMT: 18; CBT+placebo: 18	Active	K-SADS	Clinical	Individual	General	n/r /8
Chalfant et al. (2007)	28	19	Wait-list	ADIS C-P	School Outreach Service	Individual	General	12/12
Chavira et al. (2014)	24	24	Active	ADIS C-P	Clinical	Family	General	10/12
Chiu et al. (2013)	22	18	Wait-list	ADIS C-P	School	Individual	General	1-16/1-16
Cobham (2012)	43 (ICBT: 23; BT: 20)	12	Wait-list	ADIS C-P	Clinical	Individual/ therapist supported bibliotherapy	General	12/12

Conaughton et al. (2017)	21	21	Wait-list	ADIS C-P	Computer	Internet	General	10/10
Creswell et al. (2015)	CCBT: 56; MCBT: 60	62	Active	ADIS C-P	Clinical	Individual	General	8/8
Donovan and March (2014)	23	29	Wait-list	ADIS C-P	Computer	Internet	General	8/22
Esbjørn et al. (2015)	26	28	Active	ADIS C-P	Clinical	Family	General	14/ n/r
Flannery-Schroeder and Kendall (2000)	25	12	Wait-list	ADIS C-P	Clinical	Individual/ group	General	9/18
Fujii et al. (2013)	7	5	TAU	ADIS C-P	Clinical	Individual	General	32/32
Gaesser and Karan (2017)	CBT: 21; EFT: 21	21	Wait-list	n/r	School	Individual	n/r	n/r / 20
Galla et al. (2012)	n/r	n/r	Wait-list	ADIS C-P	School	Individual	General	1-16/ n/r
García-López et al. (2002); Olivares et al. (2002)	14	SET-Asv: 15; IAFS: 15; control: 15	Active/no treatment	ADIS	Clinical	Group	Social anxiety	CBGT: 16/14; SET-Asv: 29/17; IAFSG: 12/12
Garcia-Lopez, Díaz-Castela, Muela-Martinez, and Espinosa-Fernandez (2014)	32	20	Active	ADIS C-P	Clinical	Individual	Social anxiety	12/12
Gil-Bernal and Hernández-Guzmán (2009)	CBTG: 6; CBTG+parent: 6	5	Wait-list	n/r	School	Group	Social anxiety	9/5
Ginsburg and Drake (2002)	6	6	Active	ADIS C	School	Individual	General	10/ n/r
Ginsburg, Becker, Drazdowski, and Tein (2012)	17	15	Usual care	ADIS C-P	School	Individual	General	8**/12
Hancock et al. (2016)	ACT: 54; CBT: 57	46	Wait-list	ADIS	Clinical	Individual	General	10/10

Hayward et al. (2000)	12	23	No treatment	ADIS C-P	pilot study	Group	Social anxiety	16/16
Herbert et al. (2009)	ICBT: 24; GCBT: 23	26	Active	ADIS C	School	Individual/ group	Social anxiety	12/12
Hirshfeld-Becker et al. (2010)	34	30	Wait-list	K-SADS	Clinical	Individual	General	20/24
Holmes, Donovan, Farrell, and March (2014)	20	22	Wait-list	ADIS C-P	Clinical	Group	GAD	10/10
Hudson et al. (2009)	60	52	Active	ADIS C-P	Clinical	Group	General	10/10
Hudson et al. (2014)	100	109	Active	ADIS C-P	Clinical	Individual/family	General	12/12
Ingul, Aune, and Nordahl (2014)	GCBT: 21; ICBT: 20	16	Active	ADIS C	Clinical	Individual/group	General	GCBT: 10/n/r; ICBT: 12/n/r
Kendall (1994)	27	20	Wait-list	ADIS C-P	Clinical	Individual	General	16-20/16
Kendall et al. (1997)	60	34	Wait-list	ADIS C-P	Clinical	Individual	General	16-20/16
Kendall et al. (2008)	ICBT: 55; FCBT: 56	50	Active	ADIS C-P	Clinical	Individual/ family	General	16/16
Khanna and Kendall (2010)	ICBT: 17; ComCBT (CCAL): 16	16	Active	ADIS P	Clinical/ computer	Computer/ individual	General	12/15
Lau, Chan, Li, and Au (2010)	26	25	Wait-list	K-SADS	Community clinic	Individual	General	9/13
March, Spence, and Donovan (2009)	40	33	Wait-list	ADIS C-P	Clinical	Computer (internet)	General	10/10
Masia-Warner et al. (2005)	21	21	Wait-list	ADIS C-P	School	Group	Social anxiety	10/12
Masia-Warner, Fisher, Shrout, Rathor, and Klein (2007)	21	17	Active	ADIS C-P	School	Group	Social anxiety	12/12

Masia-Warner et al. (2011)	20	20	Wait-list	ADIS C-P	Clinical	Individual	General	12/10
McNally Keehn, Lincoln, Brown, and Chavira (2013)	12	10	Wait-list	ADIS P	Clinical	Individual	General	16/16
Melfsen et al. (2011)	21	23	Wait-list	ADIS	Clinical	Individual	Social anxiety	20/20
Mendlowitz et al. (1999)	Parent+ child: 18; child: 23; parent: 21	40	Wait-list	DISCAP	Clinical	Group/family	n/r	9/12
Mitchell, Newall, Broeren, and Hudson (2013)	36	28	Active	ADIS C-P	Clinical	Group	General	10/10
Muris, Meesters, and van Melick (2002)	10	Ed: 10/no trt: 10	Active/no treatment	DISC 2.3	School	Individual	General	12/6
Nauta, Scholing, Emmelkamp, and Minderaa (2003)	CBT: 29; CBT+CPT: 30	20	Wait-list	ADIS C-P	Clinical	Individual	General	12/12
Olivares Rodríguez, Alcázar, and Piqueras Rodríguez (2005)	17	17	Wait-list	ADIS C-P	Clinical	Group	Social anxiety	12/12
Sánchez-García and Olivares (2009)	IAFS(CBT): 28; IAFS ÷cog: 29	25	Wait-list	ADIS C	Clinical	Individual	Social anxiety	12/12
Schneider et al. (2011)	21	22	Wait-list	Kinder DIPS	Clinical	Individual	Separation anxiety	16/12
Schneider et al. (2013)	33	31	Active	Diagnostic Interview for Children and youth	Clinical	Individual	Separation anxiety	16/12

Sevi Tok, Arkar, and Bildik (2016)	CBT: 16	ST: 15; CBT+ST: 15	Active	n/r	Clinical	Individual	General	16/16
Shechner et al. (2014)	ABMT+CBT: 15	ABMTplacebo+CBT: 22; CBT: 18	Active	ADIS C-P	Clinical	Individual	General	16/16
Shortt et al. (2001)	54	17	Wait-list	DISCAP	Clinical	Family	General	10/10
Silk et al. (2016)	90	43	Active	K-SADS	Clinical	Individual	General	16/ n/r
Silk et al. (2013)	30	17	Active	K-SADS	Clinical	Individual	General	16/16
Silverman, Kurtines, Ginsburg, Weems, Rabian, et al. (1999)	81	23	Active	ADIS C-P	Clinical	Individual	General	10/10
Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al. (1999)	37	19	Wait-list	ADIS C-P	Clinical	Group	General	12/ n/r
Smith, Flannery-Schroeder, Gorman, and Cook (2014)	18	13	Wait-list	ADIS P	Clinical	Individual (parent)	General	10/10
Spence, Donovan, and Brechman-Toussaint (2000)	CBT: 19; CBT+parent: 17	14	Wait-list	ADIS C-P	Clinical	Individual/family	Social anxiety	12/12
Spence et al. (2006)	CBT: 22; Internet CBT: 27	23	Wait-list	ADIS P	Clinical/internet	Individual/ computer	General	10/10
Spence et al. (2011)	Internet CBT: 44; CBT: 44	27	Wait-list	ADIS C-P	Clinical	Individual/ computer	General	10/12
Spence, Donovan, March, Kenardy, and Hearn (2017)	GenCBT: 48; SAD-CBT: 47	30	Wait-list	ADIS C-P	Internet	Computer	Social anxiety	10/10

Sportel, Hullu, Jong, and Nauta (2013)	CBT: 84; CBM: 86	70	Wait-list	ADIS C	Internet/school	Computer/ individual	General	CBM: 20/10; CBT: 10/10
Storch et al. (2013)	24	21	TAU	ADIS C-P	n/r	Individual	General	16/16
Storch, Lewin, et al. (2015)	16	15	TAU	ADIS C-P	n/r	Individual	General	16/16
Storch, Salloum, et al. (2015)	49	51	TAU	ADIS C-P	Community clinic	Computer	General	12/12
Suveg et al. (2018)	43	49	Active	ADIS C-P	n/r	Individual	General	10/10
Vigerland et al. (2016)	46	47	Wait-list	ADIS C-P	n/r	Internet	General	11/10
Walkup et al. (2008);	CBT: 139	WL:76; CBT+SSRI:140; SSRI: 133	Placebo	ADIS	Clinical	Individual	General	14/12
Waters, Ford, Wharton, and Cobham (2009)	GCBT P+C: 31; GCBT C: 38	11	Wait-list	ADIS P	Clinical	Group	General	10/10
Wergeland et al. (2014)	ICBT: 77; GCBT: 67	38	Wait-list	ADIS C-P	Community clinic	Individual/group	General	10/12
White et al. (2013)	15	15	Wait-list	ADIS C-P	Clinical	Individual/group	General	13/14
Wood et al. (2009)	17	23	Wait-list	ADIS C-P	Clinical	Individual	General	16/16
Wood et al. (2015)	19	14	Wait-list	ADIS C-P	n/r	Individual	General	16/16
Wuthrich et al. (2012)	24	19	Wait-list	ADIS C-P	n/r	Computer	General	8/12

n/r= not reported

*treatment group

**modules

CBT= Cognitive behavioral therapy, ICBT= Individual cognitive behavioral therapy, GCBT= Group Cognitive behavioral therapy, ECBT= Emotion-focused cognitive behavioral therapy, CCAL= Camp Cope-A-Lot, CBT PI= Cognitive behavioral therapy parent involvement, CBT NET= Cognitive behavioral therpy internet, CBT Gen= generic cognitive behavioral therapy, CBT SAD= social anxiety specific cognitive behavioral therapy, CBM= cognitive bias modification, P+C= parent+childe, P= parent, ABMT= Attention bias modification, ABM PBO= Attention bias modification placebo, SRT= sertraline, PBO= placebo, TAU= treatment as usua

Supplement B: Information about study characteristics of participants

Table 2. Study characteristics of participants

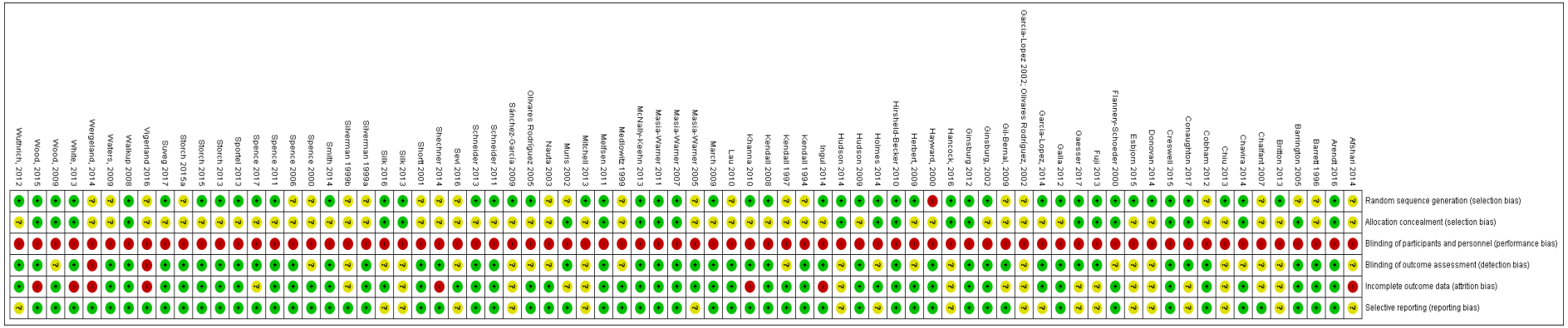
Study	Country	N	Age Range	Age M (SD)	Gender- female %	Comorbidity total %
Afshari et al. (2014)	IRN	34	9-13	10.1 (2,3)	50,0	n/r
Arendt et al. (2016)	DEN	109	7-16	11,8 (2,7)	57,0	n/r
Barrett et al. (1996)	AUS	79	7-14	9,3 (2,1)	43,0	n/r
Barrington et al. (2005)	AUS	54	7-14	10,0 (2,0)	64,8	37,0
Britton et al. (2013)	USA	53	8-17	11,1 (2,4)	58,5	n/r
Chalfant et al. (2007)	AUS	47	8-13	10,8 (1,4)	25,5	100
Chavira et al. (2014)	USA	48	8-13	9,6 (1,6)	56,3	35,4
Chiu et al. (2013)	USA	40	5-12	8,5 (1,7)	45,0	62,5
Cobham (2012)	AUS	55	7-14	9,9 (2,4)	45,5	n/r
Conaughton et al. (2017)	AUS	42	8-12	9,7 (1,3)	14,4	100
Creswell et al. (2015)	UK	178	7-12	10,2 (1,6)	52,1	n/r
Donovan and March (2014)	AUS	52	3-6	4,1 (0,8)	53,8	n/r
Esbjørn et al. (2015)	DK	54	7-12	9,6 (1,7)	48,0	n/r
Flannery-Schroeder and Kendall (2000)	USA	37	8-14	n/r	48,5	n/r
Fujii et al. (2013)	USA	12	7-11	8,8 (1,6)	25,0	100
Gaesser and Karan (2017)	USA	63	10-18	n/r	71,4	n/r
Galla et al. (2012)	USA	40	5-12	8,5 (1,7)	45,0	34,0
García-López et al. (2002); Olivares et al. (2002)	ESP	59	15-17	15,9 (0,8)	78,0	n/r
Garcia-Lopez et al. (2014)	ESP	52	13-18	15,2 (1,4)	65,4	61,5
Gil-Bernal and Hernández-Guzmán (2009)	MEX	17	7-12	9,9 (1,8)	76,5	n/r
Ginsburg and Drake (2002)	USA	12	14-17	15,6 (n/r)	83,3	n/r
Ginsburg et al. (2012)	USA	32	7-17	10,3 (2,4)	62,5	63,0
Hancock et al. (2016)	AUS	157	7-17	11,0 (2,8)	58,0	n/r

Hayward et al. (2000)	USA	35	n/r	15,8 (1,6)	100,0	n/r
Herbert et al. (2009)	USA	73	12-17	14,8 (2,1)	57,8	59,0
Hirshfeld-Becker et al. (2010)	USA	64	4-7	5,4 (1,0)	53,1	n/r
Holmes et al. (2014)	AUS	42	7-12	9,6 (1,4)	66,7	n/r
Hudson et al. (2009)	AUS	106	7-16	10,2 (n/r)	38,0	n/r
Hudson et al. (2014)	AUS	209	6-13	9,4 (1,9)	49,8	n/r
Ingul et al. (2014)	NOR	57	13-16	14,5 (1,0)	36,0	n/r
Kendall (1994)	USA	47	9-13	n/r	40,4	n/r
Kendall et al. (1997)	USA	94	9-13	n/r	38,0	n/r
Kendall et al. (2008)	USA	161	7-14	10,3 (n/r)	44,0	n/r
Khanna and Kendall (2010)	USA	49	7-13	10,1 (1,6)	32,7	53,0
Lau et al. (2010)	CHN	45	6-11	8,7 (1,2)	46,7	n/r
March et al. (2009)	AUS	73	7-12	9,5 (1,4)	54,8	n/r
Masia-Warner et al. (2005)	USA	35	13-17	14,8 (0,8)	74,3	48,6
Masia-Warner et al. (2007)	USA	36	14-16	15,1 (0,6)	83,3	41,7
Masia-Warner et al. (2011)	USA	40	8-16	12,4 (2,6)	65,0	77,5
McNally Keehn et al. (2013)	USA	22	8-14	11,3 (1,5)	4,5	n/r
Melfsen et al. (2011)	GER	44	8-14	10,7 (1,9)	47,7	n/r
Mendlowitz et al. (1999)	CAN	68	7-12	9,8 (n/r)	57,4	n/r
Mitchell et al. (2013)	AUS	64	6-13	9,8 (0,2)	51,0	n/r
Muris et al. (2002)	NLD	20	9-12	10,0 (0,8)	65,0	40
Nauta et al. (2003)	NLD	79	7-18	11,0 (2,4)	50,6	70
Olivares Rodríguez et al. (2005)	ESP	34	14-17	15,0 (0,9)	58,8	n/r
Sánchez-García and Olivares (2009)	ESP	82	10-14	11,9 (1,3)	73,2	n/r
Schneider et al. (2011)	GER	43	5-7	6,2 (0,9)	58,1	44,2
Schneider et al. (2013)	GER	64	8-13	10,4 (1,6)	51,6	61,3*
Sevi Tok et al. (2016)	TUR	46	8-12	10,0 (1,5)	56,5	50
Shechner et al. (2014)	ISR	55	6,5-18	11,5 (2,9)	43,6	12,7
Shortt et al. (2001)	AUS	71	6-10	7,9 (n/r)	59,2	72

Silk et al. (2016)	USA	133	9-14	10,9 (1,5)	56,0	n/r
Silk et al. (2013)	USA	47	9-13	10,5 (1,3)	52,0	n/r
Silverman, Kurtines, Ginsburg, Weems, Rabian, et al. (1999)	USA	104	6-16	9,8 (n/r)	48,1	72
Silverman, Kurtines, Ginsburg, Weems, Lumpkin, et al. (1999)	USA	56	6-16	10,0 (n/r)	39,3	n/r
Smith et al. (2014)	USA	31	7-13	9,8 (1,8)	39,0	n/r
Spence et al. (2000)	AUS	50	7-14	10,7 (2,1)	38,0	74
Spence et al. (2006)	AUS	72	7-14	9,9 (1,7)	41,7	n/r
Spence et al. (2011)	AUS	115	12-18	14,0 (1,6)	59,1	84
Spence et al. (2017)	AUS	125	8-17	11,3 (2,7)	60,0	n/r
Sportel et al. (2013)	NLD	240	13-15	14,1 (0,7)	73,3	n/r
Storch et al. (2013)	USA	45	7-11	8,9 (1,3)	20,0	100
Storch, Lewin, et al. (2015)	USA	31	11-16	12,7 (1,3)	19,3	100
Storch, Salloum, et al. (2015)	USA	100	7-13	9,8 (1,8)	44,0	n/r
Suveg et al. (2018)	USA	92	7-12	8,9 (1,6)	42,4	91,9
Vigerland et al. (2016)	SWE	93	8-12	10,1 (1,7)	54,8	70
Walkup et al. (2008)	USA	488	7-17	10,7 (2,8)	49,6	n/r
Waters et al. (2009)	AUS	80	4-8	6,8 (1,2)	52,5	n/r
Wergeland et al. (2014)	NOR	182	8-15	11,5 (2,1)	54,7	CBT: 81,3 / WL: 63,1
White et al. (2013)	USA	30	12-17	15,0 (n/r)	23,3	100
Wood et al. (2009)	USA	40	7-11	9,2 (1,5)	32,5	100
Wood et al. (2015)	USA	33	11-15	12,3 (1,1)	30,3	100
Wuthrich et al. (2012)	AUS	43	14-17	15,2 (1,1)	62,8	n/r

*treatment group
n/r = not reported, M= mean, SD= standard division
AUS= Australia, CAN= Canada, CHN= China, DEN= Denmark, ESP= Spain, GBR= United Kingdom, GER= Germany, IRN= Iran, ISR= Israel, MEX= Mexico, NLD= The Netherlands, NOR= Norway, SWE= Sweden, TUR= Turkey, USA= United States of America

Supplement C. Risk of bias summary:judgement about each risk of bias item for each included study



Supplement D. Primary outcome: Attrition

CBT modalities versus WL

Individual-based CBT versus WL

Meta-analysis of 11 trials demonstrated no significant increased risk of drop-out with individual-based CBT compared with WL (OR=0.78 [95%CI, 0.47 to 1.29]). There was no evidence of significant heterogeneity between trials. The attrition rates and forest plot of the individual studies can be seen in Fig. 15.

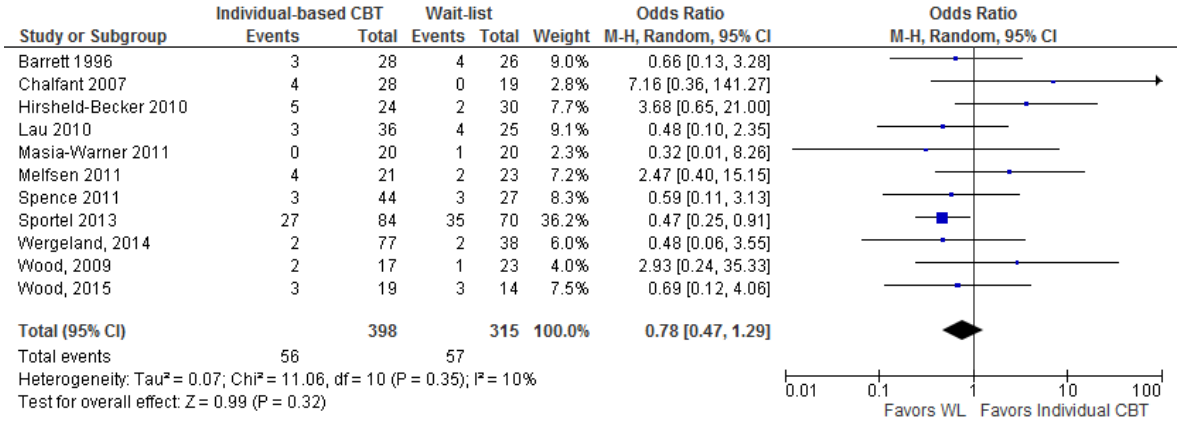


Figure 15. Forest plot: Drop-out from individual-based CBT vs. wait-list control

Group-based CBT versus WL

Meta-analysis of 8 trials demonstrated no significant increased risk of drop-out with group-based CBT compared with WL (OR=1.30 [95%CI, 0.54 to 3.12]). There was no evidence of significant heterogeneity between trials. The attrition rates and forest plot of the individual studies can be seen in Fig. 16.

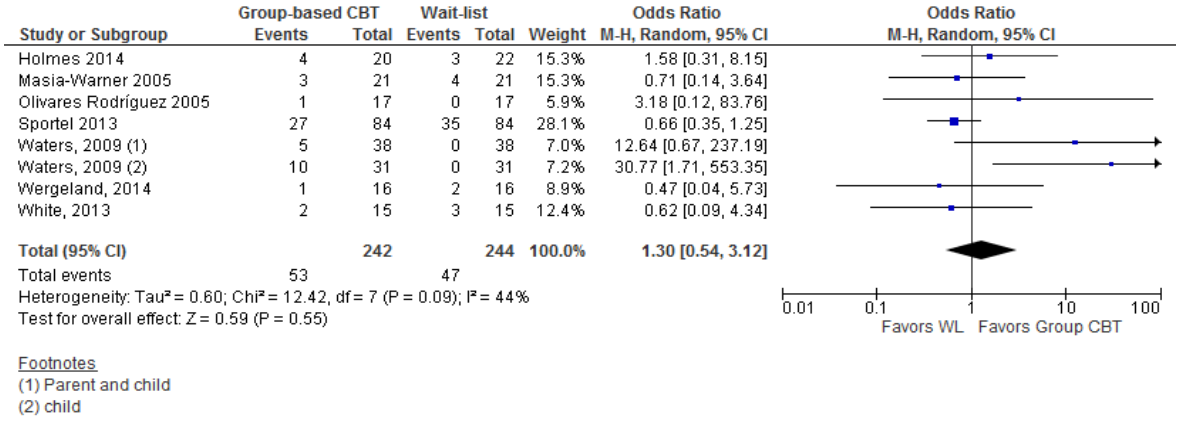


Figure 16. Forest plot: Drop-out from group-based CBT vs. wait-list control

Family-based CBT versus WL

Meta-analysis of 2 trials demonstrated no significant increased risk of drop-out with family-based CBT compared with WL (OR=0.62 [95%CI, 0.15 to 2.55]). There was no evidence of significant heterogeneity between trials. The attrition rates and forest plot of the individual studies can be seen in Fig. 17.

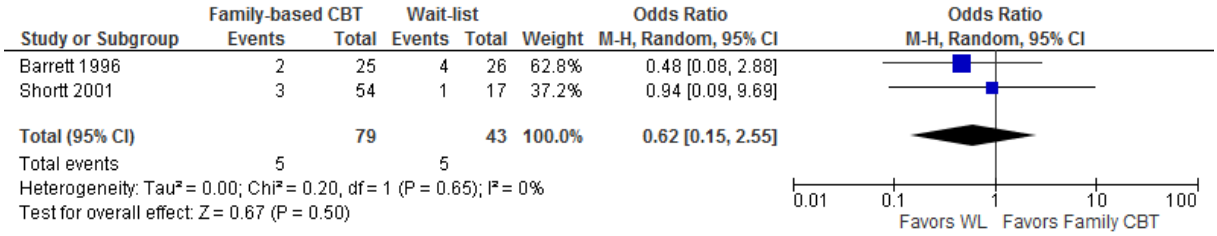


Figure 17. Forest plot: Drop-out from family-based CBT vs. wait-list control

Remote-based CBT versus WL

Meta-analysis of 7 trials demonstrated an increased risk of drop-out with remote-based CBT compared with WL (OR=1.90 [95%CI, 1.21 to 3.00]). There was no evidence of significant heterogeneity between trials. The attrition rates and forest plot of the individual studies can be seen in Fig. 18.

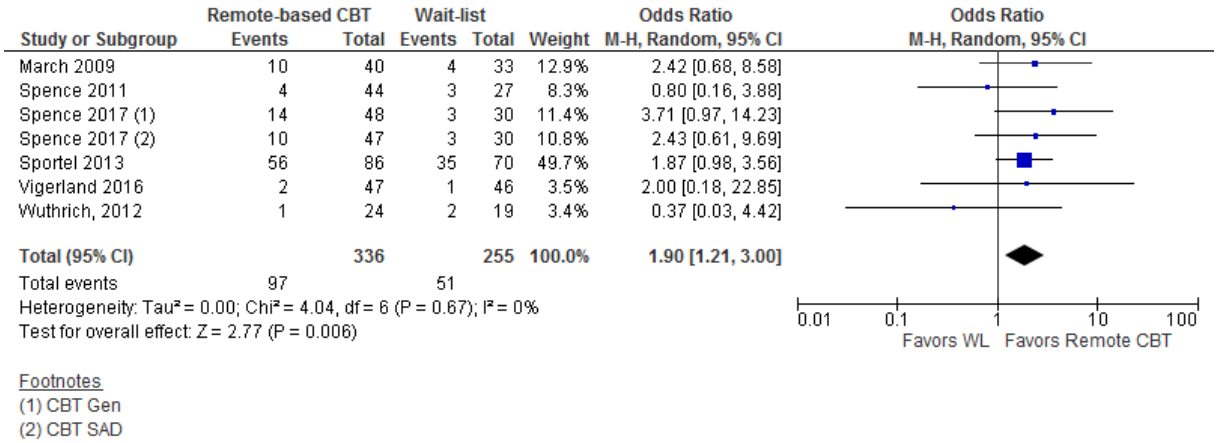


Figure 18. Forest plot: Drop-out from remote-based CBT vs. wait-list control

CBT modalities versus TAU

Only two CBT modalities (individual-based CBT and group-based CBT) had TAU comparison reported drop-out in the meta-analysis.

Individual-based CBT versus TAU

Meta-analysis of 1 trial demonstrated no significant increased risk of drop-out with individual-based CBT compared to TAU (OR=4.78 [95%CI, 0.22 to 105.36]). Only one study (Storch et al., 2013) reported attrition in individual based CBT vs. TAU comparison. Therefore, estimated effect size and heterogeneity could not be calculated.

Group-based CBT versus TAU

Meta-analysis of 1 trial demonstrated no significant increased risk of drop-out with group-based CBT compared to TAU (OR=1.04 [95%CI, 0.25 to 4.43]). Only one study (Storch, Lewin, et al., 2015) reported attrition in group-based CBT vs. TAU comparison. Therefore, estimated effect size and heterogeneity could not be calculated.

CBT modalities versus attention control

Individual-based CBT versus attention control

Meta-analysis of 4 trials demonstrated no significant increased risk of drop-out with individual-based CBT compared with attention control (OR=1.26 [95%CI, 0.60 to 2.65]). There was no evidence of significant heterogeneity between trials. The attrition rates and forest plot of the individual studies can be seen in Fig. 19.

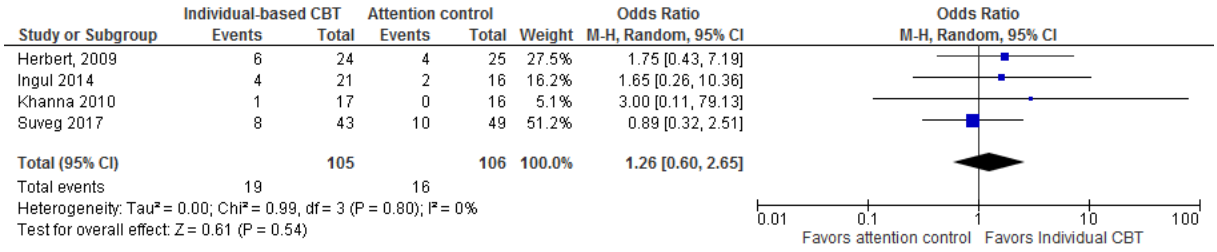


Figure 19. Forest plot: Drop-out from individual-based CBT vs. attention control

Group-based CBT versus attention control

Meta-analysis of 4 trials demonstrated no significant increased risk of drop-out with group-based CBT compared with attention control (OR=1.90 [95%CI, 0.64 to 5.64]). There was no evidence of significant heterogeneity between trials. The attrition rates and forest plot of the individual studies can be seen in Fig. 20.

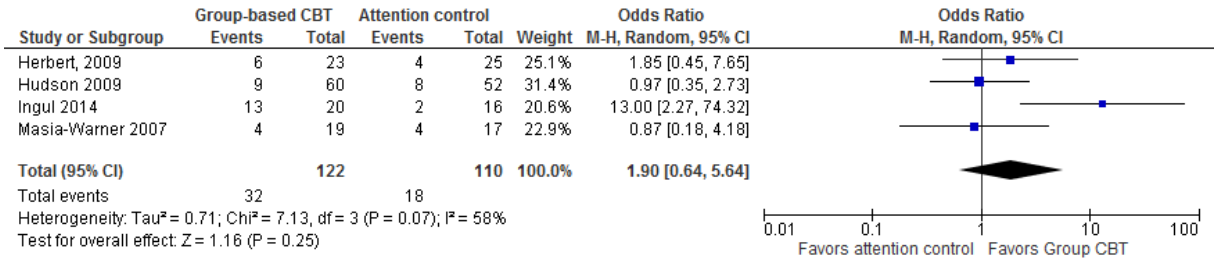


Figure 20. Forest plot: Drop-out from group-based CBT vs. attention control

Remote-based CBT versus attention control

Meta-analysis of 1 trial demonstrated no significant increased risk of drop-out with remote-based CBT compared to attention control (OR=8.56 [95%CI, 0.41 to 180.52]). Only one study (Khanna & Kendall, 2010) reported attrition in remote-based CBT vs. attention control comparison. Therefore, estimated effect size and heterogeneity could not be calculated.

CBT modalities versus SSRIs

Only one CBT modular (individual-based CBT) in comparison to SSRIs reported drop-out in the meta-analysis. Meta-analysis of 1 trial demonstrated an increased risk of drop-out with SSRIs compared with individual-based CBT (OR=0.14 [95%CI, 0.05 to 0.42]). Only one study (Walkup et al., 2008) reported attrition in individual based CBT vs. SSRIs comparison. Therefore, estimated effect size and heterogeneity could not be calculated.

CBT modalities versus combination of SSRIs and CBT

Only one CBT modular (individual-based CBT) in comparison to combination of CBT and SSRIs reported drop-out in the meta-analysis. Meta-analysis of 1 trial demonstrated no significant increased risk of drop-out with individual-based CBT compared with combination control (OR=2.30 [95%CI, 1.03 to 5.12]). Only one study (Walkup et al., 2008) reported attrition in individual based CBT vs. combination. Therefore, estimated effect size and heterogeneity could not be calculated.

Supplement E. Secondary outcome: Continuous measure

Is there a difference between CBT modalities and different control group?

CBT modalities versus WL

Individual-based CBT versus WL

Meta-analysis of 16 trials on the difference between individual-based CBT and WL showed a mean effect size (SMD) of 0.98 [95% CI, 0.50 to 1.47], demonstrating that individual-based CBT have, on average, lower anxiety score than WL control. There was a significant amount of heterogeneity between trials. The effect size estimates and forest plot of the individual studies can be seen in Fig. 21.

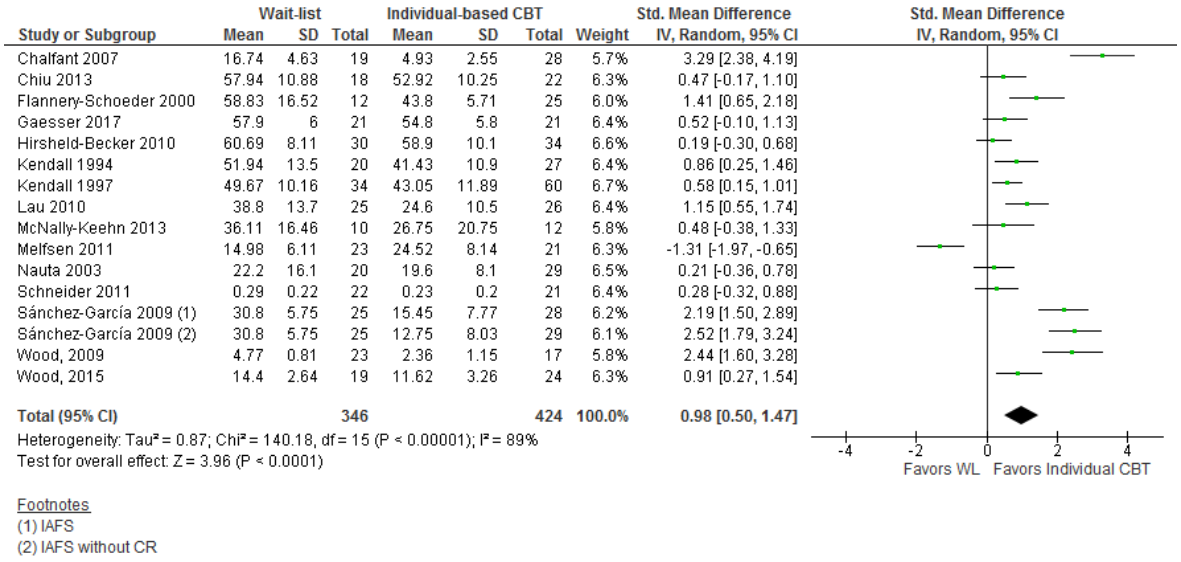


Figure 21. Forest plot: Individual-based CBT vs. wait-list control, continuous measure

Group-based CBT versus WL

Meta-analysis of 13 trials on the difference between group-based CBT and WL showed a mean effect size (SMD) of 0.74 [95% CI, 0.41 to 1.08], demonstrating that group-based CBT have, on average, lower anxiety score than WL control. There was a significant amount of heterogeneity between trials. The effect size estimates and forest plot of the individual studies can be seen in Fig. 22.

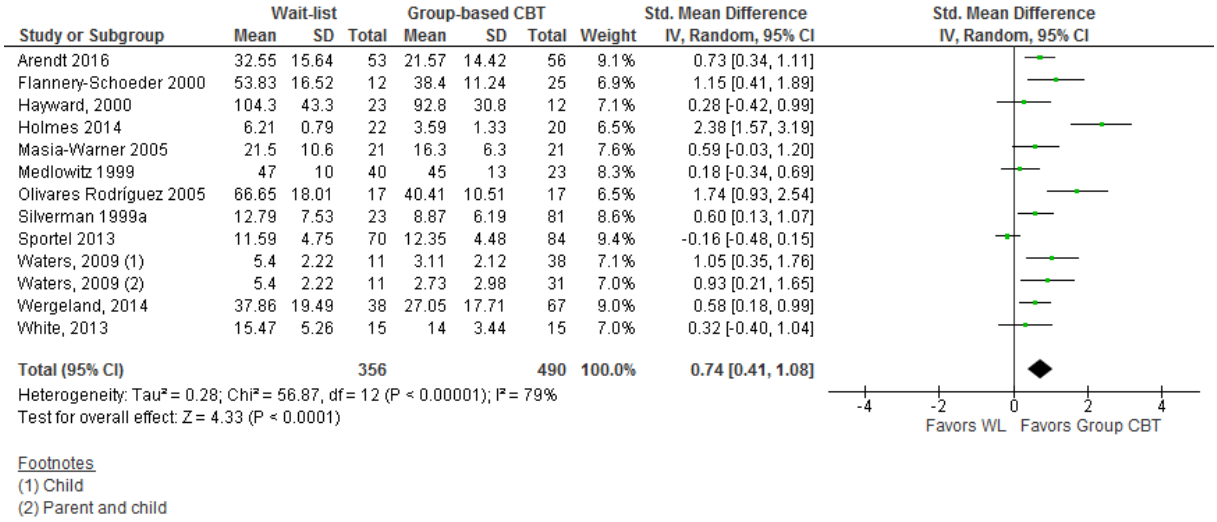


Figure 22. Forest plot: Group-based CBT vs. wait-list control, continuous measure

Family-based CBT versus WL

Meta-analysis of 6 trials on the difference between family-based CBT and WL showed a mean effect size (SMD) of 0.56 [95% CI, 0.27 to 0.86], demonstrating that family-based CBT have, on average, lower anxiety score than WL control. There was a no significant evidence of heterogeneity between trials. The effect size estimates and forest plot of the individual studies can be seen in Fig. 23.

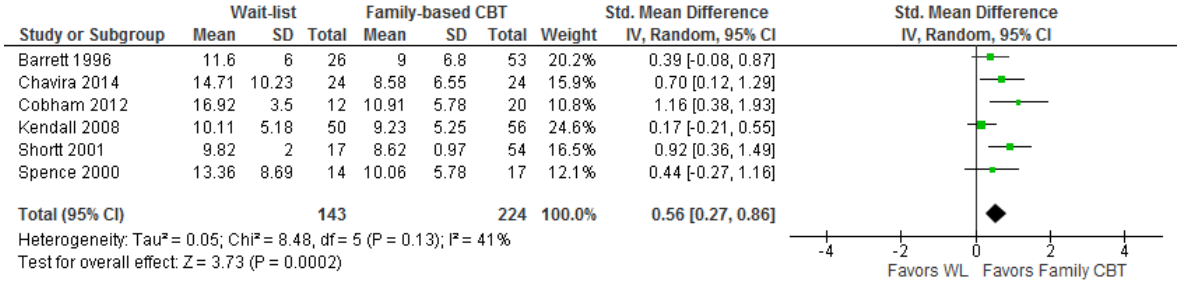


Figure 23. Forest plot: Family-based CBT vs. wait-list control, contnuous measure

Remote-based CBT versus WL

Meta-analysis of 8 trials on the difference between remote-based CBT and WL showed a mean effect size (SMD) of 1.63 [95% CI, 0.60 to 2.65], demonstrating that remote-based CBT have, on average, lower anxiety score than WL control. There was a significant amount of heterogeneity between trials. The effect size estimates and forest plot of the individual studies can be seen in Fig. 24.

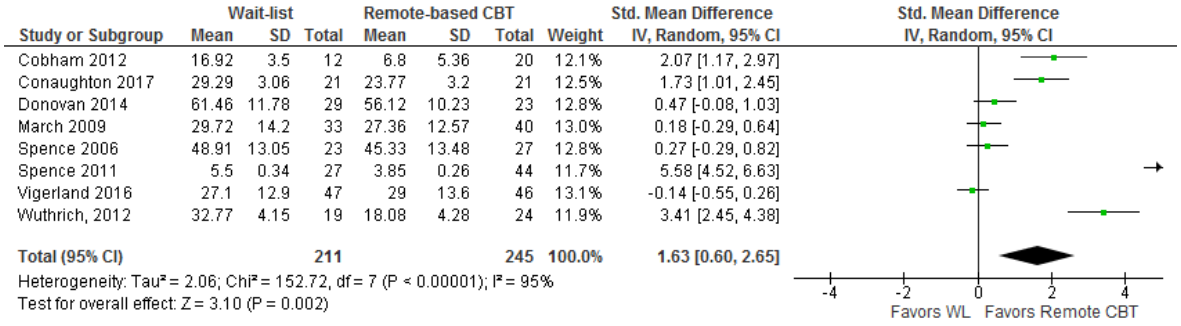


Figure 24. Forest plot: Remote-based CBT vs. wait-list control, continuous measure

CBT modalities versus TAU

Only one CBT modalities (individual-based CBT) had TAU comparison in the meta-analysis.

Individual-based CBT versus TAU

Meta-analysis of 6 trials on the difference between individual-based CBT and TAU showed a mean effect size (SMD) of 0.59 [95% CI, 0.03 to 1.15], demonstrating no significant difference between individual-based CBT and TAU. There was a significant amount of heterogeneity between trials. The effect size estimates and forest plot of the individual studies can be seen in Fig. 25.

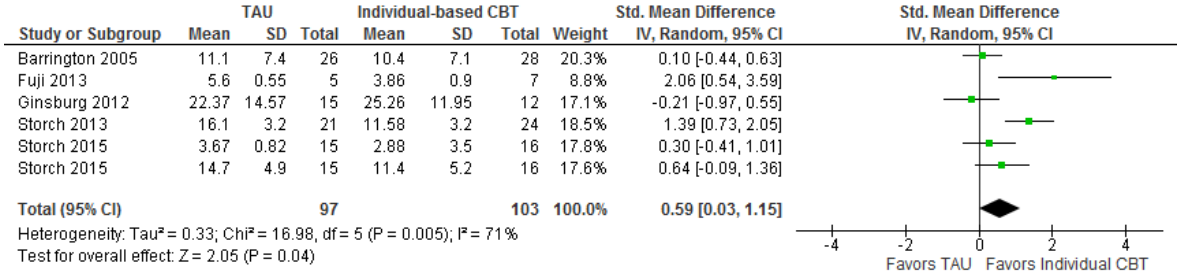


Figure 25. Forest plot: Individual-based CBT vs. TAU, continuous measure

CBT modalities versus attention control

Individual-based CBT versus attention control

Meta-analysis of 7 trial on the difference between individual-based CBT and attention control showed a mean effect size (SMD) of 0.20 [95% CI, -0.06 to 0.46], demonstrating no significant difference in efficacy between individual-based CBT and attention control. There was no evidence of significant heterogeneity between trials. The effect size estimates and forest plot of the individual studies can be seen in Fig. 26.

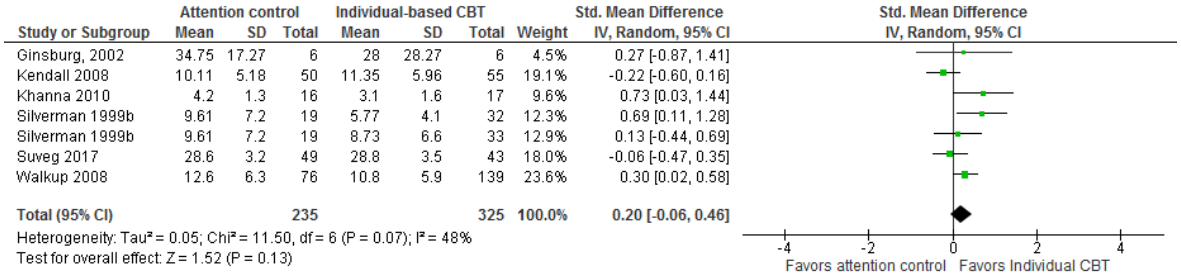


Figure 26. Forest plot: Individual-based CBT vs. attention control, continuous measure

Group-based CBT versus attention control

Meta-analysis of 4 trials on the difference between group-based CBT and attention control showed a mean effect size (SMD) of 1.30 [95% CI, -0.28 to 2.88], demonstrating no significant difference between group-based CBT and attention control. There was a significant amount of heterogeneity between trials. The effect size estimates and forest plot of the individual studies can be seen in Fig. 27.

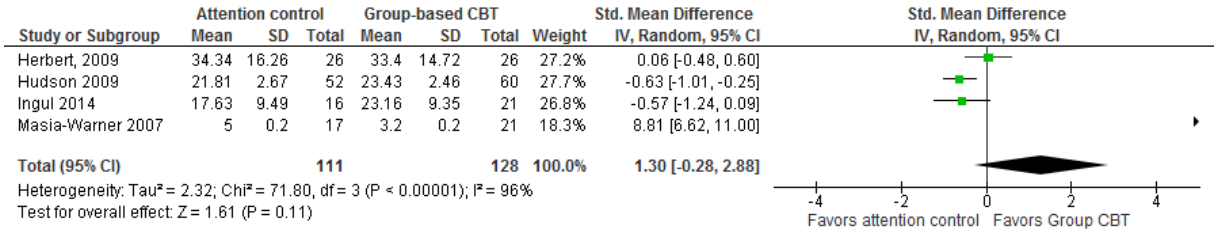


Figure 27. Forest plot: Group-based CBT vs. attention control, continuous measure

Family-based CBT versus attention control

Meta-analysis of 1 trial on the difference between family-based CBT and attention control showed a mean effect size (SMD) of 0.17 [95% CI, -0.21 to 0.55], demonstrating no significant difference in efficacy between family-based CBT and attention control. Only one study (Kendall et al., 2008) had family-based CBT vs. attention control. Therefore, estimated effect size and heterogeneity could not be calculated.

Remote-based CBT versus attention control

Meta-analysis of 1 trial on the difference between remote-based CBT and attention control showed a mean effect size (SMD) of 1.09 [95% CI, 0.34 to 1.84], demonstrating that remote-based CBT have lower anxiety score than attention control. However, only one study

(Khanna & Kendall, 2010) had remote-based CBT vs. attention control. Therefore, estimated effect size and heterogeneity could not be calculated.

CBT modalities versus SSRIs

Only one CBT modular (individual-based CBT) had SSRIs continuous measure comparison in the meta-analysis. Meta-analysis of 1 trials on the difference between individual-based CBT and SSRIs showed a mean effect size (SMD) of -0.16 [95% CI, -0.40 to 0.07], demonstrating no significant difference in efficacy between individual-based CBT and SSRIs. However, only one study (Walkup et al., 2008) had individual-based CBT vs. SSRIs comparison. Therefore, estimated effect size and heterogeneity could not be calculated.

CBT modalities versus combination of CBT and SSRIs

Only one CBT modular (individual-based CBT) had combination CBT and SSRIs continuous measure comparison in the meta-analysis. Meta-analysis of 1 trials on the difference between individual-based CBT and combination showed a mean effect size (SMD) of -0.57 [95% CI, -0.81 to -0.33], demonstrating that combination of CBT and SSRIs have, on average, lower anxiety score than individual-based CBT. Only one study (Walkup et al., 2008) had individual-based CBT vs. combination of SSRIs and CBT comparison. Therefore, estimated effect size and heterogeneity could not be calculated.