Comparative Effectiveness Review
Number 192

Anxiety in Children

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This report is based on research conducted by the Mayo Clinic Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00013-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may periodically be assessed for the currency of conclusions. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officers named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

The list of Key Informants who provided input to this report follows:

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Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Anxiety in Children

Structured Abstract

Objectives. To evaluate the comparative effectiveness and safety of treatments for childhood anxiety disorders, including panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, and separation anxiety.

Data sources. We searched MEDLINE®, Embase®, PsycINFO®, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and SciVerse Scopus through February 1, 2017, and reviewed bibliographies and the gray literature.

Review methods. We included randomized and non-randomized comparative studies that compared psychotherapy, pharmacotherapy, or a combination in children ages 3 to 18 years with panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, or separation anxiety. Pairs of independent reviewers selected studies using pre-specified inclusion and exclusion criteria.

Results. We included 206 studies. Compared with pill placebo, selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors improved primary anxiety symptoms (moderate to high strength of evidence [SOE]). Tricyclic antidepressants marginally improved clinical response (low SOE). Benzodiazepines did not show significant improvement in primary anxiety symptoms (low SOE). Data on head-to-head comparisons across drugs were sparse (only 2 RCTs; low SOE). Compared with waitlisting or no treatment, cognitive behavioral therapy (CBT) improved primary anxiety symptoms (clinician, child, and parent report), function, remission, and clinical response (low to moderate SOE). Compared with other therapies (attention control or treatment as usual), CBT reduced primary anxiety symptoms (child report; moderate SOE). Compared with CBT alone, the combination of imipramine and CBT reduced primary anxiety symptoms (child report) and function (moderate SOE). The combination of sertraline and CBT reduced primary anxiety symptoms (clinician report), improved function, and increased clinical response compared with CBT alone or sertraline alone (moderate SOE). CBT reduced primary anxiety symptoms and improved function more than fluoxetine, and was more likely to increase remission than sertraline. Medications increased short-term adverse events that were mostly not serious (low or moderate SOE). Studies were too small or too short to assess suicidality with SSRI or SNRI. One trial showed a statistically nonsignificant increase in suicidal ideation with venlafaxine (low SOE).

Conclusions. CBT is effective in reducing anxiety symptoms and improving function. Medications, primarily those targeting serotonin, are also effective and were associated with various short-term adverse events, which were mostly not serious, but studies were too small or too short to assess suicidality with SSRI or SNRI. The combination of medications and CBT is likely more effective than either treatment alone. Comparative effectiveness evidence between various medications and comparing CBT versus medications, or the combination, is limited and represents a need for research in this field. Future research is needed to evaluate components of CBT, effect modifiers of treatment, and long-term safety of drugs, and needs to be more inclusive of underserved populations and minorities.

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Introduction

Background

Childhood anxiety disorders are very common, affecting one in eight children.[1] The National Institute of Mental Health estimates a prevalence between the ages 13 and 18 years of 25.1 percent and a lifetime prevalence of 5.9 percent for severe anxiety disorder.[2] Anxiety disorders in childhood generally follow an impairing course leading to additional psychopathology and often interfere with social, emotional, and academic development.[3, 4]

Multiple treatment options are available, including psychotherapy, pharmacotherapy, and combined treatment approaches. Cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitor (SSRIs) are considered by many to be first line treatments.[5-9] CBT is generally recommended as the first-line treatment by World Health Organization (WHO), National Institute for Health and Care Excellence (NICE), and British Columbia Medical Services Commission.[10-12] In addition to CBT, other psychotherapy approaches include: psychoanalysis, family therapy, and education support. Pharmacotherapy is also widely used, including SSRIs, serotonin–norepinephrine reuptake inhibitors (SNRIs), benzodiazepines, and others. Pharmacotherapy is commonly used when psychotherapy is not available, does not lead to adequate response, or for moderate or severe symptoms at initial presentation.

There is a great deal of uncertainty regarding comparative effectiveness and safety of all treatments for childhood anxiety disorders. The potential advantage of psychotherapy is related to being safe and noninvasive.[5, 6] The potential disadvantages are that it has limited availability,[13] requires multiple appointments,[14] and requires behavioral changes by children and families. The potential disadvantages of pharmacotherapy are that it has unknown effect on brain chemistry, has the potential for adverse events (AEs),[15, 16] and that its benefits may not persist after treatment has been discontinued.[17, 18] Currently, existing treatment guidelines provide inconsistent and at times conflicting advice.[10, 11, 19] Regarding SSRIs, one guideline specifically recommends that SSRIs should not be used in children,[11] while another recommends they be used if CBT is not sufficient,[10] and the third recommends their use for more severe presentations or if CBT is not available.[19] Furthermore, despite the fact that all guidelines recommended CBT as a first line treatment, the components that comprise CBT differ between guidelines. In addition, one guideline suggested mild severity be treated with general health promotion,[10] another recommended CBT regardless of severity,[11] and the third recommended CBT as a sole intervention only for mild to moderate symptoms.[19] Regarding other behavioral interventions, one organization specifically recommended that they should not be used,[11] another did not comment,[10] and the third recommended that multiple different interventions be considered including modalities that were later in the guidelines described as having little to no empirical support.[19] In addition, there were inconsistency between several recommendations and the supporting data, particularly when discussing the role of symptom severity in treatment decisions, the comparative effectiveness of different SSRIs, the use of SSRIs in preschool age youth, and the use of non-SSRIs medications.[20-22] Finally, additional inconsistencies exists between guidelines, such as the level of empirical support ascribed to an intervention, the relative value of different treatment modalities, or the specifics of treatment protocols.

Many factors have been proposed to interfere with participation or adherence to treatment and/or response to treatments, including severity of illness, comorbid conditions, family socioeconomic status (SES), externalizing symptoms, patient age, family dysfunction or stressor, and others. For example, treatment for children under six usually involves primarily parent

training/behavior management interventions; while treatment with children 6 and up is more likely to involve working directly with children. Evidence reviews and randomized controlled trials (RCTs) reported conflicting results regarding differential response rates by age groups.[23] Severity of symptoms is generally believed to be associated with worse outcomes and guidelines suggest a different treatment approach for these children.[11, 19] Despite many available treatments, the majority of children with anxiety disorders do not receive treatment.[24]

The objectives of this systematic review are to evaluate the comparative effectiveness of psychotherapy and pharmacotherapy for childhood anxiety disorders and to evaluate the harms and safety concerns associated with these treatments.

Based on the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), we plan to study the following types of anxiety: panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, and separation anxiety. Obsessive compulsive disorder (OCD) and post-traumatic stress disorder will be excluded as their treatment approaches are generally different from other types of anxiety.

Scope and Key Questions

Scope of the Review

This systematic review addresses the comparative effectiveness and harms of commonly used types of psychotherapy and pharmacotherapy as listed in Tables 1 and 2.

Table 1. Psychotherapy used to treat childhood anxiety

Psychotherapy	Subtype
Cognitive behavioral therapy (CBT): Attempts to change cognition and behavior, generally consisting of some combination of cognitive restructuring, relaxation training, and exposure therapy. Delivered during face-to-face appointment with the child and typically some degree of parent involvement.	Exposure therapy/systematic desensitization: contingency management exposure therapy; self-control exposure therapy
	Family focused cognitive behavior therapy
	Child focused cognitive behavior therapy
Other psychotherapies: Any other intervention that included child or parents working with a therapist to address anxiety. Included parent-directed behavioral interventions, mindfulness interventions, as well as non-cognitive behavioral therapies. This was not considered a homogeneous group.	Parent child interaction therapy
	Problem solving therapy
	Third wave (mindfulness) therapies
	Psychodynamic psychotherapy
	Family therapy
	Attention modification program
	Motivational interviewing
	Eye movement desensitization reprocessing therapy (EMDR)

Table 2. Medications used to treat childhood anxiety

Drug Class	Medication (Brand Name)
Serotonin reuptake inhibitor (SRI)/Selective serotonin reuptake inhibitor (SSRI)	Sertraline (Zoloft)
	Citalopram (Celexa)
	Escitalopram (Lexapro)
	Fluoxetine (Prozac)
	Fluvoxamine (Luvox)
	Paroxetine (Paxil)

Drug Class	Medication (Brand Name)
Serotonin-norepinephrine reuptake inhibitors (SNRI)	Venlafaxine (Effexor)
	Atomoxetine (Strattera)
	Reboxetine (Edronax)
	Duloxetine (Cymbalta)
Benzodiazepine	Alprazolam (Xanax, Niravam)
	Chlordiazepoxide (Librium)
	Clonazepam (Klonopin)
Tricyclic antidepressant (TCA)	Imipramine (Tofranil)
	Clomipramine (Anafranil)
Others	Mebicarum (Mebicar)
	Buspirone (Buspar)
	Mirtazapine (Remeron)
	Nefazodone (Dutonin, Nefadar, Serzone)

Key Questions

The following Key Questions (KQs) were determined based on input from multiple key informants and members of a Technical Expert Panel. The related PICOTS (population, interventions, comparisons, outcomes, timing, and setting) are listed in Table 3.

KQ 1: What is the comparative effectiveness of the available treatments for childhood anxiety disorders, including panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, and separation anxiety?

a. What is the evidence for the comparative effectiveness of psychotherapy, pharmacotherapy, and combined treatment approaches for childhood anxiety disorders?
b. What is the evidence of differential effectiveness of different classes of medication, and for different medications within classes?
c. What is the evidence of differential effectiveness of different psychotherapy approaches, delivery mode, and components of psychotherapy for childhood anxiety disorders that are necessary and sufficient for improvement (including number of treatments and intensity of psychotherapy)?
d. How does comparative effectiveness of interventions vary according to child/family characteristics, and disease characteristics, including age, sex, race, ethnicity, SES, diagnosis, child maltreatment, parent/family comorbidity, duration, maltreatment?
e. How does comparative effectiveness of interventions vary according to child comorbid conditions, including attention deficit hyperactivity disorder (ADHD), depression, substance abuse, autism spectrum disorder, behavioral disorders, and somatic medical conditions?

f. What are the treatment burdens (for patients, providers, and health systems) and contextual factors (patient/family preference, time associated with psychotherapy) that influence treatment choices for childhood anxiety disorders?

KQ 2: What are the comparative harms and safety concerns regarding the available treatments for childhood anxiety disorders, including panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, and separation anxiety?

a. What is the evidence for short-term and long-term patient experienced harms associated with treatments for childhood anxiety disorders?

Table 3. PICOTS (population, interventions, comparisons, outcomes, timing, and setting)

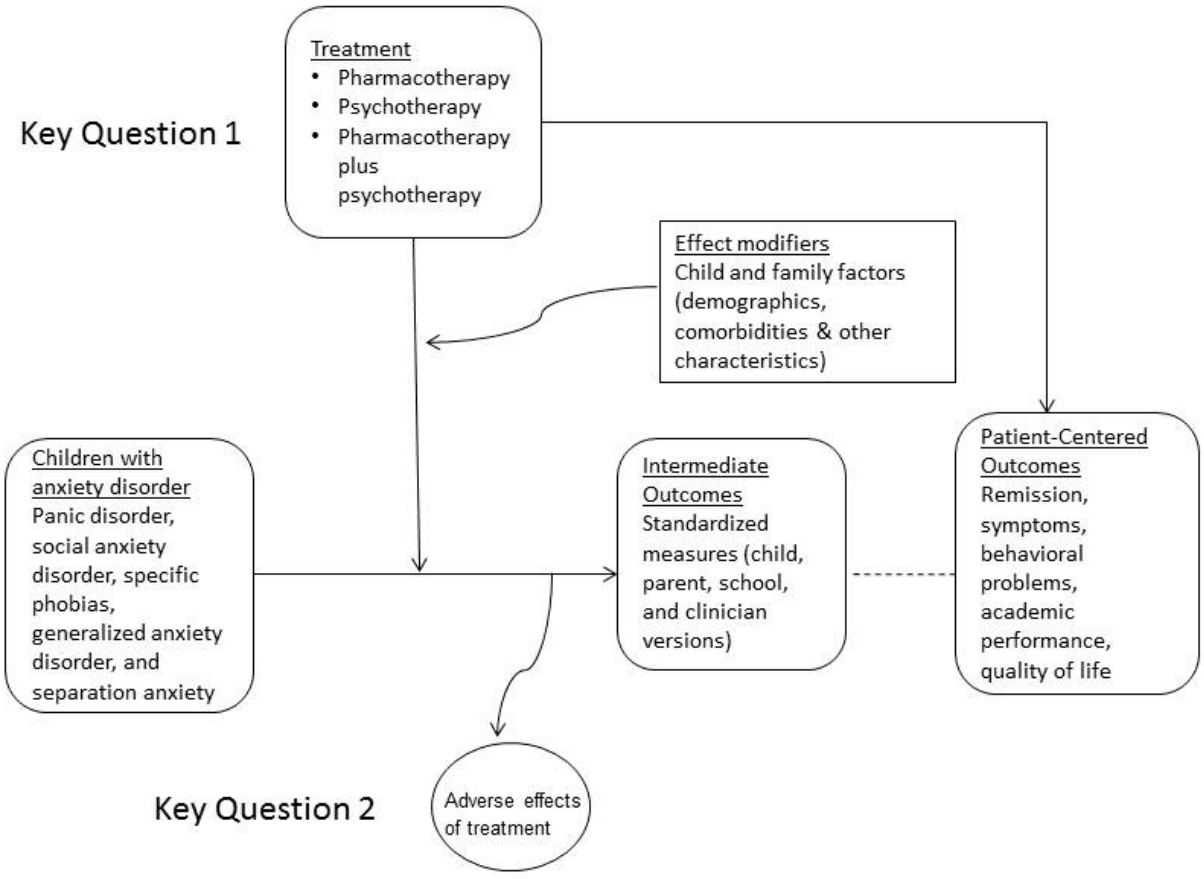
PICOTS Element	Description
Population	Children and adolescents ages 3 to 18 years with panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, and separation anxiety.
Interventions	Any psychotherapy, pharmacotherapy, alone or combined.
Comparisons	Other treatment, waitlisting or no treatment, pill placebo, attention control, or treatment as usual
Outcomes	Intermediate outcomes (standardized measures with child, parent, school, and clinician report) such as SCARED, RCMAS, Beck Anxiety Inventory, MASC, Liebowitz Social Anxiety Scale, Social Phobia and Anxiety Inventory for Children, SCAS, Fear Survey Schedule for Children – revised, STAIC, Anxiety Disorder Interview Schedule - child version. Patient centered outcomes such as remission, anxiety symptoms, diagnosis free, behavioral problems (Behavior Assessment System for Children, Achenbach Child Behavior Checklist), parent distress, therapeutic alliance, school attendance, reduction in impairment (Child Sheehan Disability Scale), quality of life (Multidimensional Child Health Questionnaire, and Youth Quality of Life Instrument – research version), avoiding hospitalization, length of treatment, availability of treatment, peer relationship. AEs, dropout from therapy.
Timing	Studies with any duration of followup.
Setting	Outpatient and hospital.

AEs: adverse events, MASC: multidimensional anxiety scale for children, RCMAS: revised children's manifest anxiety scale, SCARED: screen for anxiety-related emotional disorders, SCAS: Spence children's anxiety scale, STAIC: state trait anxiety inventory - child.

Methods

We developed an analytic framework to guide the whole process of the systematic review (Figure.1). We followed the established methodologies of systematic reviews as outlined in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Comparative Effectiveness Reviews.[25] The reporting complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements. [26] The study protocol is registered in the international prospective register of systematic reviews (PROSPERO #: CRD42016046542) and published on AHRQ Web site.

Figure 1. Analytic framework



Literature Search Strategy

Search Strategy

We conducted a comprehensive literature search of eight databases, including Ovid MEDLINE® In-Process & Other Non-Indexed Citations, Ovid MEDLINE®, Embase®,

PsycINFO®, Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and SciVerse Scopus from databases inception to February 1, 2017. We also searched U.S. Food and Drug Administration (FDA) new drug applications, ClinicalTrials.gov, Health Canada, Medicines and Healthcare Products Regulatory Agency (MHRA), AHRQ's Horizon Scanning System, conference proceedings, patient advocate group Web sites, and medical society Web sites. Relevant systematic reviews and meta-analysis, as well as reference mining of relevant publications, were used to identify additional existing and new literature. An experienced librarian, with the inputs from the study investigators, developed the search strategy (Appendix B). An independent experienced librarian peer-reviewed the search strategy.

Inclusion and Exclusion Criteria

The eligible studies had to meet all the following criteria: 1) children and adolescents between 3 and 18 years old with confirmed diagnosis of panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, or separation anxiety; 2) received any psychotherapy, pharmacotherapy, alone or combined; 3) reported outcomes of interest (standardized measures, patient centered outcomes, or safety outcomes). We included randomized controlled trials (RCTs), and comparative observational studies. Case reports or case series were used to identify additional adverse events (AEs). We did not restrict publication time, or study location. The detailed inclusion and exclusion criteria are attached in Appendix C.

Study Selection

Independent reviewers, working in duplicate and in pairs, screened the titles and abstracts of all citations using the inclusion and exclusion criteria. Studies included by either reviewer were retrieved for full-text screening. Independent reviewers, working in pairs, screened the full-text version of eligible references (Appendix Figure A.1). Discrepancies between the reviewers were resolved through discussions and consensus. If consensus was not reached, a third reviewer was added to resolve the difference.

Data Extraction

At the beginning of data extraction, we developed a standardized data extraction form to extract study characteristics (author, study design, inclusion and exclusion criteria, patient characteristics, interventions, comparisons, outcomes, and related items for assessing study quality and applicability). The standardized form was pilot-tested by all study team members using 10 randomly selected studies. We iteratively continued testing the form until no additional items or unresolved questions existed. A second reviewer verified data extraction. When there was missing information, we contacted the authors.

Assessment of Methodological Risk of Bias of Individual Studies

We evaluated the risk of bias of each included study using predefined criteria. For RCTs, we applied the Cochrane Collaboration's Risk of Bias tool (scored as high, low, unclear) to assess sequence generation; allocation concealment; participant, personnel, and outcome assessor blinding; attrition bias; incomplete outcome data; selective outcome reporting; and other sources of bias (e.g. imbalance of baseline characteristics, conflict of interest). [27] A judgment of overall risk of bias across the various domains was made focusing on random allocation, allocation

concealment and blinding (high risk of bias in any of these domains led to a high overall rating). We did not consider industry funding as an automatic indicator of high risk of bias. For observational studies, we selected appropriate items from the Newcastle-Ottawa Scale (i.e. high, moderate, low, unclear), focusing on the representativeness of the population, selection of the cohorts, ascertainment of exposure and outcomes, adequacy of follow-up land possible conflicts of interest.[28]

Data Synthesis

We summarized key features/characteristics (e.g. study populations, design, intervention, outcomes, and conclusions) of the included studies and presented data qualitatively in evidence tables for each Key Question.

We conducted meta-analyses to quantitatively summarize study findings. The main analyses were based on the effects measured post intervention, though length of followup (less than 6 months versus longer than 6 months) was evaluated in the subgroup analyses. We defined length of follow up as the time from the end of treatments to the time of outcome assessment. We used the intention-to-treat (ITT) principle. To facilitate the analyses, we categorized the standardized measures into groups: primary anxiety measure; secondary related measure; function related outcome; satisfaction with treatment; and social function (Table 4). For binary treatment response, we define it as 1) loss of principal anxiety diagnosis, or 2) Clinical Global Impression – Severity scale (CGI-S) 1 or 2; for remission, we define it as 1) loss of all anxiety diagnoses, or 2) Clinical Global Impression – Improvement scale (CGI-I) 1 or 2. We grouped AEs into symptoms related to abdominal/GI/appetite, behavior change, cold/infection/allergies, headache/dizzy/vision problems, fatigue/somnolence, difficulty sleeping, accidental injury, and suicide/suicidal ideation/self-harm. AEs were deemed to be serious if they were described as serious by the included studies, or led to discontinuation of treatment, significant morbidity, or mortality. We calculated relative risk (RR) and corresponding 95-percent confidence intervals (CIs) for binary outcomes and standardized mean difference (SMD) and related 95 percent confidence intervals for continuous outcomes. For count data (i.e. a single patient may experience more than one event), we calculated rate ratios, instead of RRs. The DerSimonian and Laird random effect method with the Knapp and Hartung adjustment of the variance was used when the number of the comparison was larger than two ($n>2$).[29] The fixed effect model based on the Mantel and Haenszel method was used when there were only two studies ($n=2$). We evaluated heterogeneity between studies using the I^2 indicator.

To further explore heterogeneity, we planned to stratify analysis conducting these subgroup analyses (based on a priori defined factors):

- Age
- Sex
- Race/ethnicity
- Household income
- Parent education level
- Family dysfunction/stressor
- Diagnosis
- Severity
- Length of follow-up
- Treatment sequence

- Comorbidities
- Provider
- Delivery mode
- Component of psychotherapy
- Cognitive behavioral therapy intensity
- Study settings

The statistical difference between subgroups was evaluated using one-way ANOVA tests

We evaluated potential publication bias by evaluating funnel plots symmetry and using the Egger linear regression test when the number of studies included in a direct comparison is large (n>=20). Two tailed p value <0.05 was considered as statistically significant. All statistical analyses were conducted using Stata version 14.2 (StataCorp LP, College Station, Texas).

Table 4. Categories of standardized outcome measures

Category	Description
Primary anxiety symptoms	All measures of child anxiety symptoms completed by the child, parent, or an examiner.
Secondary anxiety measures	Symptoms related to anxiety, but not the primary measure, such as coping, avoidance, or anxious thoughts.
Function	Measure of interference from symptoms or dysfunction in daily behaviors, such as school.
Satisfaction	Satisfaction with treatment or therapeutic alliance.
Social function	Measures of social skills or success with peer relationships.

Grading the Strength of Evidence

We graded strength of evidence (SOE) following the Methods Guide on assessing the strength of evidence.[25] The ratings were made via a consensus process among team members with expertise in evidence appraisal and guideline methodology. Randomized studies start with an initial level of high and observational studies start at a level of low. For each comparison and for the critical outcomes, we assessed the following domains for the total body of evidence addressing each outcome (all relevant studies in a particular comparison):

1) The methodological limitations of the studies (i.e., risk of bias): We lowered SOE one or two levels based on how serious the limitations in terms of their impact on inference.
2) Precision: We lowered SOE one or two levels based on the confidence intervals and sample size. If confidence intervals included appreciable benefits and harms (crossing no effect), or the total sample size was lower than 400 (an arbitrary cutoff that corresponds to a standardized small effect of 0.20 with significance of 0.05 and power of 0.80),[30] we rated SOE down by one level. When both of these situations were encountered simultaneously, we rated SOE down twice for imprecision and labeled this scenario as "severe imprecision".
3) Directness: We lowered SOE one level if the outcomes were surrogate and not patient-important.
4) Consistency: We lowered SOE one or two levels based on qualitative and statistical measures of heterogeneity (arbitrary cutoff of I-squared value of 60% or more was used as an indication for substantial heterogeneity).
5) The likelihood of publication bias: We lowered SOE one level if we suspected publication bias based on study reporting or statistical tests for publication bias.

Evidence derived from observational studies could be rated up if we observe a large effect, a dose response gradient, or if plausible confounding suggested a stronger association[31]. When judgment about two domains were borderline (for example, unclear risk of bias and possible publication bias), we opted to rate down once for both domains. Based on this assessment and the initial study design, we assigned SOE rating as high, moderate, low, or 'insufficient evidence to estimate an effect'. We produced summary of evidence tables for each comparison and for each outcome including data source, effect size and SOE rating with rationale for judgments that affected rating. We did not consider consistency in results across informants (child, parent and clinician) as a factor in rating SOE because we considered these as independent outcomes.

Assessing Applicability

Overall judgments about applicability were qualitatively made using the PICOTS framework. We focused on whether the populations, interventions, and comparisons in existing studies were representative of current practice. We reported any limitations in applicability of individual studies in evidence tables and limitations of applicability of the whole body of evidence in the discussion section. To further enhance applicability and considering that relative association measures and standardized effects are challenging to apply, we provided: 1) an approach to convert RRs to absolute effects (using baseline risks derived from the current data), and 2) an approach to convert SMDs to measures with units of scales commonly used in evaluating anxiety disorders in children (using standard deviations if such scales derived from the current data).

Results

Literature Searches and Evidence Base

The electronic search, grey literature and reference mining identified 32,156 citations. After title and abstract screening, 3,288 studies were retrieved for full text review. A total of 206 studies met eligibility criteria and were included in the analyses (Appendix A, Figure A.1).

For Key Question (KQ) 1, we identified a total of 110 randomized controlled trials (RCTs) and 4 non-randomized comparative studies. 19 RCTs compared drugs to pill placebo. 2 RCTs compared drugs to drugs. 2 RCTs compared cognitive behavioral therapy (CBT) to drugs. 88 studies (84 RCTs and 4 non-randomized comparative studies studies) compared CBT to pill placebo, waitlisting/no treatment, or attention control/treatment as usual. 3 RCTs compared combination treatment to drugs or CBT alone.

For KQ 2, 20 RCTs and non-randomized comparative studies reported adverse events (AEs). Majority of these studies compared drugs to pill placebo, while head-to-head comparisons were rare. In addition, 18 single cohort observational studies reported AEs related to different drugs.

We identified 51 studies (44 RCTs and 7 non-randomized comparative studies) that evaluated non-CBT psychotherapies. We did not quantitatively combine these studies due to the heterogeneity of the interventions. However, these studies are summarized in Appendix Table E.8—19. 52 studies (47 RCTs and 5 non-randomized comparative studies) compared different CBTs in terms of components (exposure session, cognitive strategy, and/or relaxation strategy), treatment intensity, parent involvement, and delivery mode (individual-based versus group-based).

We included 193 studies published in English, 10 studies in Spanish,[32-41] and 3 studies in German.[42-44] We excluded one study published in Turkish[45-47] and three in Persian.[48] In addition, we identified 225 relevant ongoing trials through clinicaltrials.gov.

Risk of bias in the majority of the included studies was rated as moderate to high (Appendix Table F.1 and F.2). We did not rate down strength of evidence (SOE) due to lack of blinding as this is not feasible in CBT and other psychotherapies.

Analysis Results

KQ 1: What is the comparative effectiveness of the available treatments for childhood anxiety disorders, including panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, and separation anxiety?

Drugs Versus Pill Placebo

Key Points

- Selective serotonin reuptake inhibitor (SSRIs) improved primary anxiety symptoms (clinician and parent report), function, remission, and clinical response, compared to pill placebo (moderate to high SOE).
- Serotonin–norepinephrine reuptake inhibitors (SNRIs) improved primary anxiety symptoms, compared to pill placebo (only clinician report) (high SOE).

- Tricyclic antidepressants marginally improved clinical response, compared to pill placebo (low SOE).
- Benzodiazepines did not show significant improvement in anxiety symptoms over pill placebo (low SOE).

Discussion

Nineteen RCTs[7, 22, 49-72] compared medications to pill placebo, including atomoxetine, clonazepam, clomipramine, duloxetine, fluvoxamine, fluoxetine, imipramine, paroxetine, sertraline, and venlafaxine. Overall, 2,498 patients were included with a mean age of 11.6 years old and 54.1 percent male. 13 studies[49-52, 54, 56, 58, 60-65] (68.4%) included patients without any comorbidity. 6 studies [7, 22, 53-55, 57, 66, 67, 69-73] included children with anxiety and comorbidity (attention deficit hyperactivity disorder (ADHD), autism, ODD, obsessive compulsive disorder (OCD) and other internalizing disorders). Details of the included studies can be found in Appendix Table E.1. We were unable to evaluate publication bias due to small number of studies (n<20) included in each comparisons.

As a class, SSRIs improved primary anxiety symptoms (clinician and parent report), function, remission, and clinical response, compared to pill placebo (moderate to high SOE). SNRIs improved primary anxiety symptoms (clinician report, high SOE). TCAs marginally improved clinical response (low SOE), whereas benzodiazepines did not show significant improvement in anxiety symptoms over pill placebo (low SOE). Results of the comparisons of drug classes with pill placebo and associated SOE are presented in Table 5. Results of the individual drugs comparisons with pill placebo are presented in Table 6.

Table 5. Strength of evidence for drug classes versus pill placebo

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
Benzodiazepine vs. Pill Placebo	Primary anxiety, clinician report	SMD: 0.30; 95% CI: -0.72 to 1.32; I^2=N/A	1 RCT (15 Patients)[57]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
SNRI vs. Pill Placebo	Primary anxiety, child report	SMD: -2.14; 95% CI: -9.75 to 5.48; I^2= 99.4%	3 RCTs (622 Patients)[55, 58, 62]	Severe imprecision (very wide CIs) and inconsistency	Insufficient
	Primary anxiety, parent report	SMD: -0.32; 95% CI: -0.63 to 0.00; I^2=N/A	1 RCT (153 Patients)[62]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Primary anxiety, clinician report	SMD: -0.45; 95% CI: -0.81 to -0.10; I^2=0.0%	3 RCTs (601 Patients)[55, 62, 64]	None	High (reduced anxiety)
	Function	SMD: -0.05; 95% CI: -0.24 to 0.13; I^2=93.4%	2 RCTs (448 Patients)[55, 64]	Severe imprecision (wide CIs) and inconsistency	Low (no difference)
SSRI vs. Pill Placebo	Primary anxiety, child report	SMD: -0.42; 95% CI: -0.96 to 0.12; I^2=27.5%	4 RCTs (197 Patients)[51, 53, 54, 61, 65]	Severe imprecision (small sample size and wide CIs)	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
	Primary anxiety, parent report	SMD: -0.61; 95% CI: -1.03 to -0.20; I^2=55.1%	2 RCTs (96 Patients)[53, 61]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Primary anxiety, clinician report	SMD: -0.65; 95% CI: -1.10 to -0.21; I^2=73.4%	7 RCTs (675 Patients)[7, 22, 49, 51, 53, 54, 61, 65, 67, 69-73]	Inconsistency	Moderate (reduced anxiety)
	Function	SMD: -0.59; 95% CI: to -0.85 to -0.34; I^2= 0.0%	4 RCTs (680 Patients)[7, 51, 53, 65, 67, 69-73]	None	High (improved function)
	Secondary measure	SMD: -0.19; 95% CI: -0.55 to 0.17; I^2=75.1	1 RCT (124 Patients)[51, 54]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Social function	SMD: 0.18; 95% CI: -0.26 to 0.62; I^2 = N/A	1 RCT (80 Patients)[51]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Remission	RR: 2.04; 95% CI: 1.37 to 3.04; I^2=N/A	2 RCTs (95 Patients)[53, 54]	Imprecision small sample size)	Moderate (improved remission)
	Response	RR: 1.96; 95% CI: 1.60 to 2.40; I^2=0.0%	2 RCTs (396 Patients)[53, 65]	Imprecision (small sample size)	Moderate (improved response)
TCA vs. Pill Placebo	Primary anxiety, child report	SMD: 0.36; 95% CI: -0.27 to 0.99; I^2=45.6%	2 RCTs (41 Patients)[54, 74]	Severe imprecision (small sample size and wide CIs).	Low (no difference)
	Primary anxiety, parent report	SMD: 0.46; 95% CI: -0.41 to 1.33; I^2=N/A	1 RCT (21 Patients)[74]	Methodological limitations, severe imprecision (small sample size and wide CI)	Insufficient
	Remission	RR: 1.83; 95% CI: 0.74 to 4.55; I^2=N/A	1 RCT (20 Patients)[54]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Response	RR: 1.72; 95% CI: 1.01 to 2.91; I^2=N/A	1 RCT (35 Patients)[56]	Severe imprecision (small sample size and wide CIs)	Low (improved response)

CI: confidence interval, N/A: not applicable, RCT: randomized control trial, RR: relative risk, SMD: standardized mean difference, SNRI: serotonin–norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, TCA: tricyclic antidepressants.

[a] The sample size includes the number of patients from each comparison.

[b] Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

Table 6. Strength of evidence for individual drugs versus pill placebo

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
Atomoxetine (class: SNRI)	Primary anxiety, child report	SMD: -0.29; 95% CI: -0.51	2 RCTs (331 Patients)[55, 62]	Imprecision (small sample size)	Moderate (reduced

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
vs. Pill Placebo		to - 0.08; I^2=0.0%			anxiety)
	Primary anxiety, clinician report	SMD: -0.56; 95% CI: -0.78 to -0.34; I^2=0.0%	2 RCTs (331 Patients)[55, 62]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Primary anxiety, parent report	SMD: -0.23; 95% CI: -0.55 to 0.08; I^2 = N/A	1 RCT (155 Patients)[62]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Function	SMD: -0.46; 95% CI: -0.76 to -0.16; I^2 = N/A	1 RCT (176 Patients)[55]	Imprecision (small sample size)	Moderate (improved function)
Clomipramine (class: TCA) vs. Pill Placebo	Primary anxiety, child report	SMD: -0.07; 95% CI: -0.95 to 0.81; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
Duloxetine (class: SNRI) vs. Pill Placebo	Primary anxiety, clinician report	SMD: -0.43; 95% CI: -0.67 to -0.19; I^2=N/A	1 RCT (272 Patients)[64]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Function	SMD: -0.35; 95% CI:-0.59 to -0.11; I^2=N/A	1 RCT (272 Patients)[64]	Imprecision (small sample size)	Moderate (improved function)
Fluoxetine (class: SSRI) vs. Pill Placebo	Primary anxiety, child report	SMD:-0.38; 95% CI: -1.26 to 0.50; I^2=43.3%	2 RCTs (154 Patients)[51, 53, 54]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, parent report	SMD:-0.46; 95% CI: -0.92 to 0.01; I^2=N/A	1 RCT (74 Patients)[53]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, clinician report	SMD:-0.40; 95% CI: -0.72 to -0.01; I^2=N/A	2 RCTs (154 Patients)[51, 53]	Severe imprecision (wide CIs and small sample size)	Low (reduced anxiety)
	Function	SMD: -0.75; 95% CI: -1.07 to -0.42; I^2= 0.0%	2 RCTs (154 Patients)[51, 53]	Imprecision (small sample size)	Moderate (improved function)
	Secondary measure	SMD: -0.19; 95% CI: -0.55 to 0.17; I^2=75.1%	1 RCT (124 Patients)[51, 54]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Social function	SMD: 0.18; 95% CI: -0.26 to 0.62; I^2=N/A	1 RCT (80 Patients)[51]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Remission	RR: 2.04; 95% CI: 1.32 to 3.04; I^2=N/A	2 RCTs (95 Patients)[53, 54]	Imprecision (small sample size)	Moderate (improved remission)
	Response	RR: 1.70; 95% CI: 1.01 to 2.82; I^2=0.0%	1 RCT (74 Patients)[53]	Severe imprecision (wide CIs and small	Low (improved response)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
				sample size)	
Fluvoxamine (class: SSRI) vs. Pill Placebo	Primary anxiety, clinician report	SMD: -0.97; 95% CI: -1.31 to -0.63; I^2=69.1%	2 RCTs (153 Patients)[22, 49]	Imprecision (small sample size) and inconsistency	Low (reduced anxiety)
Imipramine (class: TCA) vs. Pill Placebo	Primary anxiety, child report	SMD: 0.80; 95% CI: -0.10 to 1.70; I^2=N/A	1 RCT (21 Patients)[74]	Methodological limitations, severe imprecision (small sample size and wide CI)	Insufficient
	Primary anxiety, parent report	SMD: 0.46; 95% CI: -0.41to 1.33; I^2=N/A	1 RCT (21 Patients)[74]	Methodological limitations, severe imprecision (small sample size and wide CI)	Insufficient
Paroxetine (class: SSRI) vs. Pill Placebo	Primary anxiety, clinician report	SMD: -0.71; 95% CI: -1.06 to -0.37; I^2=N/A	1 RCT (137 Patients)[65]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Function	SMD: -0.61; 95% CI: -0.83 to -0.38; I^2=N/A	1 RCT (317 Patients)[65]	Imprecision (small sample size)	Moderate (improved function)
	Response	RR: 2.02; 95% CI:1.62 to 2.51; I^2=N/A	1 RCT (322 Patients)[65]	Imprecision (small sample size)	Moderate (improved response)
Sertraline (class: SSRI) vs. Pill Placebo	Primary anxiety, child report	SMD: -0.75; 95% CI: -1.62 to 0.12; I^2=N/A	1 RCT (22 patients)[61]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, parent report	SMD: -0.24; 95% CI: -2.16 to -0.32; I^2=N/A	1 RCT (22 Patients)[61]	Severe imprecision (wide CIs and small sample size)	Low (reduced anxiety)
	Primary anxiety, clinician report	SMD: -71; 95% CI: -0.99 to -0.42; I^2=89.9%	2 RCTs (231 Patients)[7, 61, 67, 69-73]	Imprecision (small sample size), inconsistency	Low (reduced anxiety)
	Function	SMD: -0.46; 95% CI: -0.74 to -0.17; I^2=N/A	1 RCT (209 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (improved function)
Venlafaxine (class: SNRI) vs. Pill Placebo	Primary anxiety, child report	SMD: -1.96; 95% CI: -2.23 to -1.64; I^2=99.6%	2 RCTs (443 Patients)[58, 62]	Inconsistency	Moderate (reduced anxiety)
	Primary anxiety, parent report	SMD: -0.32; 95% CI: -0.63 to 0.00; I^2=N/A	1 RCT (153 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, clinician report	SMD: -0.42; 95% CI: -0.74 to -0.10; I^2=N/A	1 RCT (153 Patients)[62]	Imprecision (small sample size)	Moderate (reduced anxiety)
Clonazepam (class: Benzodiazepine	Primary anxiety, clinician report	SMD: 0.30; 95% CI: -0.72 to 1.32; I^2=N/A	1 RCT (15 Patients)[57]	Severe imprecision (wide CIs and small	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
) vs. Pill Placebo				sample size)	
Venlafaxine (class: SNRI) vs. Attention Control or Treatment As Usual	Primary anxiety, child report	SMD: -0.40; 95% CI: -0.72 to -0.09; I^2=N/A	1 RCT (158 Patients)[62]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Primary anxiety, parent report	SMD: -0.42; 95% CI: -0.73 to -0.10; I^2=N/A	1 RCT (158 Patients)[62]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Primary anxiety, clinician report	SMD: -0.09; 95% CI: -0.40 to 0.22; I^2=N/A	1 RCT (158 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
Atomoxetine (class: SNRI) vs. Attention Control or Treatment As Usual	Primary anxiety, child report	SMD: -0.26; 95% CI: -0.57 to 0.05; I^2=N/A	1 RCT (154 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, parent report	SMD: -0.34; 95% CI: -0.65 to -0.03; I^2=N/A	1 RCT (154 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (reduced anxiety)
	Primary anxiety, clinician report	SMD: -0.33; 95% CI: -0.65 to -0.02; I^2=N/A	1 RCT (154 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (reduced anxiety)

CI: confidence interval, N/A: not applicable, RCT: randomized control trial, RR: relative risk, SMD: standardized mean difference, SNRI: serotonin–norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, TCA: tricyclic antidepressants.

[a]The sample size includes the number of patients from each comparison.

[b] Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

Drugs Versus Drugs

Key Points

- Only two RCTs conducted head-to-head comparison.
- Compared to clomipramine, fluoxetine was more effective in improving primary anxiety symptoms (child report) (low SOE).
- No significant difference was found between venlafaxine and atomoxetine on primary anxiety symptoms (child, parent, and clinician reports) (low SOE).

Discussion

One RCT[54, 62] compared fluoxetine to clomipramine[54] and another RCT compared venlafaxine to atomoxetine.[62] Overall, 39 patients were included with age range of 6-17 years old and 52.2% male. These 2 studies[54, 62] included patients without any comorbidity. Details of the included studies can be found in Appendix Table E.2. We were unable to evaluate publication bias due to small number of studies (n<20) included in each comparisons.

Compared to clomipramine, fluoxetine was more effective in improving primary anxiety symptoms (child report, low SOE); while venlafaxine and atomoxetine were not significantly

different in improving primary anxiety symptoms (low SOE). Results of the individual drugs comparisons with drugs are presented in Table 7.

Table 7. Strength of evidence for drugs versus drugs

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of evidence[b]	Overall Evidence Strength (Direction of Effect)
Fluoxetine (class: SSRI) vs. Clomipramine (class: TCA)	Primary anxiety, child report	SMD: -1.01; 95% CI: -2.02 to -0.09; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (wide CIs and small sample size)	Low (reduced anxiety)
	Remission	RR: 1.20; 95% CI: 0.69 to 2.09; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
Venlafaxine (class: SNRI) vs. Atomoxetine (class: SNRI)	Primary anxiety, child report	SMD: -0.12; 95% CI: -0.43 to 0.20; I^2=N/A	1 RCT (154 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, parent report	SMD: -0.08; 95% CI: -0.39 to 0.24; I^2=N/A	1 RCT (154 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, clinician report	SMD: 0.25; 95% CI: -0.07 to 0.57 I^2=N/A	1 RCT (154 Patients)[62]	Severe imprecision (wide CIs and small sample size)	Low (no difference)

CI: confidence interval, N/A: not applicable, RCT: randomized control trial, RR: relative risk, SMD: standardized mean difference, SNRI: serotonin–norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, TCA: tricyclic antidepressants.

[a] The sample size includes the number of patients from each comparison.

[b] Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

Drugs Versus CBT

Key Points

- Only two RCTs compared CBT to SSRIs.
- CBT reduced primary anxiety symptoms and improved function more than fluoxetine (moderate SOE).
- CBT was more likely to increase remission than sertraline (moderate SOE).

Discussion

One RCT compared CBT to fluoxetine.[51, 63] Overall, 102 patients were included with a mean age of 11.6 years old and 51.5 percent male. Details of the included study can be found in Appendix Table E.3. CBT was more effective in improving primary anxiety symptoms (clinician report), function, and secondary anxiety measures (moderate SOE). Table 8 includes summary of the results and assessment of SOE.

One RCT of 272 patients with a primary diagnosis of social anxiety disorder, generalized anxiety disorder, or social anxiety disorder (mean age: 10.7 years), compared CBT to sertraline.[7, 67, 69-73] Patients were randomized to receive either 14 sessions of CBT or sertraline (up to 200 mg per day). Details of the included study can be found in Appendix Table E.3. CBT was more likely to increase remission (moderate SOE). There were no other significant differences in other outcomes (low SOE) (Table 8).

Table 8. Strength of evidence for drugs versus CBT

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
Fluoxetine (class: SSRI) vs. CBT	Primary anxiety, child report	SMD:-0.16; 95% CI: -0.55 to 0.24; I^2=N/A	1 RCT (102 Patients)[51]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, clinician report	SMD:0.78; 95% CI: 0.37 to 1.18; I^2=N/A	1 RCT (102 Patients)[51]	Imprecision (small sample size)	Moderate (increased anxiety)
	Function	SMD: 0.54; 95% CI: 0.14 to 0.94; I^2=N/A	1 RCT (102 Patients)[51]	Imprecision (small sample size)	Moderate (reduced function)
	Secondary measure	SMD: 0.51; 95% CI: 0.11 to 0.90; I^2=N/A	1 RCT (102 Patients)[51]	Imprecision (small sample size)	Moderate (increased anxiety)
	Social function	SMD: -0.19; 95% CI: -0.58 to 0.21; I2=N/A	1 RCT (102 Patients)[51]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
Sertraline (class: SSRI) vs. CBT	Primary anxiety, clinician report	SMD: -0.15; 95% CI: -0.31 to 0.02; I^2= N/A	1 RCT (272 Patients)[7, 67, 69-73]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Function	SMD: -0.12; 95% CI: -0.35 to 0.12; I^2= N/A	1 RCT (272 Patients)[7, 67, 69-73]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Remission	RR: 0.57; 95% CI: 0.48 to 0.69; I^2=N/A	1 RCT (272 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (reduced remission)
	Response	RR: 0.97; 95% CI: 0.80 to 1.17; I^2=N/A	1 RCT (272 Patients)[7, 67, 69-73]	Severe imprecision (wide CIs and small sample size)	Low (no difference)

CI: confidence interval, CBT: cognitive behavioral therapy, N/A: not applicable, RCT: randomized control trial, RR: relative risk, SMD: standardized mean difference, SNRI: serotonin–norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, TCA: Tricyclic antidepressants

[a] The sample size includes the number of patients from each comparison.

[b] Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

CBT Versus Control (Pill Placebo, Waitlisting/No Treatment, or Attention Control/Treatment as Usual)

Key Points

- Compared to pill placebo, CBT improved secondary anxiety measures (low SOE).
- Compared to waitlisting or no treatment, CBT improved primary anxiety symptoms (clinician, child, and parent report), function, remission, and clinical response (low to moderate SOE).

- Compared to attention control or treatment as usual, CBT reduced primary anxiety symptoms (child report) (moderate SOE).

Discussion

Eighty-four RCTs and 4 non-randomized comparative studies compared CBT to controls. 29 RCTs[7, 33, 38, 41, 63, 67-72, 75-101] and 1 non-randomized comparative study [102] compared CBT to attention control/treatment as usual, 60 RCTs [33, 34, 36, 39-42, 44, 84, 86, 89, 100, 101, 103-153] and 3 non-randomized comparative study [154-156] compared CBT versus waitlisting/no treatment, and 3 RCTs compared CBT versus pill placebo.[7, 51, 63, 67-72] Overall, 6,978 patients were included with a mean age of 11.2 years and 47.9 percent male. 59 studies[33, 34, 36, 38-42, 44, 51, 63, 75-81, 83, 85-87, 89, 90, 92, 94, 96, 100, 102-105, 107-109, 110 , 113, 117, 118, 120, 123-126, 130, 131, 133, 135, 137, 139-145, 147, 154-156] (67.0%) of included patients without any comorbidity. 30 studies[7, 67-73, 82, 84, 88, 91, 93, 95, 97-99, 101, 106, 111, 112, 114-116, 119, 121, 122, 127-129, 134, 136, 138, 146, 148-150, 152, 153] included children with anxiety and other comorbidities. 8 studies[39, 42, 44, 89, 98, 99, 104, 113, 133] (9.1%) didn't provide enough quantitative data and were excluded from meta-analyses. Details of the included studies can be found in Appendix Tables E.4 to E.6. We found indications of potential publication bias when CBT was compared to waitlisting on primary anxiety symptoms (Appendix Figures H.1 to H.3). We were unable to evaluate publication bias due to small number of studies (n<20) included in other comparisons.

Compared to pill placebo, CBT improved secondary anxiety measures (low SOE). Compared to waitlisting or no treatment, CBT improved primary anxiety symptoms (clinician, child, and parent report), function, remission, and clinical response (low to moderate SOE). Compared to attention control or treatment as usual, CBT reduced primary anxiety symptoms (child report, moderate SOE). Table 9 includes summary of the results and assessment of SOE.

Table 9. Strength of evidence for CBT versus pill placebo, waitlisting/no treatment, or attention control/treatment as usual

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
CBT vs. Pill Placebo	Primary anxiety, child report	SMD: -0.22; 95% CI: -0.64 to 0.19; I^2=N/A	1 RCT (96 Patients)[51]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Primary anxiety, clinician report	SMD: -0.61; 95% CI: -0.85 to -0.37; I^2=89.1%	2 RCTs (311 Patients)[7, 51, 67, 69-73]	Methodological limitations, inconsistency, imprecision (small sample size)	Insufficient
	Function	SMD:-0.60;	2 RCTs (311	Methodological	Insufficient

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		95% CI: -0.84 to -0.36; I^2=90.5%	Patients)[7, 51, 67, 69-73]	limitations, inconsistency, imprecision (small sample size)	
	Social function	SMD: 0.35; 95% CI: -0.07, 0.76; I^2=N/A	1 RCT (96 Patients)[51]	Methodological limitations, severe imprecision (small sample size and wide CI)	Insufficient
	Secondary measure	SMD: -0.02; 95% CI: -0.42 to 0.37; I^2=99.1%	1 RCT (96 Patients)[51, 63]	Imprecision (small sample size) and inconsistency	Low (no difference)
CBT vs. Waitlisting or No Treatment	Primary anxiety, child report	SMD: -0.77; 95% CI: -1.06 to -0.47; I^2=86.5%	41 RCTs, 2 non-randomized comparative studies (2,297 Patients)[33, 36, 40, 86, 105-112, 114-117, 119, 120, 122-130, 134-139, 141-146, 150, 151, 153-155, 157, 158]	Inconsistency[c]	Moderate (reduced anxiety)
	Primary anxiety, parent report	SMD: -0.88; 95% CI: -1.23 to -0.54; I^2=81.2%	27 RCTs 2 non-randomized comparative studies (1,540 Patients)[33, 103, 105, 106, 110, 111, 114-116, 121-124, 126-128, 131, 132, 134, 136-138, 141, 143, 145, 146, 150, 151, 153, 155, 158]	Inconsistency[c]	Moderate (reduced anxiety)
	Primary anxiety, clinician report	SMD: -1.38; 95% CI: -1.95 to -0.81; I^2=88.3%	32 RCTs, 2 non-randomized comparative studies (1,926 Patients)[33, 36, 40, 86, 106, 107, 109, 111, 112, 114, 117-122, 126, 127, 129, 131, 132, 136, 137, 139, 143-146, 148-150, 152-154, 158]	Inconsistency[c]	Moderate (reduced anxiety)
	Function	SMD: -0.80, 95% CI; -1.41 to - 0.20; I^2=91.6%	18 RCTs, 1 non randomized control trial (937 Patients)[33, 36, 106, 108, 114, 117, 119, 122, 126, 128, 129, 132, 134, 136, 141, 146, 148, 152, 154]	Inconsistency	Moderate (improved function)
	Social function	SMD: -0.02; 95% CI; -0.77 to 0.74; I^2=86.1%	9 RCTs, 1 non-randomized control trial (385 Patients)[36, 41, 114-117, 119, 122, 123, 144, 154]	Severe imprecision (wide CI and small sample size), inconsistency	Insufficient
	Satisfaction	SMD: 0.90; 95% CI: -0.58 to 1.21; I^2=0.0%	2 RCTs (146 Patients)[86, 157]	Severe imprecision (wide CI and small sample size)	Low (no difference)
	Secondary measure	SMD: 0.37; 95% CI: -0.32 to 1.05; 92.4%	16 RCTs, 2 non-randomized control (1,111 Patients)[33, 36, 40, 86, 108, 110, 115, 116, 119, 121-125, 130, 135, 137, 144, 147,	Imprecision (wide CI), inconsistency	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
			154		
	Remission	RR: 4.08; 95% CI: 1.05 to 15.80; I^2=80.8%	7 RCTs (307 Patients)[33, 34, 108, 111, 122, 134, 149]	Methodological limitations, imprecision (small sample size), inconsistency	Low (improved remission)
	Response	RR: 4.72; 95% CI: 2.39 to 9.32; I^2=80.4%	14 RCTs (733 Patients)[36, 81, 86, 115, 116, 120-122, 124, 126-128, 136, 143, 144, 148, 149]	Inconsistency	Moderate (improved response)
CBT vs. Attention Control or Treatment As Usual	Primary anxiety, child report	SMD:-0.36; 95% CI: -0.67 to -0.05; I^2=60.5%	12 RCTs, 1 non-randomized comparative study (704 Patients)[38, 76, 79, 80, 82, 83, 87, 88, 92, 94-96, 102]	Borderline imprecision and inconsistency	Moderate (reduced anxiety)
	Primary anxiety clinician report	SMD:-0.11; 95% CI: -0.36 to 0.14; I^2=28.6%	9 RCTs (486 Patients)[77-79, 82, 87, 92, 94, 97, 100]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	Primary anxiety, parent report	SMD: 0.04; 95% CI: -0.17 to 0.24; I^2=0.0%	7 RCTs, 1 non-randomized comparative study (533 Patients)[78-81, 92, 94, 96, 97, 102]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	Function	SMD: -0.70, 95% CI: -1.76 to -0.36; I^2=83.5%	5 RCTs (293 Patients)[38, 82, 95, 96, 101]	Methodological limitations, imprecision (small sample size), inconsistency	Insufficient
	Social function	SMD: -0.23, 95% CI: -0.66 to 0.21; I^2=40.9%	5 RCTs (330 Patients)[38, 78, 92, 101, 102]	Methodological limitations, severe imprecision (small sample size and wide CIs)	Insufficient
	Satisfaction	SMD: -0.03, 95% CI: -0.71 to 0.65; I^2=N/A	1 RCT (33 Patients)[82]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Secondary measure	SMD: -0.50; 95% CI: -1.28 to 0.29; I^2=N/A	3 RCTs (156 Patients)[38, 80, 81, 87]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Remission	RR: 1.51; 95% CI: 0.95 to 2.40; I^2=0.0%	4 RCTs (366 Patients}[79, 90, 92, 94]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Response	RR:1.90, 95% CI: 0.68 to 5.30; I^2=67.2%	5 RCTs (374 Patients)[79-81, 92, 94, 96]	Methodological limitations, severe imprecision (small sample size and wide CIs), inconsistency	Insufficient

CI: confidence interval, CBT: cognitive behavioral therapy, N/A: not applicable, RCT: randomized control trial, RR: relative risk, SMD: standardized mean difference.

[a] The sample size includes the number of patients from each comparison.

[b] Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

[c] There was a suggestion of publication bias; however, we did not rate down SOE.

CBT Combined With Drugs

Key Points

- Compared to CBT alone, the combination of imipramine and CBT reduced primary anxiety symptoms (child report) and function (moderate SOE).
- The combination of fluoxetine and CBT was found to have lower remission rate compared to CBT alone (low SOE).
- The combination of sertraline and CBT reduced primary anxiety symptoms (clinician report), improved function, and increased clinical response, compared to CBT alone (moderate SOE).
- The combination of sertraline and CBT improved primary anxiety symptoms (clinician report), function, and clinical response (moderate SOE), compared to sertraline alone (moderate SOE).

Discussion

One RCT with 63 patients compared the combination of imipramine and CBT to CBT alone[159]. All patients had major depressive disorder and at least one anxiety disorder. The mean age of the included patients was 13.9 years and 90.5 percent were Caucasians. Details of the included study can be found in Appendix Table E.7. Compared with CBT alone, adding imipramine to CBT reduced primary anxiety symptoms (child report) and improved function (moderate SOE).

One RCT of 41 anxious school refusing adolescents compared fluoxetine plus CBT to CBT[160]. Details of the included study can be found in Appendix Table E.7. Patients in the CBT and fluoxetine group had lower remission than CBT alone (low SOE).

One RCT of 272 patients compared the combination of CBT and sertraline to CBT, or to sertraline[7, 67, 69-73]. Patients (7-17 years old; mean age: 10.7; primary diagnosis of social anxiety disorder, generalized anxiety disorder, or social anxiety disorder) were randomized to receive either 14 sessions of CBT or sertraline (up to 200 mg per day). Details of the included study can be found in Appendix Table E.7. Compared to CBT alone, adding sertraline reduced primary anxiety symptoms (clinician report), improved function, and improved clinical response (moderate SOE). The addition of CBT to sertraline (compared to sertraline alone) improved primary anxiety symptoms (clinician report), function, and likelihood of clinical response (moderate SOE) (Table 10).

Table 10. Strength of evidence for CBT combined with drugs

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
Imipramine (class: TCA) + CBT vs. CBT	Primary anxiety, child report	SMD: -0.74; 95% CI: -1.26 to -0.23; I^2=N/A	1 RCT (63 Patients)[159]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Primary anxiety. clinician report	SMD: -0.61; 95% CI: -1.11 to 0.10; I^2=N/A	1 RCT (63 Patients)[159]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Function	SMD: -1.27; 95% CI: -1.81	1 RCT (63 Patients)[159]	Imprecision (small sample size)	Moderate (improved

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		to -0.73; I^2=N/A			function)
Fluoxetine (class: SSRI) + CBT vs. CBT	Function	SMD: -0.13; 95% CI: -0.74 to 0.48; I^2=N/A	1 RCT (41 Patients)[160]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Secondary measure	SMD: -0.03; 95% CI: -0.59 to 0.64; I^2=N/A	1 RCT (41 Patients)[160]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Response	RR: 1.71; 96% CI: 0.69 to 4.24; I^2=N/A	1 RCT (41 Patients)[160]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Remission	RR: 0.24; 95% CI: 0.06 to 0.99; I^2=N/A	1 RCT (41 Patients)[160]	Severe imprecision (small sample size and wide CI)	Low (reduced remission)
CBT + Sertraline (class: SSRI) vs. CBT	Primary anxiety, clinician report	SMD: -0.69; 95% CI: -0.93 to -0.45; I^2=N/A	1 RCT (272 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Function	SMD: -0.47; 95% CI: -0.70 to -0.23; I^2=N/A	1 RCT (272 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (improved function)
	Remission	RR: 0.45; 95% CI: 0.36 to 0.59; I^2=N/A	1 RCT (272 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (reduced remission)
	Response	RR: 1.27; 95% CI: 1.09 to 1.49; I^2=N/A	1 RCT (272 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (improved response)
CBT+ Sertraline (class: SSRI) vs. Sertraline (class: SSRI)	Primary anxiety, clinician report	SMD: -0.46; 95% CI: -0.70 to -0.22; I^2=N/A	1 RCT (273 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (reduced anxiety)
	Function	SMD: -0.34; 95% CI: -0.58 to -0.10; I^2=N/A	1 RCT (273 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (improved function)
	Remission	RR: 0.78; 95% CI: 0.69, 4.24; I^2=N/A	1 RCT (273 Patients)[7, 67, 69-73]	Severe imprecision (wide CIs and small sample size)	Low (no difference)
	Response	RR: 1.32; 95% CI: 1.12 to 1.55; I^2=N/A	1 RCT (273 Patients)[7, 67, 69-73]	Imprecision (small sample size)	Moderate (improved response)

CI: confidence interval, CBT: cognitive behavioral therapy, N/A: not applicable, RCT: randomized control trial, RR: relative risk, SMD: standardized mean difference, SSRI: selective serotonin reuptake inhibitor, TCA: tricyclic antidepressants

[a] The sample size includes the number of patients from each comparison.

[b] Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

Subgroup Analysis

Key Points

- Treatment effects observed immediately post intervention were larger than those observed after a period of followup.
- Individual-based CBT had statistically significantly more improvement on function than group-based CBT.
- Relaxation and cognitive strategies in CBT were not associated with improvements on primary anxiety symptoms, function, secondary measures, social function, and clinical response; while exposure statistically significantly reduced primary anxiety symptoms (parent report).
- Compared to waitlisting or no treatment, CBT was found to have more improvement on functioning in age group 13-18 than age group 7-12.

Discussion

We were not able to conduct a large number of the planned subgroup analyses, including those based on race/ethnicity, parent education level, family income, disease severity (measured by CGI), treatment sequence, and provider. This was due to studies not providing sufficient stratified data per subgroup variable. The results of the feasible exploratory analyses are reported in Appendix Tables G.1 to G.12 and were summarized as follows:

- Age: when CBT compared to waitlisting or no treatment, we found statistically significantly more improvement in function in age group 13-18 than age group 7-12.
- Comorbidity: when CBT compared to pill placebo, patients without comorbidity had statistically significantly more improvement in secondary anxiety measures than patient with any comorbidity. However, the finding was limited by the fact that CBT delivered to children with comorbidities was different in children without comorbidities. Inference from subgroup analyses evaluating comorbidities is less reliable.
- ADHD: when fluvoxamine compared to pill placebo, we found no statistically significant difference on primary anxiety symptoms (clinician report).
- Autism: When CBT was compared to waitlisting or no treatment, we did not find statistically significant difference in outcomes (primary anxiety symptoms, clinician, child, and parent report), function, or clinical response in patients with autism than patients without autism.
- School refusal: when CBT compared to pill placebo, patients without school refusal were found to have statistically significant better outcome (secondary anxiety measures) than patient with school refusal.
- Diagnosis: when CBT compared to attention control/treatment as usual, patients with social anxiety disorder were found to have more improvement on secondary anxiety measures than patients with panic disorder.
- Treatment settings: when CBT compared to attention control or treatment as usual, we found statistically significantly more improvement in secondary anxiety measures in school settings than mental health clinic.
- Length of follow-up: when CBT compared to waitlisting or no treatment, post intervention response rate was significantly higher than those reported at less than 6-month followup. Post intervention reduction of primary anxiety symptoms (child report)

and remission rate were also significantly larger than those reported after more than 6 month followup.

- Exposure sessions in CBT: Compared with non-exposure CBT, exposure sessions statistically significant reduced primary anxiety symptoms (parent report only).
- Cognitive strategies in CBT: CBT with cognitive strategies were found to have statistically significant less improvement in primary anxiety symptoms (parent report) than CBT without cognitive strategies. No other significant differences were found on primary anxiety symptoms (clinician and child report), function, secondary measures, social function, or clinical response.
- Relaxation strategies in CBT: We found no statistically significant differences between CBT with relaxation and CBT without relaxation on primary anxiety symptoms (clinician, child, and parent report), function, secondary measures, social function, and clinical response.
- Individual-based CBT versus group-based CBT: we found that individual-based CBT had statistically significantly more improvement on function than group-based CBT.
- Treatment intensity: we found no statistically significant difference in any outcome based on treatment intensity.

KQ 2: What are the comparative harms and safety concerns regarding the available treatments for childhood anxiety disorders, including panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, and separation anxiety?

Key Points

- SSRIs and SNRIs were associated with increased risk of various short-term AEs that were overall not serious (low to moderate SOE).
- Studies were generally too small or too short to assess the effect of SSRIs on suicidal behavior. One study found that venlafaxine was associated with a statistically nonsignificant increase in the risk of suicidal ideation (low SOE).
- No differences or fewer dropout rates were found when CBT was compared to pill placebo, waitlisting, or active control therapies (low SOE).

Discussion

Twenty RCTs[7, 22, 49-51, 53-58, 60-62, 64-72, 74, 161] compared medications to pill placebo, including atomoxetine, clonazepam, clomipramine, duloxetine, fluvoxamine fluoxetine, imipramine, sertraline, and venlafaxine, and reported AEs. Overall, 2,610 patients were included with a mean age of 11.6 years old and 53.4 percent male. 14 studies [49-52, 56, 58, 60-65] [49-52, 54, 56, 58, 60-65] (70.0%) included patients without any comorbidity. 6 studies [7, 22, 53-55, 57, 66, 67, 69-73] included children with anxiety and comorbidity (ADHD, autism, ODD, OCD and other internalizing disorder). Details of the included studies can be found in Appendix Table E.1. We were unable to evaluate publication bias due to small number of studies (n<20) included in each comparisons.

Compared with pill placebo, SSRIs as a class was not significantly different on number of dropouts, dropouts due to any AEs, or any AEs. In terms of specific SSRIs, AEs that were associated with low to moderate SOE were any AEs (fluoxetine, paroxetine), AEs related to gastrointestinal symptoms (fluvoxamine), behavior change (paroxetine), cold/infection/allergies

(paroxetine), and difficulties in sleeping (paroxetine). In terms of SNRIs, AEs that were associated with moderate SOE included atomoxetine (any AE and GI AEs) and venlafaxine (gastrointestinal AE and somnolence). These adverse effects were not serious (i.e., were not described as severe by the included trials, or did not lead to discontinuation of treatment or significant morbidity or mortality). Imipramine (class: TCA) was found to have higher risk of AEs related to oral symptoms (moderate SOE). Evidence on AE of benzodiazepines was sparse and of lower quality.

CBT was associated with fewer dropouts than pill placebo or sertraline (class: SSRI) (low SOE). Compared to sertraline, CBT was found to have lower risk of any AEs, AEs related to behavior change, and difficulties in sleeping.

Three studies reported suicide/suicidal ideation/self-harm.[7, 58, 67-72, 162] The CAMS trial[7, 67-72] compared CBT, sertraline, CBT plus sertraline, and pill placebo. The study found no suicide attempts in any group and no statistical difference between groups on suicide ideation. In a RCT of 293 children with generalized social anxiety disorder, March et al. [58] compared venlafaxine ER to pill placebo and found 3 cases of suicide ideation (3/140) in the venlafaxine group and no incidence in the pill placebo group (p=0.18). In an observational study [162], Renaud et al. found no suicide attempts or ideation among 12 children treated by SSRIs and benzodiazepines.

Eighteen single-cohort observational studies reported AEs related to different drugs. Those AEs included gastrointestinal symptoms, behavior change, difficulties in sleeping, headache, fatigue, and somnolence. No serious AEs were reported. The characteristics of these studies are summarized in Appendix Table E.21.

In summary, SOE supporting specific AE for specific drugs was low in general. However, as a class, SSRIs and SNRIs increased the risk of short-term AEs that were mostly not serious with the exception of increased suicidal ideation with venlafaxine. Studies were generally too small or too short to assess the effect of SSRIs on suicidal behavior, but one study found increased suicidal behavior with venlafaxine (low SOE). Results of the AEs are presented in Tables 11 and 12.

Table 11. Strength of evidence for adverse events of drugs versus pill placebo

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
Benzodiazepine vs. Pill Placebo	Dropouts	RR: 6.22; 95% CI: 0.38 to 102.94; I^2=N/A	1 RCT (15 Patients)[57]	Severe imprecision (small sample size and wide CI)	Low (no difference)
SNRI vs. Pill Placebo	Dropouts	RR: 0.93; 95% CI: 0.70 to 1.25; I^2=0.0%	4 RCTs (786 Patients)[62 55, 58 64]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	Dropouts due to AEs	RR: 0.99; 95% CI: 0.39 to 2.47; I^2=7.9%	4 RCTs (786 Patients)[62 55, 58, 64]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	Any AEs	Rate ratio: 1.55; 95% CI: 0.35 to 6.77;	3 RCTs (786 Patients)[55, 58, 62]	Methodological limitations, imprecision (wide CIs)	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		I^2=94.8%			
	AEs related to abdominal/GI/appetite	Rate ratio: 2.15; 95% CI: 0.63 to 7.34; I^2=78.8%	3 RCTs (786 Patients)[55, 58, 62]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	AEs related to accidental injury	Rate ratio: 1.16, 95% CI: 0.58 to 2.29; I^2=N/A	21 RCTs (320 Patients)[62]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	AEs related to behavior change	Rate ratio: 1.48; 95% CI: 0.71 to 3.10; I^2=0.0%	2 RCTs (466 Patients)[55, 58]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	AEs related to cold/infection/allergies	Rate ratio: 1.05; 95% CI: 0.16 to 7.10; I^2=83.6%	3 RCTs (786 Patients)[55, 58, 62]	Methodological limitations, imprecision (wide CIs), inconsistency	Insufficient
	AEs related to fatigue/somnolence	Rate ratio: 2.14; 95% CI: 1.13 to 4.07; I^2=N/A	1 RCT (290 Patients)[58]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to headache/dizzy/vision problems	Rate ratio: 0.76; 95% CI: 0.52 to 1.11; I^2=60.2%	2 RCTs (496 Patients)[55, 62]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	AEs related to suicide/ideation/self-harm	Rate ratio: 4.29; 95% CI: 0.48 to 38.44; I^2=N/A	1 RCT (290 Patients)[58]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
SSRI vs. Pill Placebo	Dropouts	RR: 0.82; 95% CI: 0.59 to 1.13; I^2=0.0%	7 RCTs (856 Patients)[7, 22, 51, 53, 54, 61, 65, 67-72]	Imprecision (wide CIs)	Moderate (no difference)
	Dropouts due to AEs	RR: 2.60; 95% CI: 0.64 to 10.65; I^2=0.0%	4 RCTs (733 Patients)[7, 22, 53, 65, 67-72]	Severe imprecision (extremely wide CIs)	Low (no difference)
	Any AEs	Rate ratio: 1.28; 95% CI: 0.71 to 2.30; I^2=79.1%	8 RCTs (930 Patients)[7, 22, 49, 50, 53, 54, 60, 61, 65, 67-72]	Imprecision (wide CIs), inconsistency	Low (no difference)
	AEs related to abdominal/GI/appetite	Rate ratio: 1.40; 95% CI: 0.68 to 2.87; I^2=54.8%	6 RCTs (780 Patients)[7, 22, 49, 53, 61, 65, 67-72]	Imprecision (wide CIs)	Moderate (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
	AEs related to behavior change	Rate ratio: 1.66; 95% CI: 0.92 to 2.98; I^2=48.2%	7 RCTs (823 Patients)[7, 22, 49, 53, 60, 61, 65, 67-72]	Imprecision (wide CIs)	Moderate (no difference)
	AEs related to cold/infection/allergies	Rate ratio: 1.09; 95% CI: 0.67 to 1.79; I^2=36.0%	4 RCTs (684 Patients)[7, 22, 49, 65, 67-72]	Imprecision (wide CIs)	Moderate (no difference)
	AEs related to difficulties sleeping	Rate ratio: 1.24; 95% CI: 0.42 to 3.69; I^2=80.5%	5 RCTs (739 Patients)[7, 22, 49, 50, 65, 67-72]	Imprecision (wide CIs), inconsistency	Low (no difference)
	AEs related to fatigue/somnolence	Rate ratio: 1.61; 95% CI: 0.83 to 3.11; I^2=0.0%	4 RCTS (679 Patients)[7, 22, 61, 65, 67-72]	Methodological limitations, imprecision (wide CIs)	Low (no difference)
	AEs related to headache/dizzy/vision problem	Rate ratio: 1.24; 95% CI: 0.57 to 2.67; I^2=21.3%	4 RCTS (384 Patients)[7, 22, 49, 61, 67-72]	Methodological limitations, severe imprecision (small sample size and wide CIs)	Insufficient
	AEs related to accidental injury	Rate ratio: 2.29; 95% CI: 0.26 to 20.45; I^2=N/A	1 RCT (209 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to suicide/ideation/self-harm	0 case in each group	1 RCT (209 Patients)[7, 67-72]	No data	Insufficient
	AEs related to dry mouth/bad taste/oral symptoms	Rate ratio: 1.10; 95% CI: 0.34 to 3.58; I^2=62.0%	2 RCTs (47 Patients)[49, 61]	Severe imprecision (wide CI, small sample size), inconsistency	Insufficient
TCA vs. Pill Placebo	Any AEs	Rate ratio: 1.39; 95% CI: 0.82 to 2.63; I^2=86.6 %	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI), inconsistency	Insufficient
	AEs related to abdominal/GI/appetite	Rate ratio: 0.62; 95% CI: 0.21 to 1.86; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to behavior change	Rate ratio: 5.45; 95% CI: 0.66 to 45.30; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
	AEs related to difficulties sleeping	Rate ratio: 0.34; 95% CI: 0.07 to 1.63; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to fatigue/somnolence	Rate ratio: 2.73; 95% CI: 0.28 to 26.22; I^2=N/A	1 RCT (21 Patients)[74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to difficulties sleeping	Rate ratio: 0.34; 95% CI: 0.07 to 1.63; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to dry mouth/bad taste/oral symptoms	Rate ratio: 3.81; 95% CI: 1.25 to 11.62; I^2= 0.0%	2 RCTs (56 Patients)[56, 74]	Imprecision (small sample size)	Moderate (increased AEs)
Atomoxetine (class: SNRI) vs. Pill Placebo	Dropouts	RR: 1.07, 95% CI: 0.64 to 1.79; I^2=N/A	1 RCT (176 Patients)[55]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Dropouts due to AEs	RR: 0.98, 95% CI: 0.06 to 15.38; I^2=N/A	1 RCT (176 Patients)[55]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 1.74; 95% CI: 1.17 to 2.61; I^2=N/A	1 RCT (176 Patients)[55]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to abdominal/GI/appetite	Rate ratio: 2.48; 95% CI: 1.31 to 4.71; I^2=N/A	1 RCT (176 Patients)[55]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to behavior change	Rate ratio: 1.63; 95% CI: 0.39 to 6.82; I^2=N/A	1 RCT (176 Patients)[55]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to Cold/Infection/Allergies	Rate Ratio: 1.19; 95% CI: 0.59 to 2.41; I^2=N/A	1 RCT (176 Patients)[55]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to headache/dizzy/vision	Rate ratio: 1.54; 95% CI: 0.60 to 3.96;	1 RCT (176 Patients)[55]	Severe imprecision (small sample size and wide CI)	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		I^2=N/A			
Clomipramine (class: TCA) vs. Pill Placebo	Dropouts	RR: 3.60; 95% CI: 0.16 to 79.00; I^2=N/A	1 RCT (20 Patients)[54]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 0.52; 95% CI: 0.14 to 2.03; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Clonazepam (class: Benzodiazepine) vs. Pill Placebo	Dropouts	RR: 6.22; 95% CI: 0.38 to 102.94; I^2=N/A	1 RCT (15 Patients)[57]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Duloxetine (class: SNRI) vs. Pill Placebo	Dropouts	RR: 1.02; 95% CI: 0.76 to 1.35; I^2=N/A	1 RCT (272 Patients)[64]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Dropouts due to AEs	RR: 1.17; 95% CI: 0.58 to 2.37; I^2=N/A	1 RCT (272 Patients)[64]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Fluoxetine (class: SSRI) vs. Pill Placebo	Dropouts	RR: 1.39; 95% CI: 0.38 to 5.09; I^2=0.0	3 RCTs (175 Patients)[51, 53, 54]	Methodological limitations, severe imprecision (small sample size and wide CIs)	Insufficient
	Dropouts due to AEs	RR: 3.00; 95% CI: 0.13 to 71.34; I^2=N/A	1 RCT (74 Patients)[53]	Methodological limitations, severe imprecision (small sample size and wide CIs)	Insufficient
	Any AEs	Rate ratio: 2.77; 95% CI: 1.71 to 4.47; I^2=0.0%	2 RCTs (95 Patients)[53, 54]	Methodological limitations, imprecision (small sample size)	Low (increased AEs)
	AEs related to abdominal/GI/appetite	Rate ratio: 2.29; 95% CI: 0.94 to 5.56; I^2=N/A	1 RCT (74 Patients)[53]	Methodological limitations, severe imprecision (small sample size and wide CIs)	Insufficient
	AEs related to behavior Change	Rate ratio: 1.75; 95% CI: 0.51 to 5.98;	1 RCT (74 Patients)[53]	Methodological limitations, severe imprecision	Insufficient

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		I^2=N/A		(small sample size and wide CIs)	
Fluvoxamine (class: SSRI) vs. Pill Placebo	Dropouts	RR: 0.74; 95% CI: 0.35 to 1.54; I^2=N/A	1 RCT (128 Patients)[22]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Dropouts due to AEs	RR: 5.16; 95% CI: 0.62 to 42.93; I^2=N/A	1 RCT (128 Patients)[22]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 1.18; 95% CI: 0.15 to 9.45; I^2=83.5 %	4 RCTs (303 Patients)[22, 49, 50, 60]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to abdominal/GI/appetite	Rate ratio: 1.58; 95% CI: 1.13 to 2.20; I^2=0.0%	2 RCTs (153 Patients)[22, 49]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to behavior change	Rate ratio: 2.12; 95% CI: 0.08 to 54.36; I^2=79.0 %	3 RCTs (198 Patients)[22, 49, 60]	Severe imprecision (small sample size and wide CI), inconsistency	Insufficient
	AEs related to cold/infection/allergies	Rate ratio: 1.05; 95% CI: 0.75 to 1.47; I^2= 53.1%	2 RCTs (153 Patients)[22, 49]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to difficulties sleeping	Rate ratio: 0.76; 95% CI: 0.14 to 3.86; I^2=55.2%	3 RCTs (258 Patients)[22, 49, 50]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to headache/dizzy/vision	Rate ratio: 1.22; 95% CI: 0.74 to 2.00; I^2= 0.0%	2 RCTs (153 Patients)[22, 49]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to fatigue/somnolence	Rate ratio: 1.65; 95% CI: 0.87 to 3.15; I^2=N/A	1 RCT (128 Patients) [22]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to dry mouth/bad taste/oral symptoms	Rate ratio: 0.22; 95% CI: 0.02 to 2.13; I^2=N/A	1 RCT (25 Patients)[49]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Imipramine (class: TCA)	Any AEs	Rate ratio: 1.40; 95%	2 RCTs (56 Patients)[56, 74]	Severe imprecision	Insufficient

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
vs. Pill Placebo		CI: 0.82 to 2.63; I^2=86.6 %		(small sample size and wide CI), inconsistency	
	AEs related to abdominal/GI/appetite	Rate ratio: 0.62; 95% CI: 0.21 to 1.86; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to behavior change	Rate ratio: 5.45; 95% CI: 0.66 to 45.30; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to difficulties sleeping	Rate ratio: 0.34; 95% CI: 0.07 to1.63; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to fatigue/somnolence	Rate ratio: 2.73; 95% CI: 0.28 to 26.22; I^2=N/A	1 RCT (21 Patients)[74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to difficulties sleeping	Rate Ratio: 0.34; 95% CI: 0.07 to 1.63; I^2=0.0%	2 RCTs (56 Patients)[56, 74]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to dry mouth/bad taste/oral symptoms	Rate Ratio: 3.81; 95% CI: 1.25 to 11.62; I^2= 0.0%	2 RCTs (56 Patients)[56, 74]	Imprecision (small number of patients)	Moderate (increased AEs)
Paroxetine (class: SSRI) vs. Pill Placebo	Dropouts	RR: 0.71; 95% CI: 0.50 to 1.02; I^2=N/A	1 RCT (322 Patients)[65]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Dropouts due to AEs	RR: 4.28; 95% CI: 0.94 to 19.51; I^2=N/A	1 RCT (322 Patients)[65]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 1.85; 95% CI: 1.45 to 2.35; I^2=N/A	1 RCT (210 Patients)[65]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to abdominal/GI/appetite	Rate ratio: 3.49; 95% CI: 0.97 to 12.51; I^2=N/A	1 RCT (322 Patients)[65]	Severe imprecision (small sample size and wide CI)	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
	AEs related to behavior change	Rate ratio: 2.16; 95% CI: 1.06 to 4.40; I^2=N/A	1 RCT (322 Patients)[65]	Severe imprecision (small sample size and wide CI)	Low (increased AEs)
	AEs related to cold/infection/allergies	Rate ratio: 2.00; 95% CI: 1.39 to 2.89; I^2=N/A	1 RCT (274 Patients)[65]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to difficulties sleeping	Rate ratio: 6.17; 95% CI: 3.58 to 10.63; I^2=N/A	1 RCT (157 Patients)[65]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to fatigue/somnolence	Rate ratio: 1.52; 95% CI: 0.76 to 3.03; I^2=N/A	1 RCT (320 Patients)[65]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Sertraline (class: SSRI) vs. Pill Placebo	Dropouts	RR: 0.73; 95% CI: 0.38 to 1.42; I^2=0.0%	2 RCTs (231 Patients) [7, 61, 67-72]	Methodological limitations, severe imprecision (small sample size and wide CIs)	Insufficient
	Dropouts due to AEs	RR: 1.33; 95% CI: 0.36 to 5.00; I^2=N/A	1 RCT (209 Patients) [7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 1.2 95% CI: 0.94 to 1.55; I^2=50.1%	2 RCTs (231 Patients)[7, 61, 67-72]	Methodological limitations, severe imprecision (small sample size and wide CIs)	Insufficient
	AEs related to abdominal/GI/appetite	Rate ratio: 0.88; 95% CI: 0.50 to 1.53; I^2=78.6%	2 RCTs (231 Patients)[7, 61, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to behavior change	Rate ratio: 1.57; 95% CI: 0.88 to 2.81; I^2=0.00%	2 RCTs (231 Patients)[7, 61, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to cold/infection/allergies	Rate ratio: 0.86; 95% CI: 0.49 to 1.51; I^2=N/A	1 RCT (209 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to difficulties sleeping	Rate ratio: 1.94; 95%	1 RCT (209 Patients)[7, 67-72]	Severe imprecision	Low (no

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		CI: 0.72 to 5.27; I^2=N/A		(small sample size and wide CI)	difference)
	AEs related to fatigue/somnolence	Rate ratio: 1.68; 95% CI: 0.76 to 3.74; I^2=0.0%	2 RCTs (231 Patients)[7, 61, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to headache/dizzy/vision	Rate ratio: 1.29; 95% CI: 0.59 to 2.85; I^2=72.6%	2 RCTs (231 Patients)[7, 61, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to accidental injury	Rate ratio: 2.29; 95% CI: 0.26 to 20.45; I^2=N/A	1 RCT (209 patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to suicide/ideation/self-harm	0 case in each group	1 RCT (209 patients)[7, 67-72]	No data	Insufficient
	AEs related to dry mouth/bad taste/oral symptoms	Rate ratio: 2.0; 95% CI: 0.50 to 8.00; I^2=N/A	1 RCT (22 patients)[61]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Venlafaxine (class: SNRI) vs. Pill Placebo	Dropouts	RR: 0.84; 95% CI: 0.65 to 1.09; I^2=0.0%	2 RCTs (610 Patients)[62, 58]	Imprecision (wide CIs)	Moderate (no difference)
	Dropouts due to AEs	RR: 0.78; 95% CI: 0.36 to 1.66; I^2=64.9%	2 RCTs (610 Patients)[58, 62]	Imprecision (wide CIs), inconsistency	Low (no difference)
	Any AEs	Rate ratio: 1.13; 95% CI: 0.98 to 1.31; I^2=97.5%	2 RCTs (610 Patients)[58, 62]	Imprecision (wide CIs), inconsistency	Low (no difference)
	AEs related to abdominal/GI/appetite	Rate ratio: 1.92; 95% CI: 1.44 to 2.57; I^2=88.8%	2 RCTs (610 Patients)[58, 62]	Inconsistency	Moderate (increased AEs)
	AEs related to behavior change	Rate ratio: 1.43; 95% CI: 0.60 to 3.39; I^2=N/A	1 RCT (290 Patients)[58]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to cold/Infection/allergies	Rate ratio: 0.87; 95% CI: 0.57 to 1.32; I^2=	2 RCTs (610 Patients)[58, 62]	Severe imprecision (small sample size and wide	Insufficient

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		91.4%		CI), inconsistency	
	AEs related to fatigue/somnolence	Rate ratio: 2.14; 95% CI: 1.13 to 4.07; I^2=N/A	1 RCT (290 Patients)[58]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to headache/dizzy/vision	Rate ratio: 0.67; 95% CI: 0.44 to 1.01; I^2=N/A	1 RCT (320 Patients)[62]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to suicide/ideation/self-harm	Rate ratio: 4.29; 95% CI: 0.48 to 38.34; I^2=N/A	1 RCT (290 Patients)[58]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to accidental injury	Rate ratio: 1.16; 95% CI: 0.58 to 2.29; I^2=N/A	1 RCT (320 Patients)[62]	Severe imprecision (small sample size and wide CI)	Low (no difference)

AE: adverse event, CI: confidence interval, GI: gastrointestinal, N/A: not applicable, RCT: randomized controlled trial, RR: relative risk, SNRI: serotonin–norepinephrine reuptake inhibitor, SMD: standardized mean difference, SSRI: selective serotonin reuptake inhibitor, TCA: tricyclic antidepressants

[a]The sample size includes the number of patients from each comparison.

[b]Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

Table 12. Strength of evidence for adverse events reported in other comparisons, including combination treatments

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
TCA vs. SSRI	Dropouts	RR: 0.56; 95% CI: 0.06 to 5.14; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 6.90; 95% CI: 2.10 to 22.98; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (small sample size and wide CI)	Low (increased AEs)
Clomipramine (class: TCA) vs. Fluoxetine (class: SSRI)	Dropouts	RR: 0.56; 95% CI: 0.06 to 5.14; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 6.90; 95% CI: 2.10 to 22.98; I^2=N/A	1 RCT (19 Patients)[54]	Severe imprecision (small sample size and wide CI)	Low (increased AEs)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
Sertraline (class: SSRI) vs Paroxetine (class: SSRI)	Any AEs	Rate ratio: 5.00; 95% CI 0.31 to 79.94; I^2=N/A	1 RCT (19 patients)[54]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Fluoxetine (class: SSRI) vs. CBT	Dropouts	RR: 1.26; 95% CI: 0.61 to 2.58; I^2=N/A	1 RCT (102 Patients)[51]	Severe imprecision (small sample size and wide CI)	Low (no difference)
Sertraline (class: SSRI) vs CBT	Dropouts	RR: 2.79; 95% CI: 1.12 to 6.91; I^2=N/A	1 RCT (272 Patients)[7, 67-72]	Methodological limitations, imprecision (small sample size)	Low (increased dropouts)
	Dropouts due to AEs	RR: 15.67; 95% CI: 0.90 to 271.71; I^2=N/A	1 RCT (272 Patients)[7, 67-72]	Methodological limitations, severe imprecision (small sample size and wide CI)	Insufficient
	Any AEs	Rate ratio: 1.39; 95% CI: 1.09 to 1.77; I^2=N/A	1 RCT (272 Patients)[7, 67-72]	Methodological limitations, imprecision (small sample size)	Low (increased AEs)
	AEs related to abdominal/GI/appetite	Rate ratio: 0.71; 95% CI: 0.41 to 1.20; I^2=0.0%	2 RCT (274 Patients)[7, 67-72, 161]	Methodological limitations, severe imprecision (small sample size and wide CI)	Insufficient
	AEs related to behavior change	Rate ratio: 2.09; 95% CI: 1.17 to 3.74; I^2=0.0%	2 RCT (321 Patients)[7, 66-72]	Methodological limitations, imprecision (small sample size)	Low (increased AEs)
	AEs related to cold/infection/allergies	Rate ratio: 0.64; 95% CI: 0.41 to 1.01; I^2=N/A	1 RCT (272 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to difficulties sleeping	Rate ratio: 4.44; 95% CI: 1.50 to 13.20; I^2=N/A	1 RCT (272 Patients)[7, 67-72]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to headache/dizzy/vision	Rate ratio: 1.83; 95% CI: 0.90 to 3.72; I^2=N/A	1 RCT (272 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to accidental injury	Rate ratio: 1.05; 95% CI: 0.26 to 4.18;	1 RCT (272 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
		I^2=N/A			
	AEs related to suicide/ideation/self-harm	0 events	1 RCT (272 Patients)[7, 67-72]	No data	Insufficient
CBT vs. Pill Placebo	Dropouts	RR: 0.53; 95% CI: 0.30 to 0.95; I^2=74.4 %	2 RCTs (311 Patients)[7, 51, 67-72]	Severe imprecision (small sample size and wide CI)	Low (reduced dropouts)
	Dropouts due to AEs	RR: 0.08; 95% CI: 0.00 to 1.50; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	Any AEs	Rate ratio: 0.97; 95% CI: 0.71 to 1.30; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to abdominal/GI/appetite	Rate ratio: 0.84; 95% CI: 0.44 to 1.61; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to behavior change	Rate ratio: 0.72; 95% CI: 0.35 to 1.47; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to cold/infection/allergies	Rate ratio: 1.34; 95% CI: 0.80 to 2.25; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to difficulties sleeping	Rate ratio: 0.44; 95% CI: 0.12 to 1.63; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to headache/dizzy/vision	Rate ratio: 1.09; 95% CI: 0.41 to 2.92; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to suicide/ideation/self-harm	Rate ratio: 2.73; 95% CI: 0.32 to 23.40; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
	AEs related to accidental injury	Rate ratio: 2.19; 95% CI: 0.24 to 19.57; I^2=N/A	1 RCT (215 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
CBT vs. Waitlisting or	Dropouts	RR: 1.19; 95% CI:	29 RCTs (1345 Patients)[84, 105-108, 110,	Methodological limitations,	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
No Treatment		0.81 to 1.73; I^2=14.52 %	[111, 114-116, 120-122, 126, 127, 129, 136-138, 140-144, 146, 149, 152, 153]	imprecision (wide CI)	
	Dropouts due to AEs	RR: 0.31; 95% CI: 0.12 to 0.79; I^2=NA	1 RCT (125 Patients) [119]	Methodological limitations, imprecision (small sample size)	Low (reduced dropouts)
CBT vs. Attention Control or Treatment As Usual	Dropouts	RR: 0.87; 95% CI: 0.65 to 1.16 I^2=0.0%	16 RCTs and 1 non-randomized comparative study (1053 Patients)[76, 78-80, 82-84, 86, 88, 90, 92, 94-97, 100, 102]	Methodological limitations, imprecision (wide CI)	Low (no difference)
CBT+ Sertraline (class: SSRI) vs. CBT	Dropouts	RR: 1.99; 95% CI: 0.77 to 5.14; I^2=N/A	1 RCT and 1 non-randomized comparative study (327 patients)[7, 67-72, 163]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Dropouts due to AEs	RR: 2.98; 95% CI: 0.12 to 72.50; I^2=N/A	1 RCT (279 patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Any AEs	Rate ratio:1.67; 95% CI: 1.32 to 2.07 I^2=N/A	1 RCT (279 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (increased AEs)
	AEs related to abdominal/GI/appetite	Rate ratio: 1.42; 95% CI: 0.84 to 2.42; I^2=N/A	1 RCT (279 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to behavior change	Rate ratio: 3.80; 95% CI: 2.23 to 6.48; I^2=N/A	1 RCT (279 Patients)[7, 67-72]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to cold/infection/allergies	Rate ratio: 0.95; 95% CI: 0.64 to 1.42; I^2=N/A	1 RCT (279 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to difficulties sleeping	Rate ratio: 3.23; 95% CI: 1.05 to 9.90; I^2=N/A	1 RCT (279 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (increased AEs)
	AEs related to headache/dizzy/vision	Rate ratio: 1.49; 95% CI: 0.72 to 3.09; I^2=N/A	1 RCT (279 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to suicide/ideation/s	Rate ratio: 0.99; 95%	1 RCT (279 Patients)[7, 67-72]	Severe imprecision (small sample size	Low (no difference)

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
	elf-harm	CI: 0.29 to 3.43; I^2=N/A		and wide CIs)	
	AEs related to accidental injury	Rate ratio: 1.00; 95% CI: 0.25 to 3.80; I^2=N/A	1 RCT (279 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
CBT+ Sertraline (class: SSRI) vs. Sertraline (class: SSRI)	Dropouts	RR: 0.71; 95% CI: 0.35 to 1.45; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Dropouts due to AEs	RR: 0.14; 95% CI: 0.02 to 1.09; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	Any AEs	Rate ratio: 1.2; 95% CI: 0.97 to 1.45; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to abdominal/GI/appetite	Rate ratio: 1.01; 95% CI: 0.62 to 1.65; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to behavior change	Rate ratio: 1.82; 95% CI: 1.20 to 2.75; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Imprecision (small sample size)	Moderate (increased AEs)
	AEs related to cold/infection/allergies	Rate ratio: 1.49; 95% CI: 0.94 to 2.35; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to difficulties Sleeping	Rate ratio: 0.73; 95% CI: 0.35 to 1.50; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CIs)	Low (no difference)
	AEs related to fatigue/somnolence	Rate ratio: 0.20; 95% CI: 0.06 to 0.71; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Imprecision (small sample size)	Moderate (reduced AEs)
	AEs related to headache/dizzy/vision	Rate ratio: 0.81; 95% CI: 0.43 to 1.53; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low(no difference)
	AEs related to suicide/ideation/s	0 case in each group	1 RCT (273 Patients)[7, 67-72]	No data	Insufficient

Comparison	Outcome	Conclusion	Study Design and Sample Size[a]	Factors That Affect the Strength of Evidence[b]	Overall Evidence Strength (Direction of Effect)
	elf-harm				
	AEs related to accidental injury	Rate ratio: 0.95; 95% CI: 0.24 to 3.80; I^2=N/A	1 RCT (273 Patients)[7, 67-72]	Severe imprecision (small sample size and wide CI)	Low (no difference)
CBT+ Imipramine (class: TCA) vs. CBT	Dropouts	RR: 0.80; 95% CI: 0.34 to 1.89; I^2=N/A	1 RCT (63 Patients)[159]	Severe imprecision (small sample size and wide CI)	Low (no difference)
CBT+ Fluoxetine (class: SSRI) vs. CBT	Dropouts	RR: 1.54; 95% CI: 0.60 to 3.88; I^2=N/A	1 RCT(41 Patients)[160]	Severe imprecision (small sample size and wide CI)	Low (no difference)

AE: adverse event, CBT: cognitive behavioral therapy, CI: confidence interval, GI: Gastrointestinal, N/A: not applicable, RCT: randomized controlled trial, RR: relative risk, SNRI: serotonin–norepinephrine reuptake inhibitor, SMD: standardized mean difference, SSRI: selective serotonin reuptake inhibitor, TCA: tricyclic antidepressants

[a]The sample size includes the number of patients from each comparison.

[b] Only SOE domains that led to rating down SOE are reported in this column. Domains that are not reported were satisfactory.

Discussion

We conducted a systematic review and meta-analysis to examine the effectiveness and safety of treatments for anxiety disorders (i.e., separation anxiety disorder, generalized anxiety disorder, social anxiety disorder, panic disorder, and specific phobia) in children (i.e. ages 3 to 18). The systematic review examined medications (primarily selective serotonin reuptake inhibitors and selective norepinephrine reuptake inhibitors, tricyclic antidepressant, and anxiolytics) as well as psychotherapies (primarily cognitive behavioral therapy). This review constitutes the largest and most comprehensive review of the treatment literature for child anxiety disorders. In total, we examined 206 studies including 19 studies comparing medication to placebo with 2,498 patients and 88 studies comparing cognitive behavioral therapy (CBT) to a control group with 6,978 patients. To our knowledge, there has not been a systematic review of pharmacotherapy for childhood anxiety disorders since 2010. In the current review, by far, CBT was the most extensively examined intervention with over 40 studies providing outcome data for comparisons against waitlisting or no treatment.

No individual medication had evidence for significant reduction in anxiety symptoms across all three reporters (child, parent, and clinician). The finding regarding inconsistent effectiveness across reporters in trials of medications might be related to artifacts of study design including issues with blinding or may reflect that medication treatment of child anxiety is not as robust as CBT[164]. Compared to pill placebo, selective serotonin reuptake inhibitor (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) improved anxiety symptoms (evidence was available for paroxetine, fluoxetine, sertraline, fluvoxamine, duloxetine, atomoxetine, and venlafaxine). The effect of benzodiazepines and TCAs on anxiety symptoms, function and remission was only supported by insufficient or low strength of evidence. Data on head-to-head comparisons across drugs were sparse. Compared to waitlisting or no treatment, CBT significantly reduced primary anxiety symptoms based on child, parent, and clinician reports, improved function, and improved remission and clinical response. The combination of SSRIs and CBT reduced primary anxiety symptoms and improved clinical response, compared to either approach alone. Short-term AEs (mostly not serious) were common with medications but not psychotherapy. Studies were generally too small or too short to assess suicidality with SSRI or SNRIs, with the exception of venlafaxine. Exploratory subgroup analyses showed that 1) post intervention effective sizes were larger than those reported in followup, 2) individual-based CBT had statistically significantly more improvement in function than group-based CBT, 3) relaxation and cognitive strategies in CBT were not associated with improvements; while exposure statistically significantly reduced primary anxiety symptoms, and 4) CBT was found to have more improvement on functioning in age group 13-18 than age group 7-12. However, such results from subgroup analyses should be considered hypothesis generating.

Findings in Relation to What Is Known

In regards to the CBT, the current analysis is consistent with previous ones, such as a Cochrane systematic review, concluding that CBT is an effective treatment for childhood and adolescent anxiety disorders. However, the current review extends the empirical support for CBT, by finding moderate support for the superiority of CBT over treatment as usual or attention control. The current analyses also contribute additional information to the understanding of the necessary and sufficient components of CBT. Specifically, the data suggest that relaxation and cognitive-restructuring do not increase effectiveness above exposure. In fact the presence of

cognitive-restructuring was associated with worse outcomes in terms of functioning. Moreover, the current analyses found no differences or fewer dropout rates between CBT and pill placebo, waitlisting, or active control therapies. This finding refutes the belief that patients find CBT (particularly exposure) aversive and unacceptable. Finally, the current report highlights factors that may reduce the effectiveness of CBT including younger age. As such, the current review bolsters the empirical support for CBT by supporting its incremental effectiveness over common therapeutic factors, elucidating some of its active ingredients, and demonstrating its acceptability.

In regards to medication, the current analyses are consistent with previous systematic reviews of psychopharmacologic interventions suggesting that SSRIs and SNRIs have demonstrated effectiveness in the reduction of anxiety symptoms. However, the evidence support for SSRIs is somewhat lessened by the fact that superiority over pill placebo was not found with child report. This issue of inconsistent report is more concerning for SNRIs where support for effectiveness was only found through clinician report, and not through parent or child report of symptoms, or on measures of functioning. In terms of adverse events (AEs), the current review provides the most comprehensive evaluation to date and suggests that short-term AEs tended to be not serious and generally did not lead to discontinuation. Studies were generally of small sizes and short duration and did not report the incidence of serious AEs. There was no evidence of suicidal behavior or ideation associated with the use of SSRIs in children with anxiety, although one trial showed a nonsignificant increase in suicidal ideation with venlafaxine. This contrasted with the well reported two fold increase in suicidal behavior and/or suicidal thoughts associated with SSRIs used for the treatment of depression in children and adolescents, a finding which led to the black box warning. Besides the small sample sizes and short duration, this discrepancy could also be due to the lack of a standardized mechanism for coding and assessing akathisia, aggression, hostility, and suicidal events in pediatric trials and the resulting underreporting of harm events [165]. Evidence on the effectiveness of benzodiazepines and tricyclic antidepressants remains minimal and insufficient to recommend their routine use.[15, 166]

The current analysis also contributes to the understanding of effectiveness in terms of patient centered outcomes. Whereas previous analyses typically focused exclusively on reduction of anxiety symptoms, the current analyses also examined effects on functioning, anxiety related constructs (such as coping skills), social functioning, and AEs. The results suggested that both CBT and SSRIs improve functioning. The current analyses are also the first to our knowledge to examine the symptom improvement from the perspectives of each stakeholder. Specifically, rather than selecting a single outcome measure from each study, we examined the parent, child, and clinician/evaluator reported outcomes.

Overall, our findings are consistent with existing evidence synthesis reports in terms of demonstrating effectiveness of CBT, SSRIs and SNRIs and pointing out to the need for comparative effectiveness evidence and concerns about long term safety of medications. In terms of existing guidelines, the World Health Organization (WHO), National Institute for Health and Care Excellence (NICE), and British Columbia Medical Services Commission[10-12] are congruent with the current findings in that they recommend CBT as the first-line treatment with medication treatment as a reasonable alternative if preferred by the patient or if CBT was unavailable. In contrast, the American Academy of Child and Adolescent Psychiatry (AACAP) guideline recommends that treatment be multimodal (including a variety of education, psychotherapy interventions, and medications) and informed by the severity of the symptoms and level of impairment.[19] The current findings provide some data to address the need acknowledged in the

AACAP guidelines for comparative effectiveness by supporting the superiority of CBT over treatment as usual.

Limitations

Despite anxiety being a common disorder in children, the body of evidence was relatively small and had short followup. A large number of scales were used across studies in overlapping domains, which created a challenge for evidence synthesis, interpretation and translation. Components of interventions and description of participants comorbidities, demographics and social support was either lacking or was provided without stratification per intervention. This rendered numerous subgroup analyses unfeasible. Results of such subgroup analyses would have been most helpful to guideline developers, practitioners and patients because it could have led to nuanced and personalized recommendations. We found indications of potential publication bias when CBT was compared to waitlisting on primary anxiety symptoms. We were unable to statistically evaluate publication bias for most of the comparisons due to small numbers of studies ($n<20$). The synthesis of data on AEs in particular is limited by the fact that the vast majority of CBT studies do not evaluate AEs and by the lack of a structured consistent approach to measurement in medication studies.

Applicability

The results of this review are likely widely applicable to a heterogeneous population of children with separation anxiety disorder, generalized anxiety disorder, social anxiety disorder, panic disorder, and specific phobia; with minimal psychiatric comorbidities, who are on average 8-18 years old and have ready access to mental health professionals who can provide CBT or have access to psychiatrists or pediatricians who are willing to prescribe SSRIs and SNRIs. Studies published in foreign languages (Spanish and German) demonstrated similar or larger effect size (the effect was in the same direction), compared to studies published in English.

Children of younger ages (3-6) were less presented in the current literature. The majority of the studies were conducted with populations that were predominately Caucasian with limited co-morbidity. As such, it is unclear how the results would apply to more diverse populations, patients with comorbidity (especially disruptive behavior), or families with significant additional psychosocial stressors. Most studies also studied treatment naïve children. Thus it is unclear how the results apply to practitioners working with children that have received previous ineffective treatments.

A Guide To Aid in Applicability

To facilitate analysis, data had to be standardized (i.e., expressed in multiples of standard deviations and presented as a standardized mean difference called SMD) or combined using a relative association measure (e.g., relative risk). Such measures may be challenging to interpret by guideline developers or practicing clinicians and can be translated to become more clinically meaningful.[167]

One way to make SMD more clinically relevant is to translate it back to scales with which clinicians have familiarity. In Table 13, we provide the average standard deviations for commonly used scales that can be multiplied by SMD for conversion.

Table 13. Average standard deviations for commonly used scales that can be multiplied by SMD for conversion

Domain	Commonly Used Scales	Average Standard Deviation[a]
Primary Anxiety Symptoms (Clinician report)	ADIS	1.73
	CGI-Severity	1.16
	PARS	5.53
Primary Anxiety Symptoms (Child report)	SPAI	16.54
	SCAS	14.37
	FSSCR	18.61
Primary Anxiety Symptoms (Parent report)	SCAS	12.88
	SCARED	10.43
	STAI	8.50

ADIS: anxiety disorder interview schedule, CGI-Severity: clinical global impressions- severity, FSSCR: fear survey schedule for children - revised, PARS: pediatric anxiety rating scale, SCARED: screen for child anxiety related emotional disorders, SCAS: Spence children's anxiety scale, SPAI: social phobia and anxiety inventory, STAI: state-trait anxiety inventory.
[a] The standard deviation of other scales can be obtained from studies that used such scales and can be used for conversion of SMD to any scale following the same approach.

As an example of this conversion; compared with pill placebo, fluoxetine reduced primary anxiety symptoms by SMD=-0.40. Multiplying this SMD by the average standard deviation of ADIS scale (1.73) results in -0.69 (which is the expected improvement in anxiety symptoms using ADIS scale). Another approach to aid in the interpretation of the SMD is to consider the magnitude of the effect. SMD cutoffs of 0.20, 0.50, and 0.80 are considered to represent small, moderate, and large effect, respectively.

For binary outcomes presented using a relative effect measure, the effect can be multiplied by the baseline risk to produce an absolute effect and number needed to treat. Using the same example, fluoxetine improved remission by RR= 1.75. Using the average risk in the placebo arms of the included studies (36%), we obtain the absolute effect of 270 patients per 1000 achieving remission (number needed to treat =4). Such conversion can be done in each local setting differently (using a baseline risk appropriate for the setting of the stakeholder) and facilitates the applicability of the findings of this review.

Future Research Needs

Interventions for anxiety in children are complex interventions with multiple components and effect modifiers. However, few studies provided sufficient information to determine the relative effectiveness of such components (e.g. relaxation, exposure, and cognitive-restructuring) or to explore contextual factors that can modify the effectiveness of these complex interventions. Research needs to move away from the simple question of 'does this work?" to "under what circumstances do medications and psychotherapy work best for children with anxiety?" Therefore, studies need to explore the most beneficial components of CBT and the impact of comorbidities, family demographics and stressors as effect modifiers that can change the effectiveness of treatment. Knowing these effect modifiers would help in providing more individualized treatment. Further research is also needed on long term safety of drugs, treatment of refractory anxiety symptoms, and needs to be more inclusive of underserved populations and minorities. Since anxiety outcomes are measured using a variety of scales without established minimally clinically important differences, studies that establish such differences are needed to better enable clinicians and patients gauge the effectiveness of interventions and balance benefits and harms during a shared decision making process. A large number of analyses, when stratified by an individual intervention, had a small number of included patients leading to imprecise

estimates. Considering that anxiety in children is a fairly common condition, larger trials (> 400 participants) with follow up that exceeds 2-3 years are likely feasible and are needed to advance patient care.

Conclusion

CBT is effective in reducing anxiety symptoms and improving function. Medications, primarily those targeting serotonin, are also effective but were associated with various short-term AEs, which were mostly not serious, but studies were too small or too short to assess suicidality with SSRI or SNRI. One trial showed a statistically nonsignificant increase in suicidal ideation with venlafaxine. The combination of medications and CBT is likely more effective than either treatment alone. Comparative effectiveness evidence between various medications and comparing CBT versus medications, or the combination, is limited and represents a need for research in this field. Future research is needed to evaluate components of CBT, effect modifiers of treatment, and long-term safety of drugs, and needs to be more inclusive of underserved populations and minorities.

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Abbreviations

AACAP	**American Academy of Child and Adolescent Psychiatry**
ADHD	Attention Deficit Hyperactivity Disorder
ADIS	Anxiety Disorder Interview Schedule
AE	Adverse Event
CBT	Cognitive Behavioral Therapy
CGAS	Children's Global Assessment Scale
CGI-I	Clinical Global Impression - Improvement Scale
CGI-S	Clinical Global Impressions Scale - Severity Scale
CI	Confidence Interval
CMAS	Children's Manifest Anxiety Scale
DSM-5	Diagnostic and Statistical Manual of Mental Disorders
EAS Temperament Survey	Emotionality-Activity-Sociability Temperament Survey
FSSCR	Fear Survey Schedule for Children - Revised
ITT	Intention-to-treat
MASC	Multidimensional Anxiety Scale for Children
N/A	Not Applicable
NICE	National Institute for Health and Care Excellence
NIMH	The National Institute of Mental Health
OCD	Obsessive Compulsive Disorder
ODD	Oppositional Defiant Disorder
PARS	Pediatric Anxiety Rating Scale
PICOTS	Population, Interventions, Comparisons, Outcomes, Timing, and Setting
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PST	Problem Solving Therapy
RCMAS	Revised Children's Manifest Anxiety Scale
RCT	Randomized Controlled Trial
SCARED	Screen for Child Anxiety Related Emotional Disorders
SCAS	Spence Children’s Anxiety Scale
SES	Socioeconomic Status
SMD	Standardized Mean Difference
SNRI	Serotonin-Norepinephrine Reuptake Inhibitor
SOE	Strength of Evidence
SPAI	Social Phobia and Anxiety Inventory
SRI	Serotonin Reuptake Inhibitor
SSRI	Selective Serotonin Reuptake Inhibitor
STAI	State-Trait Anxiety Inventory
TCA	Tricyclic Antidepressant

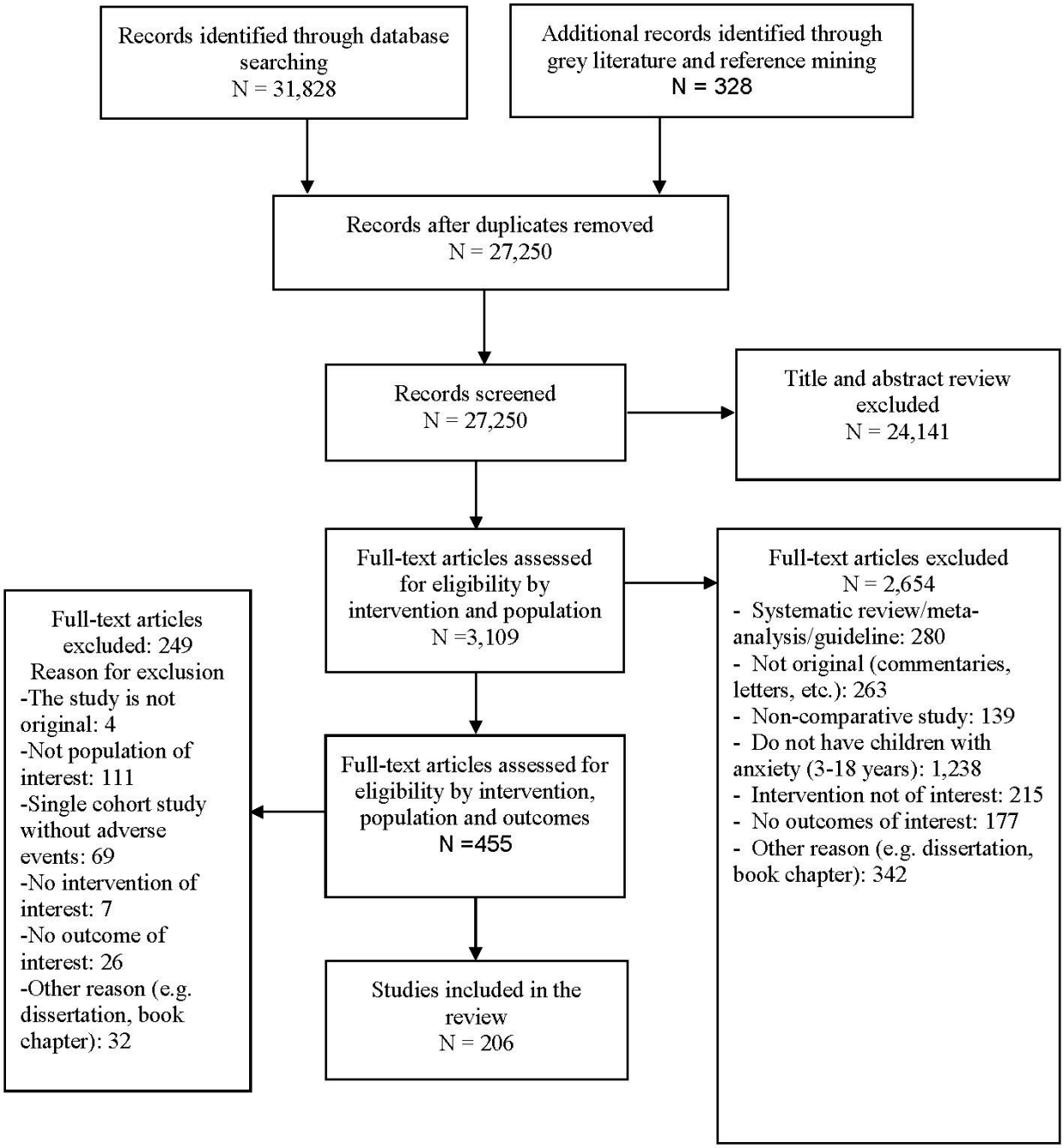
Appendixes
Contents

Tables

Figures

Appendix A. Flow Chart

Figure A.1. Flow chart



Appendix B. Search Strategy

Ovid
Database(s): Embase 1988 to 2017 Week 05, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, PsycINFO 1806 to January Week 4 2017, EBM Reviews - Cochrane Central Register of Controlled Trials November 2016, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to January 25, 2017
Search Strategy:

#	Searches	Results
1	Anxiety Disorders/dh, dt, su, th	9492
2	anxiety disorder/dm, dt, rt, su, th [Disease Management, Drug Therapy, Radiotherapy, Surgery, Therapy]	13722
3	exp Panic Disorder/dt, su, th [Drug Therapy, Surgery, Therapy]	7765
4	exp panic/dm, dt, su, th [Disease Management, Drug Therapy, Surgery, Therapy]	5422
5	exp Phobic Disorders/dh, dt, su, th [Diet Therapy, Drug Therapy, Surgery, Therapy]	3954
6	exp phobia/dm, dt, su, th [Disease Management, Drug Therapy, Surgery, Therapy]	5441
7	exp Anxiety, Separation/dt, th [Drug Therapy, Therapy]	724
8	exp separation anxiety/dm, dt, th [Disease Management, Drug Therapy, Therapy]	425
9	exp generalized anxiety disorder/dm, dt, su, th [Disease Management, Drug Therapy, Surgery, Therapy]	2415
10	((("social anxiet*" or "generalized anxiet*" or overanxious) adj3 (disorder* or neuroses or neurosis or neurotic or phobia* or phobic)) or ((anxiety or anxieties) adj3 (disorder* or neuroses or neurosis or neurotic)) or (panic adj3 (disorder* or attack*)) or Acrophobia* or agoraphobia* or claustrophobia* or homophobia* or neophobia* or Ophidiophobia* or phobia* or phobic or "separation anxiet*" or xenophobia*).mp.	244817
11	exp Psychotherapy/	569654
12	exp Electroconvulsive Shock Therapy/	20518
13	exp Electroconvulsive Therapy/	27336
14	exp brain depth stimulation/	30937
15	exp Deep Brain Stimulation/	39654
16	exp transcranial magnetic stimulation/	34619
17	exp Vagus Nerve/	40508
18	exp Vagus Nerve Stimulation/	9498
19	exp electrostimulation therapy/	181773
20	exp Electric Stimulation Therapy/	254786
21	exp electrical brain stimulation/	38192
22	exp alternative medicine/	268544
23	exp phototherapy/	102362

24	exp kinesiotherapy/	58263
25	exp Exercise Therapy/	105637
26	exp Exercise/	459889
27	exp yoga/	9351
28	exp complementary therapies/	261302
29	exp alternative medicine/	268544
30	exp Combined Modality Therapy/	300497
31	((brain adj2 excitation) or (brain adj2 stimulat*) or "12 step program*" or abreaction or acupressure* or acupuncture or "age regression" or agent* or "alternative medicine" or aromatherap* or Aromatherapy or auriculotherap* or "Balint group*" or "behavior contracting" or "behavior modification" or bibliotherapy or biofeedback or "breathing exercise*" or catharsis or chemotherap* or Chronotherapy or "cognitive rehabilitation" or "cognitive restructuring" or "combined modalit*" or "complementary medicine*" or "consciousness raising" or "contingency management" or cotherap* or counseling or countercondition* or Countertransference or "crisis intervention*" or Desensitization or drug* or "electric stimulat*" or "electrical stimulat*" or Electroacupuncture or electrosleep or electrostimulat* or electrotherap* or "empty chair" or exercise or fading or "fatty acid*" or "flower remed*" or "free association*" or gestalt or "group development" or "group dynamics" or "group intervention*" or heliotherap* or holistic or homeopathy or "human potential*" or humanis* or hypnosis or Hypnotherapy or imagery or intervention* or kinesiotherap* or kinesitherap* or Logotherapy or manag* or massage or medication* or "mental healing" or microbicid* or "mind-body" or neurofeedback or neurosurger* or operat* or overcorrection or "paradoxical technique*" or pharmacotherap* or phototherap* or phytotherap* or prevent* or Psychoanaly* or psychodrama or psychodrama* or psychotherap* or Psychotherapeutic* or radiotherap* or reflexotherap* or relaxation or resect* or "response cost" or "role play*" or "role playing" or "sensory feedback" or sociotherapy or spiritual* or "stress management" or suggestion* or "support group*" or surg* or "tai ji" or therap* or "therapeutic communit*" or "therapeutic touch*" or therapies or therapy or timeout* or training or "Transactional Analysis" or "transcranial magnetic stimulat*" or transference or treat* or treatment* or "twelve step program*" or "vagal nerve" or "vagal stimulat*" or "vagus nerve" or "vagus stimulat*" or yoga).mp.	29404851
32	or/11-31	29519244
33	10 and 32	168615
34	or/1-9	37562
35	33 or 34	170412
36	limit 35 to "all child (0 to 18 years)" [Limit not valid in Embase,PsycINFO,CCTR,CDSR; records were retained]	140150
37	limit 36 to (childhood or adolescence <13 to 17 years>) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR,CDSR;	104599

	records were retained]	
38	limit 37 to (preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,PsycINFO,CCTR,CDSR; records were retained]	34306
39	(toddler* or child* or adolescent* or paediatric* or pediatric* or girl or girls or boy or boys or teen or teens or teenager* or preschooler* or "pre-schooler*" or preteen or preteens or "pre-teen" or "pre-teens" or youth or youths).mp.	6640078
40	35 and 39	41617
41	from 38 keep 1-26193	26193
42	40 or 41	42800
43	exp meta analysis/	234764
44	exp Meta-Analysis as Topic/	53463
45	exp "systematic review"/	153050
46	((meta adj analys*) or (systematic* adj3 review*)).mp,pt.	550689
47	43 or 44 or 45 or 46	550689
48	exp controlled study/	5658493
49	exp Randomized Controlled Trial/	905465
50	exp triple blind procedure/	204
51	exp Double-Blind Method/	390501
52	exp Single-Blind Method/	68129
53	exp latin square design/	570
54	((control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square").mp,pt.	7148487
55	or/48-54	7148556
56	controlled study/	5390344
57	exp comparative study/	2718783
58	exp Cross-Sectional Studies/	447921
59	exp Cohort Studies/	2043883
60	exp longitudinal study/	327400
61	exp retrospective study/	1141189
62	exp prospective study/	905077
63	exp population research/	90005
64	exp observational study/	158991
65	clinical study/	223234
66	exp Evaluation Studies/	259715
67	exp quantitative study/	59289
68	exp validation studies/	146273

69	exp quasi experimental study/	4492
70	exp field study/	10921
71	in vivo study/	265314
72	exp panel study/	1232
73	exp prevention study/	6709
74	exp replication study/	2630
75	exp Feasibility Studies/	137033
76	exp trend study/	19095
77	exp correlational study/	24732
78	exp case-control studies/	978796
79	exp confidence interval/	320632
80	exp regression analysis/	902411
81	exp proportional hazards model/	170815
82	((control* adj3 study) or "comparative study" or "comparative survey" or "comparative analysis" or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or cohort* or longitudinal* or retrospectiv* or prospectiv* or (population adj3 (stud* or survey* or analys* or research)) or (("follow-up" or followup) adj (stud* or survey or analysis)) or ((observation or observational) adj (study or survey or analysis)) or "clinical study" or "evaluation study" or "evaluation survey" or "evaluation analysis" or "quantitative study" or "quantitative analys*" or "numerical study" or "validation study" or "validation survey" or "validation analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "field study" or "field survey" or "field analysis" or "in vivo study" or "in vivo analysis" or "panel study" or "panel survey" or "panel analysis" or ((prevention or preventive) adj3 (trial or study or analysis or survey)) or "replication study" or "replication analysis " or "replication trial" or "feasibility study" or "feasibility analysis" or "trend study" or "trend survey" or "trend analysis" or ((correlation* adj2 study) or (correlation* adj2 analys*)) or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "confidence interval" or "regression analysis" or "least square" or "least squares" or (hazard* adj (model or analys* or regression or ratio or ratios)) or "Cox model" or "Cox multivariate analyses" or "Cox multivariate analysis" or "Cox regression" or "Cox survival analyses" or "Cox survival analysis" or "Cox survival model" or ((study or trial or random* or control*) and compar*)).mp,pt.	17278574
83	or/56-82	17643418
84	47 or 55 or 83	18237284
85	42 and 84	22522
86	from 42 keep 16973-28898	11926

87	limit 86 to (clinical study or clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or controlled clinical trial or multicenter study or observational study or randomized controlled trial or pragmatic clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or observational study or randomized controlled trial or pragmatic clinical trial or systematic reviews or validation studies) [Limit not valid in Embase,PsycINFO,CCTR,CDSR; records were retained]	3206
88	85 or 87	22732
89	limit 88 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,PsycINFO,CCTR,CDSR; records were retained]	548
90	from 89 keep 1-234	234
91	88 not 90	22498
92	limit 91 to yr="2015 -Current"	4188
93	remove duplicates from 92	2858
94	limit 91 to yr="2012-2014"	5471
95	remove duplicates from 94	3662
96	limit 91 to yr="2008-2011"	4733
97	remove duplicates from 96	3267
98	limit 91 to yr="2001 -2007"	4836
99	remove duplicates from 98	3351
100	limit 91 to yr="1806 -2000"	3250
101	remove duplicates from 100	2276
102	93 or 95 or 97 or 99 or 101	15414

Scopus

1	TITLE-ABS-KEY((("social anxiet*" or "generalized anxiet*" or overanxious) W/3 (disorder* or neuroses or neurosis or neurotic or phobia* or phobic)) OR ((anxiety or anxieties) W/3 (disorder* or neuroses or neurosis or neurotic)) OR (panic W/3 (disorder* or attack*)) OR Acrophobia* OR agoraphobia* OR claustrophobia* OR homophobia* OR neophobia* OR Ophidiophobia* OR phobia* OR phobic OR "separation anxiet*" OR xenophobia*)
2	TITLE-ABS-KEY((brain W/2 excitation) or (brain W/2 stimulat*) or "12 step program*" or abreaction or acupressure* or acupuncture or "age regression" or agent* or "alternative medicine" or aromatherap* or Aromatherapy or auriculotherap* or "Balint group*" or "behavior contracting" or "behavior modification" or bibliotherapy or biofeedback or

"breathing exercise*" or catharsis or chemotherap* or Chronotherapy or "cognitive rehabilitation" or "cognitive restructuring" or "combined modalit*" or "complementary medicine*" or "consciousness raising" or "contingency management" or cotherap* or counseling or countercondition* or Countertransference or "crisis intervention*" or Desensitization or drug* or "electric stimulat*" or "electrical stimulat*" or Electroacupuncture or electrosleep or electrostimulat* or electrotherap* or "empty chair" or exercise or fading or "fatty acid*" or "flower remed*" or "free association*" or gestalt or "group development" or "group dynamics" or "group intervention*" or heliotherap* or holistic or homeopathy or "human potential*" or humanis* or hypnosis or Hypnotherapy or imagery or intervention* or kinesiotherap* or kinesitherap* or Logotherapy or manag* or massage or medication* or "mental healing" or microbicid* or "mind-body" or neurofeedback or neurosurger* or operat* or overcorrection or "paradoxical technique*" or pharmacotherap* or phototherap* or phytotherap* or prevent* or Psychoanaly* or psychodrama or psychodrama* or psychotherap* or Psychotherapeutic* or radiotherap* or reflexotherap* or relaxation or resect* or "response cost" or "role play*" or "role playing" or "sensory feedback" or sociotherapy or spiritual* or "stress management" or suggestion* or "support group*" or surg* or "tai ji" or therap* or "therapeutic communit*" or "therapeutic touch*" or therapies or therapy or timeout* or training or "Transactional Analysis" or "transcranial magnetic stimulat*" or transference or treat* or treatment* or "twelve step program*" or "vagal nerve" or "vagal stimulat*" or "vagus nerve" or "vagus stimulat*" or yoga)

3 TITLE-ABS-KEY(newborn* or neonat* or infant* or toddler* or child* or adolescent* or paediatric* or pediatric* or girl or girls or boy or boys or teen or teens or teenager* or preschooler* or "pre-schooler*" or preteen or preteens or "pre-teen" or "pre-teens" or youth or youths)

4 TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*) OR guideline* OR (control* W/3 study) OR (control* W/3 trial) OR (randomized W/3 study) OR (randomized W/3 trial) OR (randomised W/3 study) OR (randomised W/3 trial) OR "pragmatic clinical trial" OR (doubl* W/1 blind*) OR (doubl* W/1 mask*) OR (singl* W/1 blind*) OR (singl* W/1 mask*) OR (tripl* W/1 blind*) OR (tripl* W/1 mask*) OR (trebl* W/1 blind*) OR (trebl* W/1 mask*) OR "latin square" OR placebo* OR nocebo*)

5 TITLE-ABS-KEY((control* W/3 study) OR "comparative study" OR "comparative survey" OR "comparative analysis" OR "cross-sectional study" OR "cross-sectional analysis" OR "cross-sectional survey" OR "cross-sectional design" OR "prevalence study" OR "prevalence analysis" OR "prevalence survey" OR "disease frequency study" OR "disease frequency analysis" OR "disease frequency survey" OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR (population W/3 (stud* or survey* or analys* or research)) OR (("follow-up" or followup) W/1 (stud* or survey or analysis)) OR ((observation or observational) W/1 (study or survey or analysis)) OR "clinical study" OR "evaluation study" OR "evaluation survey" OR "evaluation analysis" OR "quantitative

study" OR "quantitative analys*" OR "numerical study" OR "validation study" OR "validation survey" OR "validation analysis" OR "quasi experimental study" OR "quasi experimental analysis" OR "quasiexperimental study" OR "quasiexperimental analysis" OR "field study" OR "field survey" OR "field analysis" OR "in vivo study" OR "in vivo analysis" OR "panel study" OR "panel survey" OR "panel analysis" OR ((prevention or preventive) W/3 (trial or study or analysis or survey)) OR "replication study" OR "replication analysis " OR "replication trial" OR "feasibility study" OR "feasibility analysis" OR "trend study" OR "trend survey" OR "trend analysis" OR ((correlation* W/2 study) OR (correlation* W/2 analys*)) OR "case control study" OR "case base study" OR "case referrent study" OR "case referent study" OR "case referent study" OR "case compeer study" OR "case comparison study" OR "matched case control" OR "confidence interval" OR "regression analysis" OR "least square" OR "least squares" OR (hazard* W/1 (model OR analys* OR regression or ratio or ratios)) OR "Cox model" OR "Cox multivariate analyses" OR "Cox multivariate analysis" OR "Cox regression" OR "Cox survival analyses" OR "Cox survival analysis" OR "Cox survival model" OR ((study OR trial OR random* OR control*) AND compar*))

6 1 and 2 and 3 and (4 or 5)

7 DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

8 6 and not 7

9 PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)

10 8 and not 9

ClinicalTrials.Gov

Open Studies | anxiety OR overanxious OR phobia OR acrophobia OR agoraphobia OR claustrophobia OR homophobia OR neophobia OR ophidiophobia OR xenophobia | Child
Active, not recruiting | anxiety OR overanxious OR phobia OR acrophobia OR agoraphobia OR claustrophobia OR homophobia OR neophobia OR ophidiophobia OR xenophobia | Child
Enrolling by invitation | anxiety OR overanxious OR phobia OR acrophobia OR agoraphobia OR claustrophobia OR homophobia OR neophobia OR ophidiophobia OR xenophobia | Child

Health Canada

Any of these words: anxiety overanxious phobia acrophobia agoraphobia claustrophobia homophobia neophobia ophidiophobia xenophobia
All of these words: child
Any of these words: anxiety overanxious phobia acrophobia agoraphobia claustrophobia homophobia neophobia ophidiophobia xenophobia
All of these words: children
Any of these words: anxiety overanxious phobia acrophobia agoraphobia claustrophobia homophobia neophobia ophidiophobia xenophobia
All of these words: adolescent

Any of these words: anxiety overanxious phobia acrophobia agoraphobia claustrophobia homophobia neophobia ophidiophobia xenophobia
All of these words: teen

Medicines and Healthcare Products Regulatory Agency

Any of these words: anxiety overanxious phobia acrophobia agoraphobia claustrophobia homophobia neophobia ophidiophobia xenophobia

AHRQ's Horizon Scanning System

Anxiety OR overanxious OR phobia OR acrophobia OR agoraphobia OR claustrophobia OR homophobia OR neophobia OR ophidiophobia OR xenophobia

Appendix C. Criteria for Inclusion/Exclusion of Studies

Table C.1. Inclusion and exclusion criteria

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Populations	Humans Children and adolescents between 3 and 18 years old Patients with confirmed diagnosis of panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, or separation anxiety	Animals Adults (age >= 18 years) Infants (age < 3 years) Patients without confirmed diagnosis of panic disorder, social anxiety disorder, specific phobias, generalized anxiety disorder, or separation anxiety
Interventions	Any psychotherapy, pharmacotherapy, alone or combined: Pharmacological treatments will include all formulations of: Selective reuptake inhibitor (SRI): Citalopram (Celexa), Escitalopram (Lexapro), Fluoxetine (Prozac), Fluvoxamine (Luvox), Paroxetine (Paxil), Sertraline (Zoloft) Serotonin-norepinephrine reuptake inhibitors (SNRI): Desvenlafaxine (Pristiq), Duloxetine (Cymbalta), Venlafaxine (Effexor) Tricyclic antidepressants (TCA): Amiptriptyline or Nortriptyline (Elavil or Aventyl HCI), Clomipramine (Anafranil) Benzodiazepines: Alprazolam (Xanax, Niravam), Clonazepam (Klonopin), Lorazepam (Ativan) Atypical Antipsychotics: Aripiprazole (Abilify), Olanzapine (Zyprexa Zydis), Quetiapine (Seroquel), Risperidone (Risperdal), Ziprasidone (Geodon, Zeldox, or Zipwell) Monoamine oxidase inhibitor: Phenelzine (Nardil) Others: Bupropion (Wellbutrin), Mirtazapine (Remeron), D-Cycloserine (Seromycin), N-Acetylcysteine, Methylphenidate (Ritalin, Daytrana, Concerta, Methylin, or Aptensio), Riluzole (Rilutek), Buspirone (Buspar), Propranolol (Inderal, Hemangeol, or Innopran), Prazosin (Minipress), Cyproheptadine (Periactin or Peritol), Carbamazepine (Tegretol, Carbatrol, Equetro, or Epitol), Divalproex (Alti-Valproic, Depakote, Depakote DR, Depakote ER, or Depakote Sprinkles) Psychotherapies: Cognitive and behavioral therapies (CBT) Exposure Therapy/Systematic Desensitization	None

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
	Contingency Management Exposure Therapy Self-Control Exposure Therapy Family Focused Cognitive Behavior Therapy Child Focused Cognitive Behavior Therapy Parent Child Interaction Therapy Problem solving therapy (PST) Third wave (Mindfulness) therapies Acceptance and Commitment Therapy Mindfulness Based Cognitive Therapy/Mindfulness Based Stress Reduction Psychodynamic psychotherapy Interpersonal psychotherapy (IPT) Play therapy Family therapy Behavioral Systems Family therapy Narrative Family Therapy Solution Focused Family Therapy Strategic Family Therapy Attention modification program Motivational interviewing Eye movement desensitization reprocessing therapy (EMDR) Complementary psychotherapy techniques Exercise Biofeedback Relaxation Therapies Progressive muscle relaxation Diaphramatic breathing Visualization Meditation techniques Hypnosis Or any combined of the listed treatment	
Comparators	Other treatment or no treatment	None
Outcomes	KQ 1: Intermediate outcomes: Standardized measures (child, parent, school, and clinician report) such as the Screen for Anxiety-Related Emotional Disorders (SCARED), the Revised Children's Manifest Anxiety Scale (RCMAS), the Beck Anxiety Inventory, the Multidimensional Anxiety Scale for Children (MASC), the Liebowitz Social Anxiety Scale, the Social Phobia and Anxiety Inventory for Children, the Spence Children's Anxiety Scale (child and parent report) (SCAS), Fear Survey Schedule for Children – Revised, Stait Trait Anxiety Inventory - Child (STAIC), Anxiety Disorder Interview Schedule - Child report, Pediatric Anxiety Rating Scale (PARS), Child Behavior Checklist (CBCL), Revised Child Anxiety and Depression Scale (RCADS), Pre-	None

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
	School Anxiety Scale, Clinical Global Impression Scale (CGI), Children's Anxiety Meter-State (CAM-S) Patient centered outcomes: Remission, relapse, anxiety symptoms, behavioral problems (Behavior Assessment System for Children, Achenbach Child Behavior Checklist), parental overprotection, accommodation, parent distress, therapeutic alliance, school attendance, reduction in impairment (Child Sheehan Disability Scale), quality of life (Multidimensional Child Health Questionnaire, and Youth Quality of Life Instrument – Research Version), avoiding hospitalization, length of treatment, availability of treatment, peer relationship, functional impairment (Child Anxiety Impact Scale (CAIS), Children's Global Assessment Scale (CGAS), and Child Anxiety Life Interference Scale (CALIS)), avoidance behavior in children. KQ 2: Safety outcomes such as incidence of any adverse events, GI adverse effects/discomfort, withdrawal symptoms, dropouts due to adverse events, neurological complaints, increase motor activity, suicidal ideation, homicidal behavior, treatment emergent suicidality, addiction, self-injurious behaviors, activation issues (e.g. sleep, motor activity), agitation, akathisia, mania, aggression, and psychosis.	
Timing	Any	None
Settings	Any	None
Study design	Original data Any sample size RCTs, nonrandomized comparative studies (prospective and retrospective) Relevant systematic reviews, or meta-analyses (used for identifying additional studies)	In vitro studies Non-original data (e.g. narrative reviews, editorials, letters, or erratum) Non-comparative observational studies, case series
Publications	Any	None

KQ = key question; PICOTS = populations, interventions, comparators, outcomes, timing, and settings; RCT = randomized controlled trial

Appendix D. Excluded Studies

1. Al-Namankany A, Petrie A, Ashley P. Video modelling and reducing anxiety related to dental injections - a randomised clinical trial. Br Dent J. 2014 Jun;216(12):675-9. doi: 10.1038/sj.bdj.2014.497 PMID: 24970519. *The study does not have children with anxiety (3-18 yrs).*

2. Alfano CA, Pina AA, Villalta IK, et al. Mediators and moderators of outcome in the behavioral treatment of childhood social phobia. J Am Acad Child Adolesc Psychiatry. 2009 Sep;48(9):945-53. doi: 10.1097/CHI.0b013e3181af8216 PMID: 19625981.*The study is not a comparative study (case reports only included for side effects/ harms).*

3. Anbar RD, Hummell KE. Teamwork approach to clinical hypnosis at a pediatric pulmonary center. American Journal of Clinical Hypnosis. 2005;48(1):45-9 doi:10.1080/00029157.2005.10401489 PMID: 2005408928. *The study does not have children with anxiety (3-18 yrs).*

4. Anderson RE, Spence SH, Donovan CL, et al. Working alliance in online cognitive behavior therapy for anxiety disorders in youth: comparison with clinic delivery and its role in predicting outcome. J Med Internet Res. 2012 Jun 28;14(3):e88. doi:10.1080/00029157.2005.10401489 PMID: 2012-32354-008. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

5. Andrzejewska E, Bogucka A, Losiowski Z. [Effectiveness of psychotherapy in the treatment of adolescents]. Psychiatr Pol. 1979 Jul-Aug;13(4):373-6 PMID: 515252. *Other reason for exclusion.*

6. Araya R, Fritsch R, Spears M, et al. School intervention to improve mental health of students in Santiago, Chile: a randomized clinical trial. JAMA Pediatr. 2013 Nov;167(11):1004-10. doi: 10.1001/jamapediatrics.2013.2361 PMID: 2013761184. *The study does not have children with anxiety (3-18 yrs).*

7. Attwood M, Meadows S, Stallard P, et al. Universal and targeted computerised cognitive behavioural therapy (Think, Feel, Do) for emotional health in schools: Results from two exploratory studies. Child and Adolescent Mental Health. 2012;17(3):173-8 doi:10.1111/j.1475-3588.2011.00627.x. PMID: WOS:000306402400008. *The study does not have children with anxiety (3-18 yrs).*

8. Aydin A, Tekinsav-Sütçü S, Sorias O. Evaluation of the effectiveness of a cognitive-behavioral therapy program for alleviating the symptoms of social anxiety in adolescents. Turk Psikiyatri Dergisi. 2010;21(1):1. PMID: 20204902. *Turkish study.*

9. Bar-Haim Y, Morag I, Glickman S. Training anxious children to disengage attention from threat: a randomized controlled trial. J Child Psychol Psychiatry. 2011 Aug;52(8):861-9. doi: 10.1111/j.1469-7610.2011.02368.x PMID: 21250993.*The study does not have children with anxiety (3-18 yrs).*

10. Barnes VA, Johnson MH, Williams RB, et al. Impact of Williams Lifeskills(R) Training on Anger, Anxiety and Ambulatory Blood Pressure in Adolescents. Transl Behav Med. 2012 Dec 01;2(4):401-10. doi: 10.1007/s13142-012-0162-3 PMID: 23482659. *The study does not have children with anxiety (3-18 yrs).*

11. Barrett PM, Duffy AL, Dadds MR, et al. Cognitive-behavioral treatment of anxiety disorders in children: long-term (6-year) follow-up. J Consult Clin Psychol. 2001 Feb;69(1):135-41. PMID: 11302272. *Other reason.*

12. Barrett, P M, Lock, et al. Developmental differences in universal preventive intervention for child anxiety. Clinical Child Psychology and Psychiatry. 2005 October;10(4):539-55. doi: 10.1177/1359104505056317. *The study does not have children with anxiety (3-18 yrs).*

13. Barrett, P M, Sonderegger, et al. Using FRIENDS to combat anxiety and adjustment problems among young migrants to Australia: A national trial. Clinical Child Psychology and Psychiatry. 2003 April;8(2):241-60. doi: 10.1177/1359104503008002008. *The study does not have children with anxiety (3-18 yrs).*

14. Barrington, J, Prior, et al. Effectiveness of CBT versus standard treatment for childhood anxiety disorders in a community clinic setting. Behaviour Change. 2005;22(1):29-43. doi:10.1375/bech.22.1.29.66786. *Other reason.*

15. Baumgartner JL, Emslie GJ, Crismon ML. Citalopram in children and adolescents with depression or anxiety. Ann Pharmacother. 2002 Nov;36(11):1692-7. doi:10.1345/aph.1C078 PMID: 12398561. *The study does not have children with anxiety (3-18 yrs).*

16. Becker, Emily M, Becker, et al. Modular cognitive behavioral therapy for youth with anxiety disorders: A closer look at the use of specific modules and their relation to treatment process and response. School Mental Health. 2012 Dec;4(4):243-53. doi:10.1007/s12310-012-9080-2. *The study is not a comparative study (case reports only included for side effects/ harms).*

17. Beidel DC, Turner SM, Young BJ. Social effectiveness therapy for children: five years later. Behav Ther. 2006 Dec;37(4):416-25. doi: 10.1016/j.beth.2006.06.002 PMID: 17071218. *Other reason.*

18. Beidel DC, Turner SM, Young B, et al. Social effectiveness therapy for children: three-year follow-up. J Consult Clin Psychol. 2005 Aug;73(4):721-5. doi:10.1037/0022-006X.73.4.721 PMID: 16173859. *The study is not a comparative study (case reports only included for side effects/ harms).*

19. Benjamin CL, Harrison JP, Settipani CA, et al. Anxiety and related outcomes in young adults 7 to 19 years after receiving treatment for child anxiety. J Consult Clin Psychol. 2013 Oct;81(5):865-76. doi: 10.1037/a0033048 PMID: 23688146. *The study is not a comparative study (case reports only included for side effects/ harms).*

20. Benjamin CL, O'Neil KA, Crawley SA, et al. Patterns and predictors of subjective units of distress in anxious youth. Behav Cogn Psychother. 2010 Jul;38(4):497-504. doi:10.1017/S1352465810000287 PMID: 20509987. *The study is not a comparative study (case reports only included for side effects/ harms).*

21. Berg I, Fielding D. An evaluation of hospital in-patient treatment in adolescent school phobia. Br J Psychiatry. 1978 May;132:500-5. doi: 10.1192/bjp.132.5.500 PMID:656715.*The study does not include any of the interventions listed above (pharmacotherapy or psychotherapy)*

22. Berman, S L, Weems, et al. Predictors of outcome in exposure-based cognitive and behavioral treatments for phobic and anxiety disorders in children. Behavior Therapy. 2000;31(4):713-31. doi:10.1016/S0005-7894(00)80040-4. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

23. Berney T, Kolvin I, Bhate SR, et al. School phobia: a therapeutic trial with clomipramine and short-term outcome. Br J Psychiatry. 1981 Feb;138:110-8. doi:10.1192/bjp.138.2.110 PMID: 7020816. *The study does not have children with anxiety (3-18 yrs).*

24. Bernstein GA, Anderson LK, Hektner JM, et al. Imipramine compliance in adolescents. J Am Acad Child Adolesc Psychiatry. 2000 Mar;39(3):284-91. doi:10.1097/00004583-200003000-00009 PMID: 10714047. *The study is not a comparative study (case reports only included for side effects/ harms).*

25. Bernstein GA, Hektner JM, Borchardt CM, et al. Treatment of school refusal: one-year follow-up. J Am Acad Child Adolesc Psychiatry. 2001 Feb;40(2):206-13. doi:10.1097/00004583-200102000-00015 PMID: 11211369.*The study does not have children with anxiety (3-18 yrs).*

26. Bernstein GA, Bernat DH, Victor AM, et al. School-based interventions for anxious children: 3-, 6-, and 12-month follow-ups. J Am Acad Child Adolesc Psychiatry. 2008 Sep;47(9):1039-47. doi:10.1097/CHI.ob013e31817eecco PMID: 18665000. *The study does not have children with anxiety (3-18 yrs).*

27. Bernstein GA, Layne AE, Egan EA, et al. School-based interventions for anxious children. J Am Acad Child Adolesc Psychiatry. 2005 Nov;44(11):1118-27. doi:10.1097/01.chi.0000177323.400 05.a1 PMID: 16239860. *The study does not have children with anxiety (3-18 yrs).*

28. Berry K, Hunt CJ. Evaluation of an Intervention Program for Anxious Adolescent Boys Who Are Bullied at School. Journal of Adolescent Health. 2009 Oct;45(4):376-82. doi:10.1016/j.jadohealth.2009.04.02 3 PMID: 19766942. *The study does not have children with anxiety (3-18 yrs).*

29. Bilek EL, Ehrenreich-May J. An open trial investigation of a transdiagnostic group treatment for children with anxiety and depressive symptoms. Behav Ther. 2012 Dec;43(4):887-97. doi:10.1016/j.beth.2012.04.007 PMID: 23046789. *The study is not a comparative study (case reports only included for side effects/ harms).*

30. Bjaastad JF, Haugland BS, Fjermestad KW, et al. Competence and Adherence Scale for Cognitive Behavioral Therapy (CAS-CBT) for anxiety disorders in youth: Psychometric properties. Psychol Assess. 2016 Aug;28(8):908-16. doi:10.1037/pas0000230 PMID:26460894 . *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

31. Blagg NR, Yule W. The behavioural treatment of school refusal--a comparative study. Behav Res Ther. 1984;22(2):119-27. doi:10.1016/0005-7967(84)90100-1 PMID:6712554. *The study does not have children with anxiety (3-18 yrs).*

32. Blatter M, Judith, Schneider, et al. Cognitive behavioral therapy for children suffering from separation anxiety. Journal de Therapie Comportementale et Cognitive. 2011 Sep;21(3):84-9. doi:10.1016/j.jtcc.2011.07.011. *The study is not original (commentaries, letters, etc.)*

33. Bodden DH, Bögels SM, Nauta MH, et al. Child versus family cognitive-behavioral therapy in clinically anxious youth: an efficacy and partial effectiveness study. Journal of the American Academy of Child & Adolescent Psychiatry. 2008;47(12):1384-94. doi:10.1097/CHI.0b013e318189148e PMID: 18981932. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

34. Bogels SM, Siqueland L. Family cognitive behavioral therapy for children and adolescents with clinical anxiety disorders. J Am Acad Child Adolesc Psychiatry. 2006 Feb;45(2):134-41. doi:10.1097/01.chi.0000190467.01072.ee PMID: 16429083. *The study is not a comparative study (case reports only included for side effects/ harms).*

35. Byrne SP, Rapee RM, Richardson R, et al. D-cycloserine enhances generalization of fear extinction in children. Depress Anxiety. 2015 Jun;32(6):408-14. doi:10.1002/da.22356 PMID: 25775435. *The study does not include any of the interventions listed above (pharmacotherapy or psychotherapy)*

36. Calear AL, Batterham PJ, Poyser CT, et al. Cluster randomised controlled trial of the e-couch Anxiety and Worry program in schools. J Affect Disord. 2016 May 15;196:210-7. doi:10.1016/j.jad.2016.02.049 PMID: 26926660. *The study does not have children with anxiety (3-18 yrs).*

37. Caporino, N E, Herres, et al. Dysregulation in Youth with Anxiety Disorders: Relationship to Acute and 7- to 19- Year Follow-Up Outcomes of Cognitive-Behavioral Therapy. Child Psychiatry and Human Development. 2015. doi:10.1007/s10578-015-0587-2 PMID: 26384978. Child Psychiatry and Human Development. 2015. *The study is not a comparative study (case reports only included for side effects/ harms).*

38. Caporino NE, Brodman DM, Kendall PC, et al. Defining treatment response and remission in child anxiety: signal detection analysis using the pediatric anxiety rating scale. J Am Acad Child Adolesc Psychiatry. 2013 Jan;52(1):57-67. doi:10.1016/j.jaac.2012.10.006 PMID: 23265634. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

39. Cederblad, M, Bodén, et al. Barnpsykiatrisk slutenvård i två iän reduktion av platsantalet i östergötland, effekt på klientelsammansättdng och vårdkonsumtion. Nordic Journal of Psychiatry. 1988;42(5):361-7.*The study does not have children with anxiety (3-18 yrs).*

40. Chambers, J A, Power, et al. Parental styles and long-term outcome following treatment for anxiety disorders. Clinical Psychology and Psychotherapy. 2004 May/June;11(3):187-98. doi:10.1002/cpp.406. Clinical Psychology and Psychotherapy. 2004 May/June;11(3):187-98. PMID:2004453864. *The study does not have children with anxiety (3-18 yrs).*

41. Chutko LS, Surushkina S, Nikishena IS, et al. [Adaptol in the treatment of anxiety disorders in children with school maladaptation]. Zh Nevrol Psikhiatr Im S S Korsakova. 2010;110(2):45-9. doi:10.1007/s11055-011-9448-z PMID: 20436449 *The study does not have children with anxiety (3-18 yrs).*

42. Clark DB, Birmaher B, Axelson D, et al. Fluoxetine for the treatment of childhood anxiety disorders: open-label, long-term extension to a controlled trial. J Am Acad Child Adolesc Psychiatry. 2005 Dec;44(12):1263-70. doi:10.1097/01.chi.0000183464.41777.c1 PMID: 16292118. *Other reason.*

43. Comer JS, Puliafico AC, Aschenbrand SG, et al. A pilot feasibility evaluation of the CALM Program for anxiety disorders in early childhood. J Anxiety Disord. 2012 Jan;26(1):40-9.doi:10.1016/j.janxdis.2011.08.011 PMID: 21917417. *The study is not a comparative study (case reports only included for side effects/ harms).*

44. Compton SN, Peris TS, Almirall D, et al. Predictors and moderators of treatment response in childhood anxiety disorders: results from the CAMS trial. J Consult Clin Psychol. 2014 Apr;82(2):212-24. doi:10.1037/a0035458 PMID: 24417601. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

45. Compton SN, Walkup JT, Albano AM, et al. Child/Adolescent Anxiety Multimodal Study (CAMS): rationale, design, and methods. Child Adolesc Psychiatry Ment Health. 2010 Jan 05;4:1.2010;4:1. doi: 10.1186/1753-2000-4-1 PMID: 20051130. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

46. Cooper, P J, Gallop, et al. Treatment response in child anxiety is differentially related to the form of maternal anxiety disorder. Behavioural and Cognitive Psychotherapy. 2008 January;36(1):41-8. doi:10.1017/S1352465807003943. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

47. Cotton, S, Luberto, et al. Mindfulness-based cognitive therapy for youth with anxiety disorders at risk for bipolar disorder: a pilot trial. doi:10.1111/eip.12216 PMID:25582800 Early Intervention in Psychiatry. 2015. *The study is not a comparative study (case reports only included for side effects/ harms).*

48. Crawford AM, Manassis K. Familial predictors of treatment outcome in childhood anxiety disorders. J Am Acad Child Adolesc Psychiatry. 2001 Oct;40(10):1182-9. doi:10.1097/00004583-200110000-00012 PMID: 11589531. *The study is not a comparative study (case reports only included for side effects/ harms).*

49. Crawley, S A, Beidas, et al. Treating socially phobic youth with CBT: Differential outcomes and treatment considerations. Behavioural and Cognitive Psychotherapy. 2008 July;36(4):379-89. doi:10.1017/S1352465808004542 . *The study is not a comparative study (case reports only included for side effects/ harms).*

50. Crawley SA, Kendall PC, Benjamin CL, et al. Brief Cognitive-Behavioral Therapy for Anxious Youth: Feasibility and Initial Outcomes. Cogn Behav Pract. 2013 May 01;20(2):123-33. doi:10.1016/j.cbpra.2012.07.003 PMID:24244089. *The study is not a comparative study (case reports only included for side effects/ harms).*

51. Creswell C, Willetts L, Murray L, et al. Treatment of child anxiety: an exploratory study of the role of maternal anxiety and behaviours in treatment outcome. Clin Psychol Psychother. 2008 doi:10.1002/cpp.559 PMID:19115426. *The study is not a comparative study (case reports only included for side effects/ harms).*

52. Cummings CM, Caporino NE, Settipani CA, et al. The therapeutic relationship in cognitive-behavioral therapy and pharmacotherapy for anxious youth. J Consult Clin Psychol. 2013 Oct;81(5):859-64. doi:10.1037/a0033294 PMID:23750468. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

53. Cummings CM, Fristad MA. Anxiety in children with mood disorders: a treatment help or hindrance? J Abnorm Child Psychol. 2012 Apr;40(3):339-51. doi:10.1007/s10802-011-9568-5 PMID: 21912843. *The study does not have children with anxiety (3-18 yrs).*

54. Cunningham MJ, Wuthrich V. Examination of barriers to treatment and user preferences with computer-based therapy using the Cool Teens CD for adolescent anxiety. Sensoria: A Journal of Mind, Brain & Culture. 2008;4(2):12-7 doi:10.7790/ejap.v4i2.115. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

55. Cunningham NR, Jagpal A, Tran ST, et al. Anxiety Adversely Impacts Response to Cognitive Behavioral Therapy in Children with Chronic Pain. J Pediatr. 2016 Apr;171:227-33. doi:10.1016/j.jpeds.2016.01.018 PMID: 26879812. *The study does not have children with anxiety (3-18 yrs).*

56. Dadds MR, Holland DE, Laurens KR, et al. Early intervention and prevention of anxiety disorders in children: results at 2-year follow-up. J Consult Clin Psychol. 1999 Feb;67(1):145-50. PMID:10028219. *The study does not have children with anxiety (3-18 yrs).*

57. Dadds MR, Spence SH, Holland DE, et al. Prevention and early intervention for anxiety disorders: a controlled trial. J Consult Clin Psychol. 1997 Aug;65(4):627-35. doi: 10.1037/0022-006X.65.4.627 PMID: 9256564. *The study does not have children with anxiety (3-18 yrs).*

58. Dadsetan, Parirokh, Anari, et al. Social anxiety disorders and drama-therapy. Journal of Iranian Psychologists. 2008;4(14):115-23. *Persian study.*

59. Dahlstrom H, Fedor-Freybergh P, Kareland H, et al. Benzoctamine and medazepam in treatment of anxiety of children and adolescents: a comparative study. Acta Psychiatr Scand. 1973 Jul;49(6):735-43. doi:10.1111/j.1600-0447.1973.tb04462.x PMID:4592708. *The study does not have children with anxiety (3-18 yrs).*

60. De J, P J, Andrea, et al. Spider phobia in children: Disgust and fear before and after treatment. Behaviour Research and Therapy. 1997 June;35(6):559-62. doi:10.1016/S0005-7967(97)00002-8 PMID:9159980. *The study is not a comparative study (case reports only included for side effects/ harms).*

61. De Los R, Andres, Alfano, et al. Are the clinical characteristics of anxious youths participating in non-treatment-related research comparable to those of youths receiving treatment? Child & Youth Care Forum. 2016 Apr:No Pagination Specified. doi:10.1007/s10566-016-9355-0. *The study does not include any of the interventions listed above (pharmacotherapy or psychotherapy)*

62. Díaz, Cristina. Evaluación y tratamiento cognitivo-conductual de un caso de fobia social. Psicologia. com. 1997;1(1). *The study is not a comparative study (case reports only included for side effects/ harms).*

63. Diomsina B, Vyciniene D. [Anxiety disorders in children and adolescents. Psychotherapeutic interventions]. Medicina (Kaunas). 2002;38(4):466-70. PMID:12474798. *The study does not have children with anxiety (3-18 yrs).*

64. Diukova G, Vorob'eva O, Petrova E, et al. The efficacy of alprazolam in the therapy of panic disorders. Zhurnal nevrologii i psikhiatrii imeni SS Korsakova. 1995;95(4):9-13. PMID:8533521. Other reason for exclusion

65. Dour, H J, Chorpita, et al. Sudden gains as a long-term predictor of treatment improvement among children in community mental health organizations. Behaviour Research and Therapy. 2013 September;51(9):564-72. doi:10.1016/j.brat.2013.05.012 PMID:23856657. *The study does not have children with anxiety (3-18 yrs).*

66. Drahota A, Wood JJ, Sze KM, et al. Effects of cognitive behavioral therapy on daily living skills in children with high-functioning autism and concurrent anxiety disorders. J Autism Dev Disord. 2011 Mar;41(3):257-65. doi:10.1007/s10803-010-1037-4 PMID: 20508979. *The study does not have children with anxiety (3-18 yrs).*

67. Drtílková, I, Blažek, et al. Retrospective evaluation of the effect of sertraline in different indications in children and adolescents. Ceska a Slovenska Psychiatrie. 2001;97(4):157-61.*The study does not have children with anxiety (3-18 yrs).*

68. Duan YE. [Treatment of child extensive anxiety disorder with catgut implantation of point plus western medicine]. Zhongguo Zhen Jiu. 2007 May;27(5):341-3. PMID:17645255. *The study does not have children with anxiety (3-18 yrs).*

69. Eckmann, F, Hoeppner, et al. Sulpiride treatment of children with behavior disturbances. Fortschritte der Medizin. 1975;93(9):464-5. *The study does not have children with anxiety (3-18 yrs).*

70. Eisen AR, Raleigh H, Neuhoff CC. The unique impact of parent training for separation anxiety disorder in children. Behav Ther. 2008 Jun;39(2):195-206. doi:10.1016/j.beth.2007.07.004 PMID:18502252. *The study is not a comparative study (case reports only included for side effects/ harms).*

71. Eisenberg L, Gilbert A, Cytryn L, et al. The effectiveness of psychotherapy alone and in confunction with perphenazine or placebo in the treatment of neurotic and hyperkinetic children. Am J Psychiatry. 1961 Jun;117:1088-93. doi:10.1176/ajp.117.12.1088 PMID:13726172. *The study does not have children with anxiety (3-18 yrs).*

72. Emslie, G J. Combination of cognitive behavioral therapy and sertraline is more effective than monotherapy for pediatric anxiety disorders. Journal of Pediatrics. 2009 May;154(5):775-6. doi:10.1016/j.jpeds.2009.02.045 PMID:19364568. *Conference procceeding without full text.*

73. Farrell, L J, Barrett, et al. Community trial of an evidence-based anxiety intervention for children and adolescents (the FRIENDS program): A pilot study. Behaviour Change. 2005;22(4):236-48. doi:10.1375/bech.22.4.236 *The study does not have children with anxiety (3-18 yrs).*

74. Fathi A, A, Salimi, et al. Test-anxiety in Iranian students: Cognitive therapy vs. systematic desensitisation. Archives of Medical Science. 2006 September;2(3):199-204. *The study does not have children with anxiety (3-18 yrs).*

75. Festen H, Hartman CA, Hogendoorn S, et al. Temperament and parenting predicting anxiety change in cognitive behavioral therapy: the role of mothers, fathers, and children. J Anxiety Disord. 2013 Apr;27(3):289-97. doi:10.1016/j.janxdis.2013.03.001 PMID:23602942. *The study is not a comparative study (case reports only included for side effects/ harms).*

76. Fitzgerald A, Rawdon C, Dooley B. A randomized controlled trial of attention bias modification training for socially anxious adolescents. Behav Res Ther. 2016 Sep;84:1-8. doi:10.1016/j.brat.2016.06.003 PMID: 27379745. Behaviour Research and Therapy. 2016;84:1-8. *The study does not have children with anxiety (3-18 yrs).*

77. Fjermestad KW, Lerner MD, McLeod BD, et al. Therapist-youth agreement on alliance change predicts long-term outcome in CBT for anxiety disorders. J Child Psychol Psychiatry. 2016 May;57(5):625-32. doi:10.1111/jcpp.12485 PMID:26647901. *The study is not a comparative study (case reports only included for side effects/ harms).*

78. Forbes EE, Stepp SD, Dahl RE, et al. Real-world affect and social context as predictors of treatment response in child and adolescent depression and anxiety: an ecological momentary assessment study. J Child Adolesc Psychopharmacol. 2012 Feb;22(1):37-47. doi:10.1089/cap.2011.0085 PMID:22339611. *The study does not have children with anxiety (3-18 yrs).*

79. Fox E, Zougkou K, Ashwin C, et al. Investigating the efficacy of attention bias modification in reducing high spider fear: The role of individual differences in initial bias. Journal of behavior therapy and experimental psychiatry. 2015;49:84-93 doi:10.1016/j.jbtep.2015.05.001 PMID:26060177. *The study does not have children with anxiety (3-18 yrs).*

80. Fu X, Du Y, Au S, et al. Reducing negative interpretations in adolescents with anxiety disorders: a preliminary study investigating the effects of a single session of cognitive bias modification training. Dev Cogn Neurosci. 2013 Apr;4:29-37. doi:10.1016/j.dcn.2012.11.003 PMID:23219491. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

81. Galla BM, Wood JJ, Chiu AW, et al. One year follow-up to modular cognitive behavioral therapy for the treatment of pediatric anxiety disorders in an elementary school setting. Child Psychiatry Hum Dev. 2012 Apr;43(2):219-26. doi:10.1007/s10578-011-0258-x PMID:21987227. *The study is not a comparative study (case reports only included for side effects/ harms).*

82. Garcia L, L J, Olivares, et al. A pilot study on sensitivity of outcome measures for treatments of generalized social phobia in Spanish adolescents. International journal of clinical and health psychology. 2005;5(2):385-92. *The study does not report anxiety outcomes (symptom severity and scales, behavioral outcomes, adverse effects, etc).*

83. Garcia L, L J, Olivares, et al. Results at long-term among three psychological treatments for adolescents with generalized social phobia (II): Clinical significance and effect size. Psicologia Conductual. 2002;10(2):371-85. *Other reason.*

84. García L, L J, Ruiz, et al. Transporting a school-based multicomponent treatment for adolescents to young adults with social anxiety: A pilot study. Psicologia Conductual. 2006;14(1):63-73. *The study is not a comparative study (case reports only included for side effects/ harms).*

85. Gil-Bernal F, Hernández-Guzmán L. Tratamiento cognitivo-conductual para niños mexicanos con fobia social. Anuario de Psicología. 2009;40(1). *The study does not have children with anxiety (3-18 yrs).*

86. Girling B, R D, Ronan, et al. Brief cognitive-behavioural therapy for children with anxiety disorders: Initial evaluation of a program designed for clinic settings. Behaviour Change. 2009 April;26(1):27-53. doi:10.1375/bech.26.1.27. *The study is not a comparative study (case reports only included for side effects/ harms).*

87. Gittelman K, R, Klein, et al. Controlled Imipramine Treatment of School Phobia. Archives of General Psychiatry. 1971;25(3):204-7.PMID:18730587. *The study does not have children with anxiety (3-18 yrs).*

88. GlaxoSmithKline. A 16 Week Double-Blind, Placebo Controlled Study to Investigate the Efficacy and Tolerability of Paroxetine in the Treatment of Children and Adolescents with Social Anxiety Disorder/Social Phobia (29060/676). GSK Clinical Study Register [www.gsk clinicalstudyregister.com]. 2001 *Other reason.*

89. Gonzalez A, Peris TS, Vreeland A, et al. Parental anxiety as a predictor of medication and CBT response for anxious youth. Child psychiatry and human development. 2015;46(1):84 doi:10.1007/s10578-014-0454-6 PMID:24610431. *The study does not have children with anxiety (3-18 yrs).*

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Appendix E. Description of Included Studies

Table E.1. Characteristics of the included studies comparing drugs versus pill placebo

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Abikoff, 2005 [1]	United States RCT Efficacy Mental health clinic	Anxiety disorder	SSRI: Fluvoxamine, (N=15)	Maximum of 300 mg in adolescents and 250 mg in children younger than 13 years of age.	Mean age: 10 (Range 6 – 17)	NR
			Control, (N=10)	Pill placebo		
Alfano, 2007 [2]	United States RCT Efficacy Outpatient	GAD, SAD, SoP	SSRI: Fluvoxamine, (N=54)		Age; 6 – 17 Male: 70% Caucasian: 77.1%, African American: 8.5%, Hispanic: 22.8% Other: 13.3%	NR
			Control, (N=51)	Pill placebo		
Beidel, 2007 [3]	United States RCT Efficacy Mental health clinic	GAD, SAD, SP, SoP	SSRI: Fluoxetine, (N=43)	10mg per day during week 1 and 2. Increasing dose up to 40mg/day for up to 12 weeks.	Mean age:11.56 (Range 7 – 17) Male: 53.23% Caucasian: 74.1% African American: 15.1% Hispanic: 2.1% Asian: 2.8% Other: 3.5%	52
			Child CBT, (N=59)	Social Effectiveness Therapy (SET-C) Child CBT (Parents included <20%) Group and Individual based, exposure, relaxation, and cognitive problem solving. 60 min individual session and one 150 min group session twice a week for 12 weeks.		
			Control, (N=37)	Pill placebo		
Black, 1994 [4]	United States RCT Efficacy Mental health clinic	GAD, SAD, SoP CGI>=6: NR	SSRI: Fluoxetine, (N=6)	0.2 mg/kg for 1 week, then 0.4 mg/kg for 1 week, then 0.6 mg/kg for 10 weeks.	Mean age: 9.1 Male: 50%	0
			Control: (N=9)	Placebo syrup, 0.08 mL/kg/day for 2 weeks	Mean age: 8.1 Male: 33.3%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Birmaher, 2003 [5]	United States RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	SSRI: Fluoxetine, (N=37)	Up to 200 mg per day for 12 weeks	Mean age: 11.6 Male : 46% Caucasian: 97.2%, Asian: 2.8% Low income: 27.6% ADHD: 5%, Depression: 5%, dysthymia: 8%, enuresis: 5%	52
			Control, (N=37)	Pill placebo	Mean age: 11.9 Male: 46% Caucasian: 95%, Asian: 5% ODD: 8%, enuresis:8, tics: 5%	
da Costa, 2013[6]	Brazil RCT Efficacy Mental health clinic	GAD, SAD, SP Mean CGI= 4.9	TCA: Clomipramine (N=9)	Clomipramine 118.75 mg/ day average dose, 12 weeks	Mean age: 11.2 (range: 7-17) Males: 33% Lower class: 58.7% Upper/Middle class: 14.3%	0
			SSRI: Fluoxetine, (N=10)	SRI, SSRI, fluoxetine 35 mg/ day average dose for 12 weeks.	Mean age: 11.6 (range: 7-17) Males: 50% Lower class: 50% Upper/Middle class: 50%	
			Control, (N=11)	Pill placebo	Mean age: 11.4 (range: 7-17) Males: 54% Lower class: 45.4% Upper/Middle class: 45.4%	
Geller, 2007[7]	United States RCT Efficacy Outpatient	Anxiety disorder	SNRI: Atomoxetine, (N=87)		Mean age: 12.2 (Range 8 – 17) Male: 62% Caucasian: 77% ADHD: 100%	0
			Control, (N=89)	Pill placebo Patients completing 9th visit could participate in an open-label Atomoxetine extension period.	Mean age: 11.8 (8 -17) Male: 67.4% Caucasian: 82% ADHD: 100%	
Gittelman-Klein, 1973[8]	United States RCT Efficacy Outpatient	SP	TCA: Imipramine, (N=19)	Up to 200mg/day for 6 weeks	Mean age: 10.8 (range: 6-14)	0
			Control, (N=15)	Pill placebo		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Graae, 1994[9]	United States RCT Efficacy Mental health clinic	GAD,SAD, SoP, SP CGI>=6: NR	Benzodiazepines: Clonazepam, (N=8)	One tablet of up to 2 mg/ day for 4 weeks.	Mean age: 9.8(range:7-13) Male: 53.3% Caucasian: 100% ADHD: 20%, ODD : 20%, Conduct problems: 7%	0
			Control, (N=7)	Pill placebo One tablet a day for 4 weeks		
March, 2007[10]	United States RCT Effectivness Outpatient	SoP	SSRI: Venlafaxine, (N=141)	37.5 mg/day to a maximum dose of 225mg/day over 16 weeks.	Mean age: 13.6 (Range 8 – 18) Male: 42.1% Caucasian: 74.28, African: 14.28% Hispanic: 5%, Asian: 1.4%, Other: 2.85% GCI <6 n = 155 GCI >6 n = 22	0
			Control, (N=152)	Pill placebo	Mean age: 13.6 (Range 8 -16) Male: 43.3% Caucasian: 78.5%, African: 10%, Hispanic: 11.3%, Asian: 1.3%, Other: 2.6% GCI <6 n = 119 GCI >6 n = 29	
Pine, 2001 [11, 12]	United States RCT Efficacy Outpatient	GAD,SAD, SoP	SNRI: Fluoxetine, (N=63)	Up to 250 mg per day for 8weeks	Male: 51% Caucasian: 63%, African: 10%, Hispanic : 20%, other: 7% Low income (less than 25k) : 16%, Medium income (25k-60K): 30% High income (> 60K): 46% ADHD: 17.4%, Depression: 4%, OCD: 4%, ODD: 6%	0
			Control, (N=65)	Pill placebo	Male:52% Caucasian: 62%, African: 5%, Hispanic :18%, other: 15% Low income (less than 25k) : 15%, Medium income (25k-60K): 29% High income (> 60K): 42%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					ADHD: 13%, Depression: 5%, OCD: 5%, ODD: 5%, conduct disorder: 3%	
Reinblatt, 2009[13]	United States RCT Efficacy Mental health clinic	GAD,SAD, SoP	SSRI: Fluvoxamine, (N=22)	One tablet of up to 300mg/ day for 8 weeks	Mean age: 10 (range: 6-17) Male: 54.5% Caucasian: 95.4%	0
			Control, (N=23)	Pill placebo for 8 weeks	Mean age: 9.7(range: 6-17) Male: 52.2% Caucasian: 95.6%	
Rynn, 2001[14]	United States RCT Efficacy Mental health clinic	GAD	SSRI: Sertraline, (N=11)	25 mg/day for the first week, 50mg for weeks 2-9.	Mean age: 11.7 (Range 5 -17) Male: 77.2% Caucasian: 81.8%	0
			Control, (N=11)	Pill placebo		
Rynn, 2007[15]	United States RCT Efficacy Mental health clinic	Anxiety disorder	SSRI : Venlafaxine. (N=157)	37.5 mg/day during the first week. Doses thereafter ranged from 112.5mg – 225mg.	Age: 6 – 17 Male: 57.5%	0
			Control, (N=163)	Pill placebo		
Scharfstein, 2011[16]	United States RCT Effectiveness Outpatient	SoP	Child CBT, (N=46)	Social Effectiveness Therapy (SET-C) Child CBT (parents included <20%) Exposure and cognitive problem solving. One individual and one group session per week for 12 weeks.	Male: 50%	0
			SSRI: Fluoxetine, (N=22)	One tablet of up to 40mg/ day for 12 weeks		
			Control, (N=22)	Pill placebo Identically appearing placebo capsules once a week for 12 weeks.		
Strawn, 2015[17]	United States, Mexico, South Africa RCT	SAD, SoP Mean CGI: 4.5	SNRI: Duloxetine, (N=135)		Mean age: 12.6 (range: 7-17) Male: 65% Caucasian: 83% African American: 6.7%	10

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	Efficacy Outpatient				Asian: 0.7% Other:9.6%	
			Control, (N=137)	Pill placebo	Mean age: 12.2 (range: 7-17) Male: 62% Caucasian: 81% African American: 7.3% Asian: 0.7% Other:11%	
Wagner, 2004[18]	United States, South Africa, Canada and Belgium RCT Efficacy Mental health clinic	SoP	SSRI: Paroxetine, (N=165)	10-50 mg/day for 16 weeks.	Mean age: 13 Male: 43% Caucasian: 79.4%, other: 21%	16
			Control, (N=157)	Pill placebo Matching placebo pill, once per day.	Mean age: 13.3 Male: 56.6% Caucasian: 83.4%, other: 16.6%	
Walkup, 2002[19]	United States RCT Efficacy Outpatient	GAD, SAD, SoP	SSRI: Fluvoxamine(N=35)	Up to 250 mg/day for children and 300 mg/day for 32 weeks	Mean age: 10.2 Male: 43% Caucasian: 66%, African American:8%, Hispanic: 20%, other: 6% ADHD: 14%, ODD:6	0
			SSRI: Fluvoxamine + Fluoxetine, (N=14)	Fluvoxamine was tapered off during the first 2 weeks with Fluoxetine 10-40 mg/day. for 32 weeks	Mean age: 14.1 Male: 57% Caucasian: 64%, African American:22%, Hispanic: 7%, other: 7% ADHD: 7%, ODD:0% Fluvoxamine non-responder patients	
			Pill Placebo + SSRI: Fluvoxamine, (N=48)	Fluvoxamine was increased by 50 mg/week up to 300 mg/day in adolescents and 250 mg/day for children	Mean age: 10.3 Male: 48% Caucasian: 65%, African American:6%, Hispanic: 12%,	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					other: 8% ADHD: 8%, ODD:2% Placebo non-responder patients	
Walkup, 2008[20-26]	United States RCT Efficacy Outpatient	GAD,SAD, SoP	Child CBT, (N=139)	Coping cat Child CBT (parents included <20%) Individual-based, exposure, relaxation, cognitive problem solving. 60-minute session once a week for 12 weeks.	Mean age: 10.5 Male: 49.2% Caucasian: 76.3%, African American:10.1%, Hispanic: 9.2%, other: 4.5% Low income: 23.7% ADHD: 11.5%, ODD:13.8%, Tic disorder and other internalizing disorders: 41.7%	0
			SSRI: Sertraline, (N=133)	Beginning with 25mg/day Up to 200 mg/day by 8th week, for 12 weeks.	Mean age: 10.8 Male: 51.1% Caucasian: 77.4%, African American: 9%, Hispanic: 11.3%, other: 2.3% Low income: 26.3% ADHD: 12.7%, ODD:8.2%, Tic disorder and other internalizing disorders: 55.6%	
			Combination therapy: CBT+ SSRI: Child CBT+ Sertraline, (N=140)	Coping cat, Child CBT (parents included <20%) Individual-based, exposure, relaxation and cognitive problem solving plus Sertraline. 60-minute session once a week for 12 weeks plus up to 200 mg/day for 12 weeks.	Mean age: 10.7 Male: 49.6% Caucasian: 82.9%, African American: 7.9%, Hispanic: 5.6%, other: 3.6% Low income: 25.0% ADHD: 11.4%, ODD:10%, Tic disorder and other internalizing disorders: 42.8%	
			Control, (N=76)	Pill Placebo	Mean age: 10.6 Male : 51.3% Caucasian: 79%, African American: 9%, Hispanic: 9%, other: 3%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					Low income: 27.6% ADHD: 118%, ODD:9.2%, Tic disorder and other internalizing disorders: 44.7%	

ADHD: attention deficit hyperactivity disorder, CBT: cognitive behavioral therapy, CGI: clinical global impression scale. GAD: generalized anxiety disorder, NR: not reported, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, RCT: randomized control trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia, SRI: serotonin reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor

Table E.2. Characteristics of the included studies comparing drugs versus drugs

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
da Costa, 2013[6]	Brazil RCT Efficacy Mental health clinic	GAD, SAD, SP Mean CGI= 4.9	TCA: Clomipramine, (N=9)	Clomipramine 118.75 mg/ day average dose, 12 weeks	Mean age: 11.2 (range: 7-17) Males: 33% Lower class: 58.7% Upper/Middle class: 14.3%	0
			SSRI: Fluoxetine, (N=10)	SRI, SSRI, Fluoxetine 35 mg/ day average dose for 12 weeks.	Mean age: 11.6 (range: 7-17) Males: 50% Lower class: 50% Upper/Middle class: 50%	
			Control, (N=11)	Pill Placebo	Mean age: 11.4 (range: 7-17) Males: 54% Lower class: 45.4% Upper/Middle class: 45.4%	
Rynn, 2007[15]	United States RCT Efficacy Mental health clinic	Anxiety disorder	SSRI : Venlafaxine. (N=157)	37.5 mg/day during the first week. Doses thereafter ranged from 112.5mg – 225mg.	Age: 6 – 17 Male: 57.5%	0
			Control, (N=163)	Pill placebo		

CGI: clinical global impression scale, GAD: generalized anxiety disorder, NR: not reported, OCD: obsessive compulsive disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SNRI: serotonin–norepinephrine reuptake inhibitor, SoP: social anxiety, SP: specific phobia, SRI: serotonin reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor.

Table E.3. Characteristics of the included studies comparing CBT versus drugs

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Beidel, 2007 [3]	United States RCT Efficacy Mental health clinic	GAD, SAD, SP, SoP	SSRI: Fluoxetine, (N=43)	10mg per day during week 1 and 2. Increasing dose up to 40mg/day for up to 12 weeks.	Mean age:11.56 (Range 7 – 17) Male: 53.23% Caucasian: 74.1% African American: 15.1% Hispanic: 2.1% Asian: 2.8% Other: 3.5%	52
			Child CBT, (N=59)	Social Effectiveness Therapy (SET-C) Child CBT (Parents included <20%) Group and individual based, exposure, relaxation, and cognitive problem solving. 60 min individual session and one 150 min group session twice a week for 12 weeks.		
			Control, (N=37)	Pill placebo		
Scharfstein, 2011[16]	United States RCT Effectiveness Outpatient	SoP	Child CBT, (N=46)	Social Effectiveness Therapy (SET-C) Child CBT (parents included <20%) Exposure and cognitive problem solving. One individual and one group session per week for 12 weeks.	Male: 50%	0
			SSRI: Fluoxetine, (N=22)	One tablet of up to 40mg/ day for 12 weeks		
			Control, (N=22)	Pill placebo Identically appearing placebo capsules once a week for 12 weeks.		
Walkup, 2008[20-26]	United States RCT Efficacy Outpatient	GAD,SAD, SoP	Child CBT, (N=139)	Coping cat Child CBT (parents included <20%) Individual-based, exposure, relaxation, cognitive problem solving. 60-minute session once a week for 12 weeks.	Mean age: 10.5 Male: 49.2% Caucasian: 76.3%, African American:10.1%, Hispanic: 9.2%, other: 4.5% Low income: 23.7% ADHD: 11.5%, ODD:13.8%, Tic disorder and other internalizing disorders: 41.7%	0

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			SSRI: Sertraline, (N=133)	Beginning with 25mg/day Up to 200 mg/day by 8th week, for 12 weeks.	Mean age: 10.8 Male: 51.1% Caucasian: 77.4%, African American: 9%, Hispanic: 11.3%, other: 2.3% Low income: 26.3% ADHD: 12.7%, ODD:8.2%, Tic disorder and other internalizing disorders: 55.6%	
			Combination therapy: CBT+ SSRI: Child CBT+ Sertraline, (N=140)	Coping cat, Child CBT (parents included <20%) Individual-based, exposure, relaxation and cognitive problem solving plus Sertraline. 60-minute session once a week for 12 weeks plus up to 200 mg/day for 12 weeks.	Mean age: 10.7 Male: 49.6% Caucasian: 82.9%, African American: 7.9%, Hispanic: 5.6%, other: 3.6% Low income: 25.0% ADHD: 11.4%, ODD:10%, Tic disorder and other internalizing disorders: 42.8%	
			Control, (N=76)	Pill placebo	Mean age: 10.6 Male : 51.3% Caucasian: 79%, African American: 9%, Hispanic: 9%, other: 3% Low income: 27.6% ADHD: 118%, ODD:9.2%, Tic disorder and other internalizing disorders: 44.7%	

ADHD: attention deficit hyperactivity disorder, CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, ICBT: individual cognitive behavioral therapy, ODD: oppositional defiant disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia, SSRI: selective serotonin reuptake inhibitor.

Table E.4. Characteristics of the included studies comparing CBT versus waitlisting or no treatment

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Abbasi, 2016 [27]	Iran RCT Efficacy Mental health clinic	SAD	Child CBT, (N=15)	Modular CBT Child CBT- (parents included < 20%) Individual based Exposure Cognitive problem solving 4-20 sessions, 1 hour sessions, with	Age range : 6-7 years Male: 53%	13
			Other Therapy, (N=15)	Other: Child parent relationship training Individual based 10 weekly, 1 hour sessions	Age range : 6-7 years Male: 33.3%	
			Control, (N=16)	Waitlisting or no treatment	Age range : 6-7 years Male: 48%	
Adler Nevo, 2014[28]	Canada RCT	GAD, PD,SAD, SP, SoP	Child CBT plus separate parent intervention, (N=60)	Coping Bear Individual based Exposure Relaxation Cognitive Problem Solving. 12 sessions of group or individual with 12 concurrent parent groups	Mean age:9.6 (Range 8 – 12) Male: 46.50% OCD: 4% ADHD: 3% ODD:3%	0
			Control, (N=60)	Waitlisting or no treatment	Mean age:9.6 (Range 8 – 12) Male: 58.60% OCD: 5% ADHD: 5% ODD:5% Depression: 2%	
Afshari, 2014 [29]	Iran RCT Efficacy Outpatient Mental health clinic	SAD	Child CBT, (N=12)	Coping Cat Child CBT- (parents included < 20%) Group based Exposure Relaxation Cognitive problem solving 10, 60 min weekly sessions Delivered by student/trainee	Mean age: 10.4 (range: 9-13)	12

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Child CBT, (N=12)	Other: Emotion-focused CBT Child CBT- (parents included < 20%) Group based Cognitive problem solving 12 one hour weekly sessions Delivered by student/trainee	Mean age: 11 (range: 9-13)	
			Control, (N=10)	Waitlisting or no treatment	Mean age: 10.3 (range: 9-13)	
Arendt, 2015 [30]	Denmark RCT Efficacy Mental health clinic	GAD, PD with agoraphobia, PD without agoraphobia, SAD, SoP, SP	Child and parent CBT, (N=56)	Cool Kids Group-based Exposure Cognitive problem solving 10 sessions, 2 hour weekly sessions Delivered by psychologist and student	Mean age: 11.82 (SD: 2.49) Male: 45% Low income:(<$93,109): 21.4% Medium income:($93,1009-$130,353): 71.5% High income:(>$167,597): 7.1% Less than high school or high school graduate(parent):4.5% Some college(parent): 24.45% College graduate(parent): 71.05% OCD: 7.1% Externalizing disorders: 10.7% Mood disorders: 7.1% Other comorbidities: 5.4%	52
			Control, (N=53)	Waitlisting or no treatment	Mean age: 11.73 (SD: 2.47) Male: 42% Low income:(<$93,109): 37.7% Medium income:($93,1009-$130,353): 52.9% High income:(>$167,597): 9.4% Less than high school or high school graduate(parent):12.4% Some college(parent): 29.1% College graduate(parent): 58.5%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					OCD: 7.6% Externalizing disorders: 13.2% Mood disorders: 11.3% Other comorbidities: 7.5%	
Baer, 2005 [31]	Canada RCT Efficacy Mental health clinic	SoP	Child CBT, (N=6)	Social Effectiveness Therapy (SET-C) Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving 12 weekly 1.5-hour child sessions plus one parent session Delivered by 2 psychiatrists	Mean age: 14.5 (Range 13 – 18) Male: 50%	NR
			Control, (N=6)	Waitlisting or no treatment	Mean age: 16.5 (Range 13 -18) Male: 66.6%	
Barrett, 1996 [32]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP	Child CBT, (N = 28)	Coping Koala Child CBT- (parents included < 20%) Individual based Exposure, relaxation and cognitive problem solving 12 sessions, 60-80 minute weekly; 4 sessions on anxiety management Delivered by doctoral level psychologists.	Age range: 7 – 14 years	52
			Child and parent CBT, (N = 25)	Coping Koala Individual based Exposure ,relaxation and cognitive problem solving 12 session, 70 minute weekly sessions (30 minutes for CBTand 40 minutess for family intervention) Delivered by doctoral level psychologists.		
			Control, (N=26)	Waitlisting or no treatment		
Barrett, 1998	Australia	GAD, SAD, SP,	Child CBT,	Coping Koala	Age range: 7 – 14 years	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
[33]	RCT Efficacy Mental health clinic	SoP.	(N=23)	Child CBT- (parents included < 20%) Group based Exposure Relaxation Cognitive problem solving 12 sessions, 2 hours weekly sessions Delivered by 4 clinical psychologists.	Male: 53.3%	
			Child and parent together CBT, (N=17)	Coping koala Group-CBT and family management training Group based Exposure Relaxation Cognitive problem solving 12 sessions, 2 hour weekly sessions Delivered by therapists		
			Control, (N=20)	Waitlisting or no treatment		
Chalfant, 2007 [34]	Australia RCT Effectiveness Mental health clinic	GAD ,PD (agoraphobia is not specified) SAD, SP , SoP.	Child CBT plus separate parent intervention, (N=28)	Cool Kids Adaptation of the program for children with autism Group based Exposure Relaxation Cognitive problem solving 12 sessions, 9 weekly plus 3 booster monthly sessions Delivered by a doctoral level psychologist and Masters level clinicians.	Age: 10.8 (Range 8 – 13)	NR
			Control, (N=19)	Waitlisting or no treatment		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Chiu, 2013 [35]	United States RCT Effectiveness School	GAD, SAD, SoP	Child CBT, (N=22)	Building confidence Child CBT- (parents included < 20%) Individual based Exposure Cognitive problem solving 10 to 16 60-minute sessions Delivered by student/trainee	Mean age: 8.51 (range: 5-12) Males: 55% Caucasian: 40% African American: 15% Hispanic: 18% Asian: 5% Other: 23% Low income (<$40,000)= 17.5% Medium income ($40,000-$70,000)=17.5% High income (>$90,000): 67.5% ADHD: 15% OCD: 5% ODD: 7.5%	0
			Control, (N=18)	Waitlisting or no treatment		
Cobham, 2012 [36]	Australia RCT Efficacy Mental health clinic	GAD, PD, PD with agoraphobia, SAD, SoP, SP	Child CBT plus separate parent intervention, (N=23)	Do as I do Individual-based Exposure Cognitive problem solving 6 90-minutes sessions for parent and 6 60-minutes for child, weekly Delivered by Masters level clinicians	Mean age: 9.70 (range: 7-14) Males: 50% Caucasian 92% Asian: 8% PTSD: 4% ADHD: 7% Dysthymia: 4% Enuresis: 4%	26
			Distance Therapy, (N=20)	Do as I do "Do as I Do" and "Facing your Fears" bibliotherapy programs Exposure Cognitive problem solving 2 hour parent group, every other week 12 min phone calls for 12 weeks Delivered by parent and therapist	Mean age: 10.20 (range: 7-14) Males: 55% Caucasian 92% Asian: 8% ADHD: 5% PTSD: 5% Dysthymia: 5% Sleep terrors: 5%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=12)	Waitlisting or no treatment	Mean age: 9.83 (range: 7-14) Males: 57% Caucasian 92% Asian: 8% PTSD: 4%	
Dewis, 2001[37]	Australia RCT Efficacy Mental health clinic	SP	Child CBT, (N=9)	Generic CBT Live graded exposure Child CBT- (parents included < 20%) Individual based Exposure Three 45-min treatment sessions every 3–4 days Provided by clinical psychologists	Male: 35.7% Caucasian: 100% Mean age: 12.3 (Range 10-17)	4
			Distance Therapy, (N=10)	Other: Computer-aided vicarious Exposure Individual computer based Three 45-min treatment sessions every 3–4 days	Male: 35.7% Caucasian: 100% Mean age: 13.8 (Range 10-17)	
			Control, (N=9)	Waitlisting or no treatment	Male: 35.7% Caucasian: 100% Mean age: 13.3 (Range 10 – 17)	
Donovan, 2015[38]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Child and parent together CBT, (N=21)	Other: SHY Group based Exposure Relaxation Cognitive problem solving 4 3-hour sessions over 3 consecutive weekends Delivered by psychologist, student/trainee	Mean age: 9.43 (range: 7-12) Males: 37.5% Caucasian: 97.5% Asian: 2.5% Low income(<74,000): 45% High income(>74,000): 55% ADHD: 5% OCD: 5% ODD: 5% PTSD: 2.5%	26
			Control, (N=19)	Waitlisting or no treatment		
Flannery-Schroeder,	United States RCT	GAD,SAD, SoP, SP	Child CBT, (N=18)	Coping Cat Child CBT- (parents included < 20%)	Male: 33.3% Caucasian: 94.4%, Other: 5.6%	13

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
2000[39, 40]	Efficacy Outpatient			Individual based Exposure Relaxation Cognitive problem solving 18 sessions, 50-60 minute weekly sessions Delivered by Mastersstudents	ADHD: 11%, Depression: 5.6%	
			Child CBT, (N=13)	Coping Cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 18 sessions, 90 minute weekly sessions Delivered by Mastersstudents	Male: 61.5% Caucasian: 84.6%, Other: 15.4% ADHD: 30.7%, Depression: 15.3%, ODD: 23%	
			Control, (N=14)	Waitlisting or no treatment	Male: 42.8% Caucasian: 92.8%, Other: 7.2% ADHD: 21.4%	
Gallagher, 2004[41]	United States RCT Efficacy Mental health clinic	GAD, SP, SAD, SoP.	Child CBT, (N=12)	Generic CBT Child CBT-(parents included < 20%) Group based Exposure Cognitive problem solving 3 sessions, 3-hour weekly sessions	Age (range 8 – 11)	3
			Control, (N=11)	Waitlisting or no treatment	Age (range 8 – 11)	
Gallo, 2012[42]	United States RCT Efficacy Mental health clinic	PD with agoraphobia, PD without agoraphobia	Child CBT, (N=39)	Other: Immediate 8-day intensive treatment Child CBT- (parents included < 20%) Individual based Exposure and cognitive problem solving 8 days of 2 to 6 hours of treatment (20 hours total) followed by 4 weeks of phone contact	Mean age: 15.1 (range 12 – 17) Male: 40% Caucasian: 49% Hispanic: 4%	
			Control,	Waitlisting or no treatment		

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			(N=16)			
Gil-Bernal, 2009[43]	Mexico RCT Efficacy Public schools in low income district	SoP	Child CBT, (N=6)	IAFS Child CBT- (parents included < 20%) Group based Exposure and cognitive problem solving Nine 90-minutes sessions during 5 weeks Delivered by therapists	Age: Range 7 – 12 Male: 36.36%	36
			Child CBT plus separate parent intervention, (N=5)	IAFS Combined therapy: IAFS + Parent education Group based Exposure Relaxation Cognitive problem solving Nine 90-minutes sessions during 5 weeks Delivered by therapists		
			Control, (N=6)	Waitlisting or no treatment		
Hancock, 2016 [44]	Australia RCT Effectiveness Mental health clinic	GAD, SAD	ACT, (N=68)	Acceptance and commitment therapy (ACT) Group based Relaxation 10 sessions, 90-minute weekly sessions Delivered by doctoral level psychologist	Mean age: 11.15 (range: 7-17) Male: 45.5% Caucasian: 87%, Asian: 3%, Other: 10% ADHD: 6%, Depression, 18%, OCD: 7.3% Treatment naïve: 27.9%	13
			Child and parent together CBT, (N=63)	Cool Kids Group based Exposure Cognitive problem solving 10 sessions, 90-minute weekly sessions Delivered by doctoral level psychologist	Mean age: 10.81 (range: 7-17) Male: 39.6% Caucasian: 94.4%, Other: 5.6% ADHD: 10%, Depression, 13%, OCD: 3% Treatment naïve: 22.2%	
			Control, (N=62)	Waitlisting or no treatment	Mean age: 11.66 (range: 7-17) Male: 41.9%	

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					Caucasian: 84%, Other: 16% Depression: 24%, OCD: 8% Treatment naïve: 70.9	
Hayward, 2000[45]	United States RCT Efficacy Mental health clinic	SoP	Child CBT- (parents included < 20%), (N=12)	Generic CBT Group based Exposure Cognitive problem solving 16 90–minute weekly sessions Delivered by 2 doctoral level psychologist and 2 students/trainee	Mean age: 15.8 Low income: n= 29 Medium income: n= 23 High income: n= 11	52
			Control, (N=3)	Waitlisting or no treatment		
Holmes, 2014[46]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Child CBT plus separate parent intervention, (N= 20)	No worries Group based Relaxation Cognitive problem solving 10 weekly 90-min child sessions plus two boosters, and 7 90-minute parent sessions with 2 boosters Delivered by Masters level clinician	Mean age: 9.65 (range: 7-12) Males: 25% Caucasian: 100% Low income (<$29,875): 0% Medium income ($30,622-$ 59750): 10% High income (>$60,497): 90% Less than high school or high school graduate (parent): 35% Some college (parent): 25% College graduate (parent): 40% ADHD: 45% Depression: 25% ODD: 30%	13
			Control, (N=22)	Waitlisting or no treatment	Mean age: 9.64 (range: 7-12) Males: 40.9% Caucasian: 95.5% African American: 4.5 Low income (<$29,875): 9.1% Medium income ($30,622-$	

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					59750): 13.6% High income (>$60,497): 77.3% Less than high school or high school graduate (parent): 34% Some college (parent): 31.8% College graduate (parent): 31.8% ADHD: 45% Depression: 25% ODD: 30%	
Hirshfeld-Becker, 2010[47]	United States RCT Efficacy Outpatient	GAD, PD with agoraphobia, SAD, SoP, SP	Child and parent together CBT, (N=34)	Being Brave Individual based Exposure Relaxation Cognitive problem solving Up to 20 weekly sessions Delivered by psychologist, student/ trainee	Mean age: 5.4 (range: 4-7) Males:50% Caucasian: 79% Hispanic:3% Asian: 8.8% Other: 8.8% Less than high school or high school graduate (parent): 6.55% Some college (parent): 15.5% College graduate (parent): 78%	12
			Control, (N=30)	Waitlisting or no treatment	Mean age: 6.2 (range: 4-7) Males: 43% Caucasian: 80% Hispanic:3.3% Asian: 6.6% Other: 10% Less than high school or high school graduate (parent): 6.55% Some college (parent): 15.5% College graduate (parent): 78%	
Kendall,	United States RCT	GAD,SAD, SoP, SP	Child CBT, (N=27)	Coping Cat Child CBT- (parents included < 20%)	Age range: 9-13 years Male: 51.8%	52

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1995[48]	Effectiveness Mental health clinic			Individual based Exposure Relaxation Cognitive problem solving 17 50-60-minute weekly sessions Delivered by student	Caucasian: 78%, African American: 22%	
			Control, (N=20)	Waitlisting or no treatment	Age range: 9-13 years Male: 60% Caucasian: 80%, African American: 20%	
Kendall, 1997 [49]	United States RCT Effectiveness Mental health clinic	GAD, SAD, SP, SoP	Child CBT, (N=60)	Coping Cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 16 60-minute weekly sessions Delivered by doctoral level psychologists	Age range: 9 – 13 years Low income: 32% Medium income 31% High income: 28% Male: 58.3% Caucasian: 86.6% African American: 6.6 Hispanic: 1.6 Asian: 1.6	52
			Control, (N=34)	Waitlisting or no treatment	Age range: 9 – 13 years Low income: 32% Medium income 31% High income: 28% Male: 67.6% Caucasian: 82.35% African American: 2.9% Hispanic: 2.9% Asians: 5.8 Others: 5.8%	
Leutgeb, 2011[50]	Austria RCT Efficacy Mental health clinic	SP	Child CBT, (N=16)	OST Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving	Mean age: 11.44 (range: 8-14)	0

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				1 session, up to 4 hours		
			Control, (N=14)	Waitlisting or no treatment	Mean age: 11.54 (range: 8-14)	
Masia-Warner, 2005[51]	United States RCT Efficacy School	GAD, PD with agoraphobia, SoP	Child CBT, (N=21)	Skills for Social and Academic Success Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving School settings for about 3 months. 12 40-minutes weekly session, 2 brief individual meetings (15 minutes), 2 group boosters; 4 weekend social events (90 minutes); 2 Parents groups (45 minutes); 2 teacher groups (30 minutes) Delivered by a doctoral level psychologist and a student/trainee	Mean age: 15 (Range 13 -17) Male: 19% Caucasian: 76.19% African Americans: 9.5%	NR
			Control, (N=21)	Waitlisting or no treatment	Mean age: 14.5 (Range 13-17) Male: 23.8% Caucasian: 61.9% African Americans: 4.7% Hispanics: 4.7% Asians: 4.7% Others: 4.7%	
McConachie, 2014[52]	United Kingdom RCT Effectiveness Mental health clinic	GAD, PD with agoraphobia, SAD SoP, SP	Child CBT plus separate parent intervention, (N=17)	Exploring feelings Group based 7 2-hours sessions with separate parent and child groups Delivered by psychologist	Mean age: 11.7 (range: 9-13) Males: 88% College graduate (parent): 47% ADHD: 30% Depression: 12% Autism: 100% OCD: 18% ODD:6%	39

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			Control, (N=15)	Waitlisting or no treatment	Mean age: 11.8 (range: 9-13) Males: 87% College graduate (parent): 80% ADHD: 33% Autism: 100% OCD: 7% ODD:7%	
McNally Keehn, 2013[53] United States RCT Effectiveness Mental health clinic		GAD, SAD, SoP, SP	Child CBT-: (N=12)	Coping Cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving Delivered by psychologist 16 sessions, 60 to 90-minute weekly sessions	Mean age: 11.65 (range: 8-14) Males: 100% Caucasian: 66% Hispanic: 17% Others: 17% Less than high school or high school graduate (parent): 33% College graduate (parent): 67% Depression: 8% Autism: 100% OCD:17% ADHD: 67% ODD: 33%	8
			Control, (N=10)	Waitlisting or no treatment	Mean age; 11.02 (range: 8-14) Males: 90% Caucasian: 40% Hispanic: 10% Others: 17% Less than high school or high school graduate (parent): 10% College graduate (parent): 90% Autism: 90% ADHD: 80% ODD: 50%	
Melfsen, 2011[54] Germany RCT Effectiveness Mental health		SoP	Child CBT, (N=21)	Generic CBT Child CBT- (parents included < 20%) Individual based Exposure	Mean age: 10.6 (range 8-14) Males: 62% Caucasian: 100% Sleeping disorder: 9.5%	43

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	clinic			Cognitive problem solving 20 50-minute weekly sessions and 4 parent sessions Delivered by student/trainee	ODD: 4.7% Tic disorder: 4.7%	
			Control, (N=23)	Waitlisting or no treatment	Mean age: 10.76 (range 8-14) Males: 43% Caucasian: 100% Affective disorder: 4.3% Sleeping disorder: 4.3% ADHD: 4.3% ODD: 4.3% Elimination disorder: 8.6%	
Mendez, 2003 [55]	Spain RCT Efficacy Schools	SP	Child and Parent Together CBT (N=NR)	Emotive staging Exposure Individual based Delivered by psychologist 12, 30 min sessions over 3 weeks	Total number of patients: 64 Male: 50%	0
			Child and Parent Together CBT (N=NR)	Emotive staging Exposure, cognitive problem solving Individual based 12, 30 min sessions over 3 weeks		
			Control, (N=NR)	Waitlisting or no treatment		
Mendlowitz, 1999 [56]	Canada RCT Efficacy Outpatient		Child CBT, (N=23)	Coping Bear Child CBT- (parents included < 20%) Group based Relaxation, cognitive problem solving 12 1.5-hour weekly sessions Delivered by 3 psychologists, 1 student/trainee, 1 youth worker	Mean age: 9.5 (Range 7- 12) Male: 28.4%	NR
			Parent only intervention, (N=21)	Generic CBT Group based 12 1.5-hour weekly sessions Delivered by doctoral level psychologist, and student/trainee		

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			Child CBT plus separate parent intervention, (N=18)	Coping bear Group based Relaxation Cognitive problem solving 12 1.5-hour weekly sessions (one for kids, one for parents) Delivered by doctoral level psychologist, student/trainee, youth worker		
			Control, (N=40)	Waitlisting or no treatment		
Menzies, 1993[57]	Australia RCT Efficacy Outpatient	SP	Child CBT, (N=13)	In vivo exposure plus vicarious exposure Child CBT- (parents included < 20%) Individual based Delivered by student therapist 3 15-minute weekly session	Mean age: 5.5 (range:3-8) Male: 50.7% Caucasian: 96%, Hispanic:4% Depression: 10% Treatment non responder: 100%	12
			Control, (N=13)	Attention control or treatment as usual Only vicarious exposure 3 30-minute weekly session Delivered by student therapist		
			Child CBT, (N=13)	In vivo exposure Child CBT- (parents included < 20%) Individual based Exposure 3 30-minute weekly session Delivered by student		
			Control, (N=12)	Waitlisting or no treatment Only assessment		
Miller, 1972[58, 59]	United States RCT Efficacy Outpatient	SP	Child CBT, (N=NR)	Total number of patients: 67 Reciprocal inhibition: individual-based relaxation, exposure Delivered by doctoral psychologist 60 min session 3 times per week for 8 weeks	Mean age: 10.8 (range: 6-14) Male: 55% Caucasian: 95.5%, African American: 4.5% Socioeconomic status: Lower: 7% Middle:75% High: 8%	104

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			Other therapy, (N=NR)	Individual, play psychotherapy directed toward inner experiences 60 min session 3 times per week for 8 weeks		
			Control, (N=NR)	Waitlisting or no treatment		
Obler, 1970[60]	United States RCT Efficacy Mental health clinic	SP	Child CBT, (N=15)	Reciprocal inhibition Child CBT- (parents included < 20%) Individual based Exposure 10 5-hour weekly sessions Delivered by therapist	Mean age: 9.5 (range: 7-12)	NR
			Control, (N=15)	Waitlisting or no treatment	Mean age: 9.3 (range: 7-12)	
Olivares, 2002[61]	Spain Non-Randomized comparative studies Efficacy School	GAD, PD with agoraphobia, SoP,SP	Child CBT, (N=14)	SET-C Spanish Child CBT- (parents included < 20%) Exposure 29 treatment sessions over a period of 17 weeks, generally twice weekly	mean age: 15.57 (range: 15-17) Male: 28.5% Depression: 35.7%, OCD: 7%, Substance abuse : 7%, PTSD: 7%, avoidant personality disorder: 100%, selective mutism: 7%	52
			Child CBT, (N=15)	Group based Child CBT- (parents included < 20%) Exposure Cognitive problem solving 16 90-minute sessions over 14 weeks	mean age: 16.07 (range: 15-17) Male: 35.7% Depression: 60%, OCD: 6%, Substance abuse : 6%, PTSD: 6%, avoidant personality disorder: 94%, selective mutism: 12%	
			Child CBT, (N=15)	IAFS Child CBT- (parents included < 20%) Exposure, cognitive problem solving 12 90-minute weekly group sessions, and optional individual sessions	mean age: 15.87 (range: 15-17) Male: 26.6% Depression: 40%, OCD: 6%, Substance abuse : 6%, PTSD: 6%, avoidant personality disorder: 100%, selective	

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					mutism: 6%	
			Control, (N=15)	Waitlisting or no treatment	mean age: 15.87 (range: 15-17) Male: 35.7% Depression: 46%, OCD: 6%, Substance abuse : 12%, PTSD: 6%, avoidant personality disorder: 100%, selective mutism: 12%	
Olivares, 2014[62]	Spain RCT Efficacy Mental health clinic	SoP	Child CBT, (N=38)	IAFS Child CBT- (parents included < 20%) Delivered by experienced psychologist Group based Exposure Cognitive problem solving 12 90-minute weekly sessions	Mean age: 15.58 (SD: 0.76) Males: 36.81%	52
			Child CBT, (N=37)	IAFS Child CBT- (parents included < 20%) Delivered by inexperienced psychologist Group based Exposure Cognitive problem solving 12 90-minute weekly sessions	Mean age: 15.30 (SD: 0.81) Males: 29.74%	
			Control, (N=35)	Waitlisting or no treatment	Mean age: 15.23 (SD: 1.26) Males: 37.1%	
Ollendick, 2009[63]	United States and Sweden RCT Efficacy Outpatient Mental health clinic	SP, SoP, SAD, GAD	Child CBT, (N=85)	OST Child CBT- (parents included < 20%) One session treatment Individual based Exposure 1 session of 3 hours Delivered by Masters level clinicians	Caucasian: 90%, African American: 2.5% Hispanic:: 2% Other: 4.5% Age range 7 -16 years Male: 45.8%	36
			Control, (N=70)	Attention control or treatment as usual Education support treatment 1, 3 hour session of Delivered by Master level clinicians	Caucasian: 90%, African American: 2.5% Hispanic:: 2% Other: 4.5%	

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					Range 7 – 16 Male: 44.2%	
			Control, (N= 41)	Waitlisting or no treatment	Age range 7 -16 years Male: 46.3%	
Ortbandt, 2009[64, 65]	Germany RCT Efficacy Mental health clinic	GAD,SAD, SoP	Child CBT plus separate parent intervention, (N=10)	Generic CBT Individual training is at least 8 50-minute Weekly sessions or 4 100-minute weekly sessions Group training is at least 12 50-minutes weekly sessions or 6 100-minute weekly sessions	Mean age: 9.25 (range: 7.2-12.7) Male: 50%	26
			Control, (N=9)	Waitlisting or no treatment	Mean age: 9.96 (range: 7.9-11.1) Male: 44.4%	
Ost, 2001[66]	Sweden RCT Efficacy Mental health clinic	GAD,SAD, SoP, SP	Child CBT, (N=21)	OST Child CBT- (parents included < 20%) One session treatment - Child alone Individual based Exposure 1 session of 3 hours Delivered by doctoral level Psychologist	mean age: 11.7 (range: 7-17) Male: 33	52
			Child and parent together CBT, (N=20)	OST One session exposure - Parent present Individual based Exposure 1 session of 3 hours Delivered by doctoral level Psychologist	mean age: 11.7 (range: 7-17) Male: 45%	
			Control, (N=19)	Waitlisting or no treatment	mean age: 11.7 (range: 7-17) Male: 36%	
Ost, 2015[67]	Sweden RCT Efficacy Mental health clinic	GAD, PD, SAD, SP	Child CBT, (N=16)	SET-C Child CBT- (parents included < 20%) Exposure 12 individual weekly sessions plus 12 social skills group weekly session Delivered by Psychologist	Mean age: 11.6 (range: 8-14) Depression: 15% OCD: 5% ODD: 2% Neurodevelopmental Disorder:9%	52

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			Child CBT plus separate parent intervention, (N=16)	SET-C Exposure 12 individual weekly sessions plus 12 social skills group weekly session; plus 8 90-minute parent group sessions Delivered by psychologist		
			Control, (N=23)	Waitlisting or no treatment		
Rapee, 2000[68]	Australia non randomized comparative Efficacy Outpatient	NR	Child and parent together CBT, (N=95)	Other: Family CBT Group based Exposure Cognitive problem solving 9, 90 minute treatment sessions, over 11 weeks Delivered by student/trainee	Mean age: 10.46 (range: 7-16) Males: 41%	52 (only for CBT arm)
			Control, (N=15)	Waitlisting or no treatment	Mean age: 11.1 (range: 7-16) Males: 33.3%	
Rapee, 2006[69]	Australia RCT Efficacy Mental health clinic	GAD, PD (agoraphobia is not specified), SAD, SP, SoP.	Child and parent together CBT, (N=90)	Cool Kids Group based Exposure Cognitive problem solving 9 2-hour sessions over 12 weeks Delivered by student trainee.	Mean age: 9.475 (Range: 6 -12) Male: 66.6% Low income: n= 26 (<$30,000)	36
			Distance Therapy, (N=90)	Other: Bibliotherapy Individual based Exposure Relaxation Cognitive problem solving Treatment duration is 12 weeks at own pace	Mean age: 9.558 (Range: 6 – 12) Male: 64.44% Low income: n= 9 (<$30,000)	
			Control, (N=87)	Waitlisting or no treatment	Mean age: 9.5 (Range: 6 – 12) Male: 48.2% Low income: n= 15(<$30,000)	

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Reaven, 2009[70]	United States RCT Efficacy Outpatient	GAD,SAD, SoP	Child and parent together CBT, (N=10)	Generic CBT Exposure Relaxation Cognitive problem solving 12 1.5-hour weekly sessions (included large group time, separate parent and child group meetings, and parent-child dyads). Delivered by doctoral level psychologist	Mean age: 11 (range: 8-14) Male: 70% Caucasian: 80%, African American:10%, Hispanic: 10% Parent education level: Some college:30%, collage grade: 40% Autism: 100%	0
			Control, (N=23)	Waitlisting or no treatment	Mean age: 11 (range: 8-14) Male: 83% Caucasian: 83%, African American:4.5%, Hispanic: 4.5%, Other: 8 Some college:26%, collage grade: 35% Autism: 100%	
Ritter, 1968[71]	United States RCT Efficacy Outpatient	SP	Child CBT, (N=7)	Other: Only contact desensitization Child CBT- (parents included < 20%) Group based Exposure 2, 35-minute weekly sessions Delivered by psychiatrist	Age range: 5-11 years	0
			Control, (N=8)	Attention control or treatment as usual Only vicarious desensitization Group based 2, 35-minute weekly sessions Delivered by psychiatrist		
			Control, (N=7)	Waitlisting or no treatment		
Rosa-Alcazar, 2009[72]	Spain RCT Efficacy Schools	GAD, PD without agoraphobia, PD (agoraphobia is not specified) SP	Child CBT, (N=20)	IAFS Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving	Mean age 15 (Range 14 -17) Male:25%	52

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				12 90-minute weekly sessions Delivered by practicing clinician		
			Control, (N=19)	Attention Control or Treatment as Usual Educational Treatment on anxiety and relaxation 12 90-minute weekly sessions	Mean age 14.94 (14- 17) Male: 31.5%	
			Control, (N=18)	Attention Control or Treatment as Usual Education as Placebo 12 sessions of health education	Mean age 14.75 (14-17) Male: 16.6%	
			Control, (N=20)	Waitlisting or no treatment	Mean age 14.77 Male: 40%	
Rodriguez, 2005[73]	Spain RCT Efficacy High school	GAD, PD without agoraphobia, SP ,SoP, social anxiety disorder	Child CBT, (N=17)	IAFS Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving 12 90-minute weekly sessions Delivered by two experienced psychologists	Mean age: 15 Male: 41.17%	6
			Control, (N=17)	Waitlisting or no treatment	Mean age: 15.06 Male: 41.17%	
Sanchez-Garcia, 2009[74]	Spain RCT Efficacy Schools	SoP	Child CBT, (N=NR)	IAFS Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving 12 90-minute weekly sessions	Total number of patients: 45 Mean age: 12 Male: 24.4%	26
			Control, (N=NR)	Waitlisting or no treatment		
Sánchez-García, 2009[75]	Spain RCT Efficacy Schools	SAD	Child CBT, (N=28)	IAFS Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving 12 90-minute weekly sessions	Mean age: 11.91 Male: 38% White: 82%	52

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				Delivered by Practicing clinician		
			Child CBT, (N=29)	IAFS Child CBT- (parents included < 20%) Incomplete (IAFS without Cognitive restructuring) Group based Exposure 12 90-minute weekly sessions		
			Control, (N=25)	Waitlisting or no treatment		
Santucci, 2013[76]	United States RCT Efficacy Mental health clinic	SAD	Child CBT, (N=15)	Generic CBT Child CBT- (parents included < 20%) Group based Exposure Relaxation Cognitive problem solving 7 sessions, 3 to 5 hour daily sessions. Plus 2 additional 60 to 90 minute parent sessions Delivered by psychologist and student/trainee	Mean age: 9.43 (range: 7-12) Males: 0% Caucasian: 80% Asian: 13%	6
			Control, (N=14)	Waitlisting or no treatment	Mean age: 8.92 (range: 7-12) Males: 0% Caucasian: 93% Asian: 7%	
Schneider, 2011[77]	Germany RCT Efficacy Mental health clinic	SAD	Child and parent together CBT, (N=21)	Other: Parent coached exposure Individual based Exposure Cognitive problem solving 4 weekly 50-min sessions with the child alone and 50-min parents alone. Then 8 weekly 50-min family sessions, each split into two parts: one with parents and	Mean age: 6.29 (range: 5-7)	4

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				child together, and a second with the parents only Delivered by psychologist		
			Control, (N=22)	Waitlisting or no treatment	Mean age: 6.18 (range:5-7)	
Shortt, 2001[78]	Australia RCT Efficacy NR	GAD, SAD, SP, SoP.	Child CBT plus separate parent intervention, (N=54)	Friends Group based, Exposure Relaxation Cognitive problem solving 10 weekly sessions and 2 booster sessions; and 10 parent sessions (each of about 40 minutes)	Male: 40.8% Caucasian: 25.3% Asian: 1.4% Mean age: 7.83 (Range 6.5-10)	52
			Control, (N=17)	Waitlisting or no treatment	Male: 40.8% Caucasian: 25.3% Asian: 1.4% Mean age: 7.88 (Range 6.5-10)	
Silverman, 1999 [79]	United States RCT Efficacy Mental health clinic	GAD, SoP	Child CBT plus separate parent intervention, (N=37)	Generic CBT Group based Exposure Cognitive problem solving Unclear number of sessions, 65 minutes Delivered by doctoral level psychologist and student trainee	Mean age: 10.14 (range: 6-16) Males: 54% Caucasian: 47% Hispanic: 40% Other: 4% Low income (<$15,000):27% Medium income: ($15,000-$30,000):27% High income: (>$30,000): 34%	52
			Control, (N=19)	Waitlisting or no treatment	Mean age: 9.63 (range: 6-16) Males: 74% Caucasian: 44% Hispanic: 58% Low income (<$15,000):5% Medium income: ($15,000-$30,000):32% High income: (>$30,000): 63%	
Spence,	Australia RCT	GAD, SAD, SP, SoP	Child CBT plus separate	Generic CBT CBT with parent Involvement	Mean age: 10.49 (range: 7-14) Males: 59%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
2000 [80]	Efficacy Mental health clinic		parent intervention, (N=17)	Group based Exposure Relaxation Cognitive problem solving 12 1.5-hour weekly sessions, 2 1.5-hour boosters; parents observe 60 minutes of child group, then have 30 minute sessions Delivered by 2 doctoral level psychologists	ODD: 12% ADHD: 6%	
			Child CBT, (N=19)	Generic CBT Child CBT- (parents included < 20%) CBT without parent involvement Group based Exposure Relaxation Cognitive problem solving 12 1.5-hour weekly sessions, 2 1.5-hour boosters Delivered by 2 doctoral level psychologists.	Mean age: 11 (range: 7-14) Males: 53% ODD: 10% Dysthymia: 5%	
			Control, (N=14)	Waitlisting or no treatment	Mean age: 9.93 (range: 7-14) Males: 79% Dysthymia: 7%	
Spence, 2006[81]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SP SoP	Child CBT plus separate parent intervention, (N=22)	Generic CBT Group based Exposure Relaxation Cognitive problem solving 10 60-minute weekly child sessions and 6 60-minute weekly parent sessions, plus booster sessions at 1 and 3 months Delivered by 5 doctoral level psychologists.	Mean age: 10.26 (Range 7-14) Male: 59%	12

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Distance Therapy, (N=27)	Generic CBT Internet CBT Group based Exposure Relaxation Cognitive problem solving 5 of the 10 child sessions plus the 3-month booster via Internet, with the remaining sessions being conducted in the clinic; 3 of the 6 parents sessions and the 3-month via Internet Delivered through the internet	Mean age: 9.8 (Range 7-14) Male: 59.2%	
			Control, (N=23)	Waitlisting or no treatment	Mean age: 9.8 (Range 7-14) Male: 56.5%	
Spence, 2011[82]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Distance Therapy, (N=44)	Brave online Technology-based Individual based Exposure Relaxation Cognitive problem solving 10 adolescents weekly sessions and 5 parent sessions (60 minutes each) over 12 weeks; 1 15-minute phone call, email feedback after each session Delivered by psychologist, Masters level clinician	Mean age: 13.98 (range: 12-18) Males: 41% High income(>$76,910): 47% College graduate (parent): 58% Depression: 2.6% ODD: 1.7% Dysthymic disorder: 9.7%	52
			Child CBT plus separate parent intervention, (N=44)	Individual based Exposure Relaxation Cognitive problem solving 10 adolescents weekly sessions and 5 parent sessions (60 minutes each) over 12 weeks Delivered by psychologist, Masters level clinician		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=27)	Waitlisting or no treatment		
Treadwell, 1996[83]	United States RCT Efficacy Outpatient Mental health clinic	GAD, SAD	Child CBT, (N=35)	Coping Cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 16 sessions, 50-60 minute weekly sessions Delivered by Masters level clinicians	Mean age: 11.7 Male: 67.6% Caucasian: 76% African Americans: 23.9% Low income: n= 23 Medium income: n= 14 High income: n= 33	NR
			Control, (N=36)	Waitlisting or no treatment		
Valles-Arandiga, 2014 [84]	Spain RCT Efficacy Schools	SoP	Child CBT, (N=17)	IAFS Child CBT- (parents included < 20%) Group based 12, 90-minute weekly sessions Delivered by therapist	Mean age: 14.9 (range: 14-16) Males:25%	26
			Control, (N=17)	Attention Control or Treatment as Usual Education Support Individual based 12 90-minute weekly sessions		
			Control, (N=17)	Waitlisting or no treatment		
van Steensel, 2015[85]	Netherlands Non-Randomized comparative studies Effectiveness Outpatient	NR	Child and parent together CBT, (N=62)	Discussing plus Doing Individual based Exposure Relaxation Cognitive problem solving 12 weekly sessions Delivered by Masters level clinicians	Age range: 7-18 years	0
			Control, (N=17)	Waitlisting or no treatment		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Waters, 2009[86]	Australia RCT Efficacy Outpatient	GAD, SAD, SoP, SP	Child CBT plus separate parent intervention, (N=38)	Take action Group based Exposure Relaxation Cognitive problem solving 10 weekly 1-hour child and one hour parents sessions Delivered by psychologist	Mean age: 6.89 (range: 4-8) Males: 37% Caucasian: 97%	52
			Parent only intervention, (N=31)	Take action Group based Exposure Relaxation Cognitive problem solving 10 weekly 1-hour child and one hour parents sessions Delivered by psychologist	Mean age: 6.68 (range: 4-8) Males: 58% Caucasian: 97%	
			Control, (N=11)	Waitlisting or no treatment	Mean age: 6.79 (range 4-8) Males: 55% Caucasian: 91%	
Warner, 2011[87]	United States RCT Efficacy Outpatient	GAD, SAD, SoP, SP	Child CBT, (N=20)	TAPS Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 12 individual sessions (45–60 minutes each) with 3 parent meetings (45 minutes each) over 10 weeks Delivered by psychologist	Mean age: 12.4 (range: 8-16) Males: 35% Caucasian: 73.5% African American: 2.5% Hispanic: 15% Other: 10% Income range: $31,000-$120,000	13
			Control, (N=20)	Waitlisting or no treatment		
Wergeland, 2014[88, 89]	Norway RCT Efficacy	GAD, SAD, SoP	Child CBT, (N=91)	Friends Child CBT- (parents included < 20%) Individual based	Mean age: 11.4 (range: 8-15) Males: 48% Caucasian: 76%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	Outpatient			Exposure Relaxation Cognitive problem solving 10 weekly sessions, lasting 60 min (ICBT), plus 2 parent only sessions Delivered by psychologist, Masters level clinician	Hispanic: 0.5% Asian: 3% ADHD: 5% Depression: 8% ODD: 9% Tic disorder: 7%	
			Child CBT, (N=88)	Friends Child CBT- (parents included < 20%) Group based Exposure Relaxation Cognitive problem solving 10 weekly sessions, lasting 90 minutes, plus 2 parents sessions Delivered by psychologist, Masters level clinician	Mean age: 11.7 (range: 8-15) Males: 45% Caucasian: 76% Hispanic: 0.5% Asian: 3% ADHD: 6% Depression: 16% ODD: 2% Tic disorder: 7%	
			Control, (N=38)	Waitlisting or no treatment	Mean age: 11.4 (range: 8-15) Males: 50% Caucasian: 76% Hispanic: 0.5% Asian: 3% ADHD: 3% Depression: 11% ODD: 8% Tic disorder: 5%	
White, 2013[90]	United States RCT Effectiveness Mental health clinic	GAD, PD with agoraphobia, SAD, SoP, SP	Child CBT plus separate parent intervention, (N=15)	Social Skills training Exposure Cognitive problem solving Individual therapy (up to 13 sessions), group therapy (skills practice, 7 sessions), and parent education and coaching (after each individual therapy session) Delivered by student/trainee	Mean age: 14 (range: 12-17) Males: 73% Caucasian: 80% Asian: 7% African American: 7% Other: 7% Autism: 100% OCD: 20%	0

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=15)	Waitlisting or no treatment	Mean age: 15 (range: 12-17) Males: 80% Caucasian: 93% African American: 7% Autism: 100% OCD: 20% PTSD: 7%	
Wood, 2009 [91] United States RCT Efficacy Outpatient		GAD, SAD, SoP	Child and parent together CBT, (N=17)	Building confidence Individual based Exposure Cognitive problem solving 16 session 90 minutes (about 30 minutes with the child and 60 minutes with the parents/family Delivered by psychologist, student/trainee	Mean age: 9.2 (Range 7-11) Males: 71% Caucasian: 47% Hispanic: 12% Asian:24% Others: 18% Low income (<$40,000):22% Medium Income ($40,000-$90,000):25% High Income (>$90,000):45% College Graduate (parent); 71% Autism: 100% ADHD: 53% OCD: 47% ODD: 12% Dysthymia: 18%	0
			Control, (N=23)	Waitlisting or no treatment	Mean age: 9.18 (Range 7-11) Males: 65% Caucasian: 48% African American: 4% Hispanic: 13% Low income (<$40,000):22% Medium Income ($40,000-$90,000):25% High Income (>$90,000):45% Asian:9% Others: 26% College Graduate (parent): 60%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					Autism: 100% ADHD:65% OCD: 39% ODD: 26% PTSD: 4%	

ACT: acceptance and commitment theory, ADHD: attention deficit hyperactivity disorder, IAFS: intervencion en adolescents con fobia social (treatment for adolescents with social phobia), CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, NR: not reported, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, OST: one session treatment, PD: panic disorder, PTSD: post-traumatic stress disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SET-C: social effectiveness therapy, SHY: the SHY manual for social anxiety, SoP: social anxiety, SP: specific phobia. TAPS: treatment of anxiety and physical symptoms

Table E.5. Characteristics of the included studies comparing CBT versus pill placebo

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Beidel, 2007 [3]	United States RCT Efficacy Mental health clinic	GAD, SAD, SP, SoP	SSRI: Fluoxetine, (N=43)	10mg per day during week 1 and 2. Increasing dose up to 40mg/day for up to 12 weeks.	Mean age:11.56 (Range 7 – 17) Male: 53.23% Caucasian: 74.1% African American: 15.1% Hispanic: 2.1% Asian: 2.8% Other: 3.5%	52
			Child CBT, (N=59)	Social effectiveness therapy (SET-C) Child CBT (Parents included <20%) Group and Individual based, Exposure Relaxation Cognitive Problem Solving. 60 min individual session and one 150 min group session twice a week for 12 weeks.		
			Control, (N=37)	Pill Placebo		
Scharfstein, 2011[16]	United States RCT Effectiveness Outpatient	SoP	Child CBT, (N=46)	Social Effectiveness Therapy (SET-C) Child CBT (parents included <20%) Exposure Cognitive Problem Solving. One individual and one group session per week for 12 weeks.	Male: 50%	0
			SSRI: Fluoxetine, (N=22)	One tablet of up to 40mg/ day for 12 weeks		
			Control, (N=22)	Pill Placebo Identically appearing placebo capsules once a week for 12 weeks.		
Walkup, 2008[20-26]	United States RCT Efficacy Outpatient	GAD,SAD, SoP	Child CBT, (N=139)	Coping Cat Child CBT (parents included <20%) Individual-based Exposure, relaxation, cognitive problem solving. 60-minute session once a week for 12 weeks.	Mean age: 10.5 Male: 49.2% Caucasian: 76.3%, African American:10.1%, Hispanic: 9.2%, other: 4.5% Low income: 23.7% ADHD: 11.5%, ODD:13.8%, Tic	0

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					disorder and other internalizing disorders: 41.7%	
			SSRI: Sertraline, (N=133)	Beginning with 25mg/day Up to 200 mg/day by 8th week, for 12 weeks.	Mean age: 10.8 Male: 51.1% Caucasian: 77.4%, African American: 9%, Hispanic: 11.3%, other: 2.3% Low income: 26.3% ADHD: 12.7%, ODD:8.2%, Tic disorder and other internalizing disorders: 55.6%	
			Combination therapy: CBT+ SSRI: Child CBT+ Sertraline, (N=140)	Coping Cat, Child CBT (parents included <20%) Individual-based Exposure, relaxation and cognitive problem solving plus Sertraline. 60-minute session once a week for 12 weeks plus up to 200 mg/day for 12 weeks.	Mean age: 10.7 Male: 49.6% Caucasian: 82.9%, African American: 7.9%, Hispanic: 5.6%, other: 3.6% Low income: 25.0% ADHD: 11.4%, ODD:10%, Tic disorder and other internalizing disorders: 42.8%	
			Controil, (N=76)	Pill Placebo	Mean age: 10.6 Male : 51.3% Caucasian: 79%, African American: 9%, Hispanic: 9%, other: 3% Low income: 27.6% ADHD: 118%, ODD:9.2%, Tic disorder and other internalizing disorders: 44.7%	

ACT: acceptance and commitment theory, ADHD: attention deficit hyperactivity disorder, IAFS: intervencion en adolescents con fobia social (treatment for adolescents with social phobia), CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, NR: not reported, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, OST: one session treatment, PD: panic disorder, PTSD: post-traumatic stress disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SET-C: social effectiveness therapy, SHY: the SHY manual for social anxiety, SoP: social anxiety, SP: specific phobia. TAPS: treatment of anxiety and physical symptoms

Table E.6. Characteristics of the included studies comparing CBT versus attention control or treatment as usual

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Beidel, 2000 [92]	United States RCT Eficacy Mental health clinic	GAD, PD (agoraphobia is not specified), SAD, SP, SoP	Child CBT, (N=36)	Social effectiveness yherapy for Children (SET-C) Individual and group based Exposure Cognitive problem solving Two weekly sessions (one group session and one individual session) for 12 weeks. Group sessions could be 60 minutes (social skill training) or 90 minutes (peer generalization experiences). Individual sessions were 60 minutes	Mean age: 10.5 Male: 38.8% Caucasian: 97.7% African American: 30.5% Hispanic: 5.5% GCI: 5.5	26
			Control, (N=31)	Attention control or treatment as usual Testbusters program for study skills and test taking strategy	Mean age: 10.5 Male: 19.3% Caucasian: 58% African American: 25% Hispanic: 9.6% Biracial: 5.5% CGI: 5.6	
Fujii, 2013 [93]	United States RCT Efficacy Mental health clinic	GAD, SAD, SoP	Child and parent together CBT, (N=7)	Other: Coping skills exposure Individual based Exposure Cognitive problem solving 32 90-minute weekly sessions, first 16 sessions, modular CBT, second 16 sessions social skills Delivered by student/trainee	Mean age: 8.7 (range: 7-11) Males: 71% Caucasian: 86% Asian: 14% College graduate (parent): 71% Autism: 57% OCD: 14%	0
			Control, (N=5)	Attention Control or Treatment as Usual	Mean age: 9 (range: 7-11) Males: 80% Caucasian: 60% African American: 20% Other: 20% College graduate (parent): 60% Autism: 100%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Ginsburg, 2002[94]	United States RCT Efficacy School	GAD, SP, SoP, PD (agoraphobia)	Child CBT, (N=6)	Group-based Exposure Relaxation Cognitive problem solving. 45 min session over 10 weeks delivered by psychiatrists. No parent involvement.	Mean age: 15.6 (Range 14-17) Male: 16.6% African Americans: 100%	10
			Control, (N=6)	Attention control or treatment as usual Group based. 45-50 min session, one session a week, 10 sessions delivered by student trainee.		
Ginsburg, 2012[95]	United States RCT Effectiveness School-based Mental health clinics	GAD,SAD, SoP, SP	Child CBT, (N=17)	Modular CBT Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 8 modules over 12 weeks (average 7.29); 20-45min sessions in school; efforts to involve parents in at least 3 sessions Delivered by doctoral psychologist	Mean age: 11.12 Male: 29.4% African American: 82%, other: 18% Low income: 23.5% Family stress: 100%	4
			Control, (N=15)	Attention control or treatment as usual	Mean age: 9.33 Male: 46.6% African American: 87%, other: 13% Low income: 40% Family stress: 100%	
Halldorsdottir, 2016[96]	United States RCT Efficacy Outpatient	GAD, SoP	Child CBT, (N=50)	OST Exposure Relaxation Cognitive problem solving Individual-based 180 minute one session only	Mean age: 9.24 Male: 88% Mean income: 71.450	208
			Control,	Attention control or treatment as usual	Mean age: 8.97	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			(N=33)	Individual-based	Male: 90% Mean income: $73,232	
Herbert, 2009[97]	United States RCT Efficacy Mental health clinic	GAD , PD (agoraphobia is not specified), SAD, SP, SoP	Child CBT, (N= 23)	Generic CBT Group based Relaxation, exposure, Cognitive problem solving Delivered by Masters level clinicians. 120 min session per week for 12 weeks	Mean age: 14.6 (range 12 -17) Male : 56.5% Caucasian: 52%, African Americans: 39%, Asian: 8.6%	52
			Child CBT, (N= 24)	Generic CBT Individual based Relaxation, exposure, cognitive problem solving Delivered by Masters level clinicians. 60 min session per week for 12 weeks.	Mean age: 14.3 (range 12 -17) Male: 25% Caucasian: 54.2%, African Americans: 45.8%	
			Control, (N=26)	Attention control or treatment as usual Psychoeducational-supportive therapy Group based Delivered by Masters level clinicians 120 min session per week for 12 weeks	Mean age: 15.1 (range 12-17) Male: 53.8% Caucasian: 34.6%, African American: 50%, Hispanics: 7.69% Asians: 7.69%	
Hudson, 2009[98]	Australia RCT Efficacy Mental health clinic	GAD ,SAD, PD, SP, SoP	Child and parent together CBT, (N= 60)	Cool kids Group based Exposure Cognitive problem solving. 120 min session per week for 10 weeks.	Mean age; 10.2 (SD 2.4) (Range 7-16) Male: 53.3% Caucasian: 75%, Asian 6.6%, other:3.3% Low income: n= 8 Medium income: n= 21 High income: n= 22	13
			Control, (N=52)	Attention control or treatment as usual Group support and attention, group based 120 min session per week for 10 weeks	Mean age: 10.2 (SD 2.7) (Range 7-16) Male: 40.3% Caucasian: 65.3%%, Asian: 11.5%, others 5.7% Low income: n=16 Medium income: n=11	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					High income: n=17	
Ingul, 2014[99]	Norway RCT Efficacy Mental health clinic	SoP	Child CBT, (N=36)	Other CBT Exposure Cognitive problem solving Individual-based Delivered by psychologist and Masters level clinician 12, 50 min weekly sessions	Age mean: 14.98 (SD:0.94) Males: 43% ADHD: 14.29% Depression: 9.52% PTSD: 4.76%	52
			Child CBT, (N=58)	Cat Project Exposure Cognitive problem solving Group based 10, 90 min sessions	Age mean: 14.30(SD:0.89) Males: 40% ADHD: 5% Depression: 10%	
			Control, (N=34)	Attention control or treatment as usual 10, 90 min sessions	Age mean: 14.16 (SD:1.08) Males: 43% ADHD: 6.25% Depression: 6.25% OCD: 6.25% PTSD: 6.25%	
Kendall, 2008 [100, 101]	United States RCT Efficacy Mental health clinic	GAD,SAD, SoP,SP	Child CBT, (N=55)	Coping Cat: xposure Relaxation Cognitive problem solving Individual-based Weekly for 16 weeks, 60 min each session, parents at two	Age mean (years): 10.37 range (7-14) Caucasian: 83% Other:16% Low income (<$40,000): 20% Medium income ($40,000-$90,000):34% High income (>$90,000):38%	52
			Child and parent together CBT, (N=56)	CC derivative Exposure Relaxation Cognitive problem solving Individual-based, family based Weekly for 16 weeks, 60 min each	Age mean (years): 10.41 range (7-14) Caucasian: 80% Other: 16% Low income (<$40,000): 14% Medium income ($40,000-	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				session	$90,000):46% High income (>$90,000):32%	
			Control, (N=50)	Attention control or treatment as usual Family education, support, and attention Weekly for 16 weeks, 60 min each session	Age mean (years): 10.03 range (7-14) Caucasian: 88% Other:12% Low income (<$40,000): 10% Medium income ($40,000-$90,000):50% High income (>$90,000):30%	
Khanna, 2010[102]	United States RCT Efficacy Mental health clinic	GAD, PD, SAD, SoP, SP	Child CBT, (N=17)	Coping cat Exposure Relaxation Cognitive problem solving Individual-based Delivered by psychologist, student/ trainee Weekly for 12 weeks, 50 minute sessions	Age mean (years): 10.1 (range: 7-13) Males: 67% Caucasian: 83% African American: 14% Hispanic: 2% ADHD: 16% ODD:4% Tic disorder: 2%	13
			Distance, (N=16)	Camp cope a lot Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist, student/ trainee Weekly for 12 weeks		
			Control, (N=16)	Attention control or treatment as usual Individual-based, technology-based Delivered by psychologist, student/ trainee Weekly for 12 weeks, 60 minute sessions. 30 minutes of support and 30 minutes of computer.		
Last, 1998[103]	United States	SoP	Child and	Generic CBT	Age mean (years): 11.67	4

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	RCT Efficacy Mental health clinic		Parent together CBT, (N=32)	Exposure Cognitive problem solving Delivered by therapists and school contact person. 12, 60 min weekly sessions	Male: 59.3% Caucasian: 65.6% Hispanic: 3.1% African American: 3.1%	
			Control, (N=24)	Attention control or treatment as usual 12, 60 min weekly sessions	Age mean (years): 12.4 Male: 37.5% Caucasian: 87.5% African American: 4.1% Hispanic: 8.2%	
Masia-Warner, 2007[104]	United States RCT School	GAD, SAD, SoP	Child CBT, (N=19)	SASS: skills for academic and social success, Individual-based, group-based, Exposure Cognitive problem solving, 12 group sessions (40 minutes) and 2 individuals delivered by 2 doctoral level psychologists	Age mean (years): 15 (Range 14 -16) Male: 15.7% Caucasian: 73.6%, African: 5.2% African:15.78%, other: 5.2%	6
			Control, (N=17)	Attention control or treatment as usual Educational supportive group function (ESGF), Individual-based, group-based, Relaxation Cognitive strategies 12 group sessions and 2 individual delivered by 2 doctoral level psychologists.	Age mean (years): 15.1 (Range 14-16) Male: 17.64 Caucasian: 70.5%, African: 5.88% Hispanic: 17.6%, other: 5.88%	
Menzies, 1993[57]	Australia RCT Efficacy Outpatient	SP	Child CBT, (N=13)	In vivo exposure plus vicarious exposure Child CBT- (parents included < 20%) Individual based Delivered by student therapist 3 15-minute weekly session	Age mean (years): 5.5 (range:3-8) Male: 50.7% Caucasian: 96%, Hispanic:4% Depression: 10% Treatment non responder: 100%	12
			Control, (N=13)	Attention control or treatment as usual Only vicarious exposure		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				3 30-minute weekly session Delivered by student therapist		
			Child CBT, (N=13)	In vivo exposure Child CBT- (parents included < 20%) Individual based Exposure 3 30-minute weekly session Delivered by student		
			Control, (N=12)	Waitlisting or no treatment		
Muris, 2002 [105]	Netherlands RCT Efficacy School	GAD, SAD, SoP	Child CBT, (N=10)	Coping Koala Group based Exposure Relaxation Cognitive problem solving 12 30-minute sessions. 2 sessions per week delivered by student/trainee	Age range (9-12) years Caucasian: 90% Other: 10% Low income: 13 Medium income: 6 High income: 1 Male int1 ; 30% Male Int2 : 40%	13
			Control, (N=10)	Attention control or treatment as usual Emotional disclosure treatment program. Group based. 12 30-minute sessions over 6 weeks		
O'Brien, 2007 [106]	Ireland RCT Efficacy Mental health clinic	Anxiety disorder	Child CBT, (N=7)	Friends Child CBT- (parents included < 20%) Group based Exposure Relaxation Cognitive problem solving 10 90-minute weekly sessions, plus three parent session Delivered by 2 Masters level clinicians	Age mean (years): 13.8 (Range 7 – 15) Male: 28.57%	4
			Control, (N=7)	Attention Control or Treatment as Usual	Age mean (years): 12.5 (Range 7 – 15) Male: 57.14%	
Ollendick, 2009 [63]	United States and Sweden RCT	SP, SoP, SAD, GAD	Child CBT, (N=85)	OST Child CBT- (parents included < 20%) One session treatment	Caucasian: 90%, African American: 2.5% Hispanic:: 2%	36

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	Efficacy Outpatient Mental health clinic			Individual based Exposure 1 session of 3 hours Delivered by Masters level clinicians	Other: 4.5% Age range 7 -16 years Male: 45.8%	
			Control, (N=70)	Attention control or treatment as usual Education support treatment 1 session of 3 hours Delivered by Masters level clinicians	Caucasian: 90%, African American: 2.5% Hispanic:: 2% Other: 4.5% Range 7 – 16 Male: 44.2%	
			Control, (N= 41)	Waitlisting or no treatment	Age range 7 -16 years Male: 46.3%	
Pincus, 2010[107]	United States RCT Efficacy Mental health clinic	PD	Child CBT, (N=13)	Panic control treatment Exposure Relaxation Cognitive problem solving Individual-based Delivered by psychologist 11 sessions over 12 weeks, 50 min	Age mean (years): 15.75 (range: 14-17) Males: 23% Caucasian: 100% Mean income: $97,500 (SD: $65,486)	26
			Control, (N=13)	Attention control or treatment as usual		
Reigada, 2015[108]	United States RCT Efficacy Mental health clinic	GAD,PD with agoraphobia, PD without agoraphobia, SAD, SoP	Child CBT plus separate parent intervention, (N=11)	TAPS Individual based Exposure Relaxation Cognitive problem solving 15 sessions; 13 1-hour weekly sessions and 2 boosters; parents received three 1-hr sessions. Delivered by doctoral psychologist	Age mean (years): 13.65(range: 9-17) Caucasian: 82%, Other: 18% Low income (Less than $30,000): 10% Medium income ($30,000-$90,000) : 20% High income (more than $90,000) : 70% Depression:18%	13
			Control, (N=11)	Attention control or treatment as usual Offered social and emotional support	Age mean (years): 13.65(range: 9-17) Caucasian: 55%, African American: 9%, Hispanic: 18%,	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					other : 18% Low income (Less than $30,000): 9% Medium income ($30,000-$90,000) : 36% High income (more than $90,000) : 55% Depression: 27%	
Ritter, 1968[71]	United States RCT Efficacy Outpatient	SP	Child CBT, (N=7)	Other: Only contact desensitization Child CBT- (parents included < 20%) Group based Exposure 2, 35-minute weekly sessions Delivered by psychiatrist	Age range: 5-11 years	0
			Control, (N=8)	Attention control or treatment as usual Only vicarious desensitization Group based 2, 35-minute weekly sessions Delivered by psychiatrist		
			Control, (N=7)	Waitlisting or no treatment		
Rosa-Alcazar, 2007[109]	Spain RCT Efficacy Schools	SoP	Child CBT, (N=12)	IAFS Group based Exposure Cognitive problem solving Delivered by practicing clinician, 12 weekly sessions for 90 minutes each	Age mean (years) 15 Male:29%	26
			Control, (N=13)	Attention control or treatment as usual Educational treatment, individual treatment-based 12 weekly sessions for 90 minutes each		
Rosa-Alcazar, 2009[72]	Spain RCT Efficacy schools	GAD, PD without agoraphobia, PD (agoraphobia is not specified) SP	Child CBT, (N=20)	IAFS Child CBT- (parents included < 20%) Group based Exposure	Age mean (years) 15 (Range 14 -17) Male:25%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				Cognitive problem solving 12 90-minute weekly sessions Delivered by practicing clinician		
			Control, (N=19)	Attention control or treatment as usual Educational treatment on anxiety and relaxation 12 90-minute weekly sessions	Age mean (years) 14.94 (14-17) Male: 31.5%	
			Control, (N=18)	Attention control or treatment as usual Education as placebo 12 sessions of health education	Age mean (years) 14.75 (14-17) Male: 16.6%	
			Control, (N=20)	Waitlisting or no treatment	Age mean (years) 14.77 Male: 40%	
Southam-Gerow, 2010[110]	United States RCT Effectiveness Mental health clinic	GAD, PD without agoraphobia, SAD, SoP, SP	Child CBT, (N=24)	Coping Cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 14 sessions, 1 hour sessions over 12 weeks Delivered by psychologist, Masters level clinicians, social workers	Total population N = 48 Age mean (years): 10.9 (range: 8-15) Males: 44% Caucasian: 48% African American: 12.5% Hispanic: 27% Other: 10% Low income (<30,000): 73% Medium income (30,000-90,000): 16% High income (>90,000): 10% ADHD: 42% Depression: 8% OCD:4.2% ODD:37.5% PTSD:6.25% Dysthymic disorder: 2%	0
			Control, (N=24)	Attention control or treatment as usual		
Silk, 2016 [111]	United States RCT Efficacy Outpatient	GAD,SAD, SoP	Child CBT, (N=90)	Coping Cat Individual-based Exposure Relaxation Cognitive problem solving	Age mean (years): 10.94 Male: 45% Caucasian: 91%, African American :2% , Hispanic: 1%, Other: 6%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				One session per week for 16 week	Mean income: 94.155	
			Control (N=43)	Attention control or treatment as Usual supportive child centered therapy (CCT) One session per week for 16 week	Age mean (years): 10.98 Male: 41% Caucasian: 88%, African American :6% , Hispanic: 2%, Other:4% Mean income: 78.632	
Storch, 2015[112]	United States RCT Efficacy Mental health clinic	GAD, PD, PD with agoraphobia, PD without agoraphobia, SAD, SoP, SP Mean CGI=3.45	Child CBT, (N=49)	Camp Cope a Lot Computerized CBT Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving Technology based 12 60-minute weekly sessions Delivered by Masters level clinicians	Age mean (years): 9.4 (range: 7-13) Male: 53.1% College graduate(parent): 51% Caucasian: 77.6% Hispanic: 10.2% African American: 8.2% Low income (<$40,000): 44.4% Medium income ($40,000-$90,000):33.3% High income: (>$90,000): 22.2% OCD: 4.1% PTSD: 4.1% Depression: 6.1% ADHD: 34.2% ODD: 6.1% Selective mutism: 4.1% Enuresis: 4.1%	110
			Control, (N=51)	Attention control or treatment as usual	Age mean (years): 10.2 (range: 7-13) Male: 58.8% College graduate(parent): 51% Caucasian: 66.7% Hispanic: 13.7% African American: 13.7% Low income (<$40,000): 62.2% Medium income ($40,000-	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					$90,000):20% High income: (>$90,000): 18% OCD: 7.8% Dysthymia: 5.9% Depression: 5.9% ADHD: 31.4% Conduct disorder: 2% ODD: 7.8% Selective mutism: 5.9% Enuresis: 4.1%	
Storch, 2013[113]	United States RCT Efficacy Outpatient	GAD,SAD, SoP,SP	Child CBT plus separate parent intervention, (N=24)	Other: Behavioral interventions for anxiety in children with autism (BIACA) program Individual based Exposure Relaxation Cognitive problem solving 16 60-90 minute weekly sessions over 12 weeks Delivered by psychologist, student/trainee	Age mean (years): 8.83 (range: 7-11) Male: 79% Caucasian: 92% Hispanic: 4% Asian: 4% Low income (<$40,000): 4% Medium income ($40,000-$90,000):25% High income: (>$90,000):71% ADHD: 71% Depression: 4% Autism: 100% OCD: 46% ODD: 37.5%	13
			Control, (N=21)	Attention control or treatment as usual	Age mean (years): 8.89 (range: 7-11) Males: 81% Caucasian: 76% Hispanic: 19% Asian: 5% ADHD: 76% Depression: 9% Autism: 100% OCD: 62%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					ODD: 52% Low income (<$40,000): 14% Medium income ($40,000-$90,000): 28% High income: (>$90,000): 52%	
Suveg, 2009[114]	United States RCT Outpatient	GAD, SAD, SoP, SP	Child CBT, (N=55)	Coping Cat Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist, Masters level clinician 16, 60 min weekly sessions	Age range: 7-14 years ADHD: 32% Depression: 11% ODD: 14% Conduct disorder: 1%	52
			Child and parent together CBT, (N=56)	Coping Cat Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist, Masters level clinician 16, 60 min weekly		
			Control, (N=50)	Attention control or treatment as usual Weekly for 16 weeks		
Valles-Arandiga, 2014 [84]	Spain RCT Efficacy Schools	SoP	Child CBT, (N=17)	IAFS Child CBT- (parents included < 20%) Group based 12 90-minute weekly sessions Delivered by therapist	Age mean (years): 14.9 (range: 14-16) Males:25%	26
			Control, (N=17)	Attention control or treatment as usual Education Support Individual based 12 90-minute weekly sessions		
			Control, (N=17)	Waitlisting or no treatment		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Van Steensel, 2014[115]	Netherlands RCT Effectiveness Outpatient	GAD, SAD, SoP, SP	Child and parent together CBT, (N=24)	Discussing plus doing Individual based 15 sessions over 3 months	Age mean (years): 11 (range:8-18) Males: 83.3% Autism: 100%	26
			Control, (N=25)	Attention control or treatment as usual	Age mean (years): 10.72 (range:8-18) Males: 80% Autism: 100%	
			Pill Placebo, (N=76)	Pill placebo	Age mean (years): 10.6 Male : 51.3% Caucasian: 79%, African American: 9%, Hispanic: 9%, other: 3% Low income: 27.6% ADHD: 118%, ODD:9.2%, Tic disorder and other internalizing disorders: 44.7%	
Warner, 2016[116]	United States RCT Efficacy Outpatient	GAD, PD, SAD, SP, SoP	Child CBT, (N=46)	SASS: Group-based, exposure, cognitive problem solving (Skills for academic and social success provided by psychologists) Delivered by doctoral level psychologist 12 in school group sessions (ranged from 50- 90 mints)	Age mean (years): 15.5 Male: 30.4% Caucasian: 74%, African American :4% , Hispanic: 4%, Asian: 12%, Other: 4% Mean income: 94.155	20
			Child CBT, (N=47)	SASS: Group-based, exposure, cognitive problem solving Delivered by doctoral level psychologist 12 in school group sessions (ranged from 50- 90 mints)	Age mean (years): 15.34 Male: 29.7% Caucasian: 75%, African American :8% , Hispanic: 5%, Asian: 6%, Other: 6%	
			Control, (N=43)	Attention control or treatment as usual Relaxation Cognitive problem solving.	Age mean (years): 15.37 Male: 37% Caucasian: 67%, African	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				A nonspecific counseling program, SFL, controlled for the attention and group involvement.	American :2% , Hispanic: 14%, Asian: 7%, Other: 9%	
Yen, 2014[117]	Taiwan Non-Randomized comparative studies Efficacy Outpatient	GAD, SAD, SoP	Child CBT, (N=30)	Coping cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 17 weekly sessions Delivered by Psychologist	Age mean (years): 9.1 (range: 7-12)\ Males:40%	0
			Control, (N=32)	Attention control or treatment as usual	Age mean (years): 9.5 (range: 7-12) Males: 38%	

ADHD: attention deficit hyperactivity disorder, CC: coping cat, CCC: child centered therapy, IAFS: intervencion en adolescents con fobia social (treatment for adolescents with social phobia), CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, NR: not reported, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, PD: panic disorder, PTSD: post-traumatic stress disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SASS: skills for academic social success, SET-C: social effectiveness therapy, SFL: skills for life, SoP: social anxiety, SP: specific phobia, SSRI: selective serotonin reuptake inhibitor. TAPS: treatment of anxiety and physical symptoms.

Table E.7. Characteristics of studies evaluating combination of CBT with drugs versus CBT

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Bernstein, 2000 [118]	United States RCT Outpatient	SP	Combination therapy: CBT+ Other Medication: imipramine+ child CBT, (N=31)	Generic CBT CBT protocol for school refusal, but each subject had an anxiety disorder Exposure Individual-based 8, 45 to 60 min weekly sessions 25 mg bid. Delivered by 2 doctoral level psychologists a Masters level clinician	Age mean (years); 13.9 Male: 39.6% Caucasian: 90% African Americans: 7.9% Hispanic: 1.5%	
			Combination therapy Placebo Pill plus child CBT, (N=31)	Generic CBT CBT protocol for school refusal, but each subject had an anxiety disorder Exposure, Individual-based 8, 45 to 60 min weekly sessions level psychologists a Masters level clinician.		
Eichstedt, 2011[119]	Canada Non randomized comparative study Mental health clinic	GAD, SAD, SoP, SP	Therapy only Child CBT plus separate parent intervention, (N=35)	Worry warriors program Exposure Relaxation Cognitive problem solving Group-based Delivered by psychologist, student/trainee, nurse Weekly 1.5 hr sessions for 12 weeks	Age mean (years): 10.49 (range 8-13) Males: 46%	182
			Combination therapy: CBT+ SSRI: Child CBT plus separate parent intervention various SSRI , (N=13)	Worry warriors program Exposure Relaxation Cognitive problem solving Group-based Delivered by psychologist, student/trainee, nurse Weekly 1.5hr sessions for 12 weeks	Age mean (years): 10.21 (range 8-13) Males: 92%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Klein, 1992[120]	United States RCT Efficacy Mental health clinic	SAD	Other Medication+ therapy: Imipramine plus child CBT, (N=11)	Other Medication+ Imipramine Exposure, cognitive problem solving max of 5 mg/kg/day plus weekly therapy session for 6 weeks	Age mean (years): 9.5 (range:6-15) Male: 67% Caucasian: 100%	0
			Placebo Pill+ Child CBT, (N=10)	Placebo plus exposure, cognitive problem solving max of 5 mg/kg/day plus weekly therapy session for 6 weeks		
Melvin, 2016[121]	Australia RCT Efficacy Mental health clinic	GAD SAD SoP	Child CBT plus separate parent intervention : (N=20)	Other Therapy Exposure Relaxation Cognitive problem solving Individual based Psychologist , Masters level clinician and student/trainee 24, 50-60 min sessions, bi weekly and then weekly	Age mean (years): 14 (Range: 11-16.5) Males: 50% Caucasian: 94% Asian: 6%	52
			Child CBT plus separate parent intervention + pill placebo: (N=21)	Other Therapy + Pill Placebo Exposure Relaxation Cognitive problem solving Individual based Psychologist , Masters level clinician and Student/trainee 24, 50-60min sessions, bi weekly and then weekly	Age mean (years): 13.4 (Range:11-16.5) Males: 48% Caucasian: 94% Asian: 6%	
			Child CBT plus separate parent intervention plus Fluoxetine : (N=21)	Other Therapy + SSRI: Fluoxetine Exposure Relaxation Cognitive problem solving Individual based Psychologist , Masters level clinician and student/trainee 24, 50-60min sessions, bi weekly and then weekly	Age mean (years): 13.3 (Range:11-16.5) Males: 66% Caucasian: 94% Asian: 6%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Walkup, 2008[20-26]	United States RCT Efficacy Outpatient	GAD,SAD, SoP	Child CBT, (N=139)	Coping Cat Child CBT (parents included <20%) Individual-based. Exposure Relaxation Cognitive problem solving. 60-minute session once a week for 12 weeks.	Age mean (years): 10.5 Male: 49.2% Caucasian: 76.3%, African American:10.1%, Hispanic: 9.2%, other: 4.5% Low income: 23.7% ADHD: 11.5%, ODD:13.8%, Tic disorder and other internalizing disorders: 41.7%	0
			SSRI: Sertraline, (N=133)	Beginning with 25mg/day Up to 200 mg/day by 8th week, for 12 weeks.	Age mean (years): 10.8 Male: 51.1% Caucasian: 77.4%, African American: 9%, Hispanic: 11.3%, other: 2.3% Low income: 26.3% ADHD: 12.7%, ODD:8.2%, Tic disorder and other internalizing disorders: 55.6%	
			Combination therapy: CBT+ SSRI: Child CBT+ Sertraline, (N=140)	Coping Cat, Child CBT (parents included <20%) Individual-based Exposure, relaxation and cognitive problem solving plus Sertraline. 60-minute session once a week for 12 weeks plus up to 200 mg/day for 12 weeks.	Age mean (years): 10.7 Male: 49.6% Caucasian: 82.9%, African American: 7.9%, Hispanic: 5.6%, other: 3.6% Low income: 25.0% ADHD: 11.4%, ODD:10%, Tic disorder and other internalizing disorders: 42.8%	
			Control, (N=76)	Pill placebo	Age mean (years): 10.6 Male : 51.3% Caucasian: 79%, African American: 9%, Hispanic: 9%, other: 3% Low income: 27.6% ADHD: 118%, ODD:9.2%, Tic disorder and other internalizing disorders: 44.7%	

ADHD: attention deficit hyperactivity disorder, CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, NR: not reported, ODD: oppositional defiant disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia, SSRI: selective serotonin reuptake inhibitor.

Table E.8. Characteristics of studies comparing parent only intervention versus waitlisting

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Cartwright-Hatton, 2011 [122]	England RCT Effectiveness Mental health clinic	GAD, PD, PD with agoraphobia, PD without agoraphobia, SAD, SoP, SP	Parent only intervention, (N=38)	Timid to Tiger Group based Exposure Cognitive problem solving 10 2-hour weekly sessions Delivered by psychologist	Age mean (years): 6.66 (range: 2.7-9) Males: 47% Caucasian: 76% Other: 24% Struggling financially (parent): 24% Managing financially (parent):34% Comfortable financially (parent):34% Less than high school or high school graduate (parent): 45% College graduate (parent): 42% OCD: 15% ODD: 27% PTSD: 5% Selective mutism: 11% Depression: 23%	52
			Control, (N=36)	Waitlisting or no treatment	Age mean (years): 6.47 (range: 2.7-9) Males: 39% Caucasian: 72% Other: 28% Struggling financially (parent): 11% Managing financially (parent):36% Comfortable financially (parent):28% Less than high school or high school graduate (parent):33% College graduate (parent): 39% OCD: 15% ODD: 27%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					PTSD: 5% Selective mutism: 11% Depression: 23%	
Medlowitz, 1999[56]	Canada RCT Efficacy Outpatient		Child CBT, (N=23)	Coping bear Child CBT- (parents included < 20%) Group based Relaxation Cognitive problem solving 12 1.5-hour weekly sessions Delivered by 3 psychologists, 1 student/trainee, 1 youth worker	Age mean (years): 9.5 (Range 7-12) Male: 28.4%	NR
			Parent only intervention, (N=21)	Generic CBT Group based 12 1.5-hour weekly sessions Delivered by doctoral level psychologist, and student/trainee		
			Child CBT plus separate parent intervention, (N=18)	Coping Bear Group based Relaxation Cognitive problem solving 12 1.5-hour weekly sessions (one for kids, one for parents) Delivered by doctoral level psychologist, student/trainee, youth worker		
			Control, (N=40)	Waitlisting or no treatment		
Ozyurt, 2015[123]	Turkey RCT Efficacy Outpatient	GAD, SAD, SoP, SP	Parent only intervention, (N=37)	Triple P Technology based Group based 5 group sessions (2 hours), 3 telephone consultations	Age mean (years): 9.65 (range: 8-12) Male: 82%	17
			Control, (N=37)	Waitlisting or no treatment	Age mean (years): 9.83 (range: 8-12) Male: 71%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Santacruz, 2006[124]	Spain RCT Efficacy Home	SP	Parent only intervention, (N=27)	Uncle lightfoot Bibliotherapy and games Individual based Exposure 5 45-minute weekly sessions over a 1 month period Delivered by the parents	Age mean (years): 6.49% Male patients: 52.5%	12
			Parent only intervention, (N=28)	Other: Emotive performances Individual based Exposure 5 45-minute weekly sessions over a 1 month period Delivered by the parents		
			Control, (N=23)	Waitlisting or no treatment		
Smith, 2014[125]	United States RCT Efficacy Outpatient	GAD, SAD, SoP, SP	Parent only intervention, (N=18)	CC derivative Individual based Exposure Relaxation Cognitive problem solving 10 weekly one hour sessions Delivered by student/trainee	Age mean (years): 10.04 (range: 7-13) Males:61% Caucasian: 94% Hispanic: 6% Mean income: $131,000 (SD: 82,417) Externalizing disorder: 22%	13
			Control, (N=13)	Waitlisting or no treatment	Age mean (years): 9.46 (range: 7-13) Males: 62% Caucasian: 100% Mean income: $123,571 (SD: 74,202) Externalizing disorder: 15%	
Thirlwall, 2013[126, 127]	United Kingdoms RCT Efficacy	GAD, SAD,SoP	Parent only intervention, (N=64)	Generic CBT Individual based Exposure Cognitive problem solving	Males: 53% Caucasian: 86% Unemployed (parent): 6.3% Other employed (parent): 26.6%	26

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	Outpatient			8 1-hour face-to-face weekly and 4 20-minute telephone sessions Delivered by psychologist, student/trainee	Higher professional (parent): 57.8% Less than high school or high school graduate (parent): 20.3% Some college (parent): 40.6% College graduate (parent): 29.7% Depression: 7.8% ADHD: 7.8% ODD: 14.1%	
			Parent only intervention, (N=61)	Other: Brief guided parent-delivered CBT Individual based Exposure Cognitive problem solving 2 1-hour face-to-face weekly and 2 20-minute telephone sessions Delivered by psychologist, student/trainee	Males: 51% Caucasian: 87% Unemployed (parent): 8.2% Other employed (parent): 23% Higher professional (parent): 63.9% Less than high school or high school graduate (parent): 24.6% Some college (parent): 44.3% College graduate (parent): 26.2% Depression: 9.8% ADHD: 11.5% ODD: 14.8%	
			Control, (N=69)	Waitlisting or no treatment	Males: 51% Caucasian: 84% Unemployed (parent): 2.9% Other employed (parent): 26.1% Higher professional (parent): 62.3% Less than high school or high school graduate (parent): 15.9% Some college (parent): 47.8% College graduate (parent): 28.9% Depression:15.9% ADHD:11.5%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					ODD: 15.9%	
Waters, 2009[86]	Australia RCT Efficacy Outpatient	GAD, SAD, SoP, SP	Child CBT plus separate parent intervention, (N=38)	Take Action Group based Exposure Relaxation Cognitive problem solving 10 weekly 1-hour child and one hour parents sessions Delivered by psychologist	Age mean (years): 6.89 (range: 4-8) Males: 37% Caucasian: 97%	52
			Parent only intervention, (N=31)	Take Action Group based Exposure Relaxation Cognitive problem solving 10 weekly 1-hour child and one hour parents sessions Delivered by psychologist	Age mean (years): 6.68 (range: 4-8) Males: 58% Caucasian: 97%	
			Control, (N=11)	Waitlisting or no treatment	Age mean (years): 6.79 (range 4-8) Males: 55% Caucasian: 91%	

ADHD: attention deficit hyperactivity disorder, CBT: cognitive behavioral therapy, CC: coping cat, CGI: clinical global impression scale, GAD: generalized anxiety disorder, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, PD: panic disorder, PTSD: posttraumatic stress disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia, Triple P: positive parenting program.

Table E.9. Characteristics of studies comparing different components of parent only interventions

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Hiller, 2016[128]	United Kingdom RCT Efficacy Mental health clinic	GAD, PD, SAD, SoP	Parent only intervention, (N=32)	Generic CBT Exposure Cognitive problem solving Individual based 9, 90 min weekly sessions	Age mean (years): 9.78 (range: 7-12) Males: 87.5% ODD: 18.75% Agoraphobia: 3%	26
			Parent only intervention, (N=28)	Other Therapy Exposure Cognitive problem solving Delivered by parent 9, 90 min weekly sessions	Age mean (years): 9.32 (range: 7-12) Males: 86% ODD: 21.4% Agoraphobia: 3.6%	
Thirlwall, 2013[126, 127]	United Kingdoms RCT Efficacy Outpatient	GAD, SAD, SoP	Parent only intervention, (N=64)	Generic CBT Individual based Exposure Cognitive problem solving 8 1-hour face-to-face weekly and 4 20-minute telephone sessions Delivered by psychologist, student/trainee	Males: 53% Caucasian: 86% Unemployed (parent): 6.3% Other employed (parent): 26.6% Higher professional (parent): 57.8% Less than high school or high school graduate (parent): 20.3% Some college (parent): 40.6% College graduate (parent): 29.7% Depression: 7.8% ADHD: 7.8% ODD: 14.1%	26
			Parent only intervention, (N=61)	Other: Brief guided parent-delivered CBT Individual based Exposure Cognitive problem solving 2 1-hour face-to-face weekly and 2 20-minute telephone sessions Delivered by psychologist, student/trainee	Males: 51% Caucasian: 87% Unemployed (parent): 8.2% Other employed (parent): 23% Higher professional (parent): 63.9% Less than high school or high school graduate (parent): 24.6% Some college (parent): 44.3% College graduate (parent): 26.2% Depression: 9.8%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					ADHD: 11.5% ODD: 14.8%	
			Control, (N=69)	Waitlisting or no treatment	Males: 51% Caucasian: 84% Unemployed (parent): 2.9% Other employed (parent): 26.1% Higher professional (parent): 62.3% Less than high school or high school graduate (parent): 15.9% Some college (parent): 47.8% College graduate (parent): 28.9% Depression:15.9% ADHD:11.5% ODD: 15.9%	

ADHD: attention deficit hyperactivity disorder, CBT: cognitive behavioral therapy, CGI: Clinical Global Impression scale, GAD: Generalized anxiety disorder, ODD: oppositional defiant disorder, PD: panic disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia.

Table E.10. Characteristics of studies comparing distance therapy versus waitlisting

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Cobham, 2012 [36]	Australia RCT Efficacy Mental health clinic	GAD, PD, PD with agoraphobia, SAD, SoP, SP	Child CBT plus separate parent intervention, (N=23)	Do as I do Individual-based Exposure Cognitive problem solving 6 90-minutes sessions for parent and 6 60-minutes for child, weekly Delivered by Masters level clinicians	Age mean (years): 9.70 (range: 7-14) Males: 50% Caucasian 92% Asian: 8% PTSD: 4% ADHD: 7% Dysthymia: 4% Enuresis: 4%	26
			Distance Therapy, (N=20)	Do as I do "Do as I Do" and "Facing your Fears" bibliotherapy programs Exposure Cognitive problem solving 2 hour parent group, every other week 12 min phone calls for 12 weeks Delivered by parent and therapist	Age mean (years): 10.20 (range: 7-14) Males: 55% Caucasian 92% Asian: 8% ADHD: 5% PTSD: 5% Dysthymia: 5% Sleep terrors: 5%	
			Control, (N=12)	Waitlisting or no treatment	Age mean (years): 9.83 (range: 7-14) Males: 57% Caucasian 92% Asian: 8% PTSD: 4%	
Dewis, 2001[37]	Australia RCT Efficacy Mental health clinic	SP	Child CBT, (N=9)	Generic CBT Live graded exposure Child CBT- (parents included < 20%) Individual based Exposure Three 45-min treatment sessions every 3–4 days Provided by clinical psychologists	Male: 35.7% Caucasian: 100% Age mean (years): 12.3 (Range 10-17)	4
			Distance Therapy,	Other: Computer-aided vicarious exposure	Male: 35.7% Caucasian: 100%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			(N=10)	Individual computer based Exposure Three 45-min treatment sessions every 3–4 days	Age mean (years): 13.8 (Range 10-17)	
			Control, (N=9)	Waitlisting or no treatment	Male: 35.7% Caucasian: 100% Age mean (years): 13.3 (Range 10 – 17)	
Donovan, 2014[129]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Distance Therapy, (N=23)	Brave online Individual based Exposure Relaxation Cognitive problem solving 6 1-hour parent sessions and 2 boosters, one phone call and weekly emails	Age mean (years): 4.08 (range: 3-6) Males: 46% Low income: (<$29,875): 5.8% Medium income: ($30,622-$ 74,688): 38.5% High income: (>$74,688): 55.8% Selective mutism: 3%	26
			Control, (N=29)	Waitlisting or no treatment		
Infantino, 2016[130]	Australia RCT Efficacy Mental health clinic	GAD,SAD, SoP, SP	Distance Therapy, (N=12)	Other: Audio Intervention Technology based Individual based Exposure Relaxation Cognitive problem solving 10 audio lessons, 20-30 minutes each, 2 lessons a week during 5 weeks	Age mean (years): 7.3 (range: 6-12) Males: 50% Caucasian: 100% Low income: 0% Medium income 33.3% High income: 66.7% Less than high school or high school graduate (parent): 29% Some college (parent): 4% College graduate (parent): 67%	13
			Control, (N=12)	Waitlisting or no treatment	Age mean (years): 7.7 (range: 6-12) Males: 42% Caucasian: 100% Low income: 8% Medium income: 25%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					High income: 67% Less than high school or high school graduate (parent): 8% Some college (parent): 17% College graduate (parent): 71%	
Khanna, 2010[102]	United States RCT Efficacy Mental health clinic	GAD, PD, SAD, SoP, SP	Child CBT, (N=17)	Coping Cat Exposure Relaxation Cognitive problem solving Individual-based Delivered by psychologist, student/ trainee Weekly for 12 weeks, 50 minute sessions		
			Distance, (N=16)	Camp Cope a Lot Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist, student/ trainee Weekly for 12 weeks,		
			Control, (N=16)	Attention control or treatment as usual Individual-based Technology-based Delivered by psychologist, student/ trainee Weekly for 12 weeks, 60 minute sessions. 30 minutes of support and 30 minutes of computer.		
Lyneham,	Australia RCT	GAD, PD (agoraphobia is	Distance Therapy,	Other: Client initiated Individual based	Age mean (years): 9.42 (Range 6-12)	12

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
2006[131]	Efficacy Mental health clinic	not specified), SAD, SP, SoP	(N=28)	Contact as needed by phone/email over 12 weeks work Delivered by a Masters level clinician	Male: 49% Caucasian; 96% Asian: 1% Other: 3% Low income: n= 26 Medium income: n= 42 High income: n= 26	
			Distance Therapy, (N=21)	Other: Telephone CBT Technology based Individual based 9 scheduled telephone calls; weekly sessions for the first 6 weeks and bi-weekly for the final 6 weeks Delivered by a Masters level clinician		
			Distance Therapy, (N=29)	Other: Email Psychotherapy, Technology based Individual based 9 scheduled emails, plus ad hoc replies; weekly sessions for the first 6 weeks and bi-weekly for the final 6 weeks Delivered by a Master level clinician		
			Control, (N=22)	Waitlisting or no treatment		
March, 2009[132]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SP, SoP.	Distance Therapy, (N=40)	Brave online Individual based Technology based Exposure Relaxation Cognitive problem solving 10 weekly, 60-min child sessions and 6 weekly, 60-min parent sessions. Two booster sessions con- ducted 1 and 3 months; weekly online contact, 2 telephone calls Delivered by a doctoral level psychologist	Age mean (years): 9.75 (Range 7 -12) Male: 47.5% Low income: n= 8 Medium income: n= 17 High income: n= 15	36

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=33)	Waitlisting or no treatment	Age mean (years): 9.09 (Range 7 – 12) Male: 42.4% Low income: n= 4 Medium income: n= 16 High income: n= 13	
Rapee, 2006[69]	Australia RCT Efficacy Mental health clinic	GAD, PD (agoraphobia is not specified), SAD, SP, SoP.	Child and parent together CBT, (N=90)	Cool Kids Group based Exposure Cognitive problem solving 9 2-hour sessions over 12 weeks Delivered by student trainee.	Age mean (years): 9.475 (Range: 6 -12) Male: 66.6% Low income: n= 26 (<$30,000)	36
			Distance Therapy, (N=90)	Other: Bibliotherapy Individual based Exposure Relaxation Cognitive problem solving Treatment duration is 12 weeks at own pace	Age mean (years): 9.558 (Range: 6 – 12) Male: 64.44% Low income: n= 9 (<$30,000)	
			Control, (N=87)	Waitlisting or no treatment	Age mean (years): 9.5 (Range: 6 – 12) Male: 48.2% Low income: n= 15(<$30,000)	
Spence, 2006[81]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SP SoP	Child CBT plus separate parent intervention, (N=22)	Generic CBT Group based Exposure Relaxation Cognitive problem solving 10 60-minute weekly child sessions and 6 60-minute weekly parent sessions, plus booster sessions at 1 and 3 months Delivered by 5 doctoral level psychologists.	Age mean (years): 10.26 (Range 7-14) Male: 59%	12

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Distance Therapy, (N=27)	Generic CBT Internet CBT Group based Exposure Relaxation Cognitive problem solving 5 of the 10 child sessions plus the 3-month booster via Internet, with the remaining sessions being conducted in the clinic; 3 of the 6 parents sessions and the 3-month via Internet Delivered through the internet	Age mean (years): 9.8 (Range 7-14) Male: 59.2%	
			Control, (N=23)	Waitlisting or no treatment	Age mean (years): 9.8 (Range 7-14) Male: 56.5%	
Spence, 2011[82]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Distance Therapy, (N=44)	Brave online Technology-based Individual based Exposure Relaxation Cognitive problem solving 10 adolescents weekly sessions and 5 parent sessions (60 minutes each) over 12 weeks; 1 15-minute phone call, email feedback after each session Delivered by psychologist, Masters level clinician	Age mean (years): 13.98 (range: 12-18) Males: 41% High income(>$76,910): 47% College graduate (parent): 58% Depression: 2.6% ODD: 1.7% Dysthymic disorder: 9.7%	52
			Child CBT plus separate parent intervention, (N=44)	Individual based Exposure Relaxation Cognitive problem solving 10 adolescents weekly sessions and 5 parent sessions (60 minutes each)		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				over 12 weeks Delivered by psychologist, Masters level clinician		
			Control, (N=27)	Waitlisting or no treatment		
Spence, 2017[133]	Australia RCT Efficacy Mental health clinic	GAD SAD SoP SP	Distance Therapy: (N=48)	BRAVE online Exposure Relaxation Cognitive problem solving Individual based Delivered by doctoral level psychologists 10, 60min weekly sessions, 5-6 parent sessions	Age mean (years): 11.02 (Range 8-17) Males:46% Caucasian: 92% African Americans: 4% Asian: 4% Low income (<76,761.50): 58% High income (>$76761.50): 37.5% Other comorbidities: 10%	26
			Distance Therapy: (N=47)	Other Therapy Exposure Relaxation Cognitive problem solving Individual based Delivered by doctoral level psychologists 10, 60min weekly sessions, 5-6 parent sessions	Age mean (years): 11.34 (Range 8-17) Males: 30% Caucasian: 98% Asian: 2% Low income (<76,761.50): 5% High income (>$76761.50): 36% Dysthymia:11% Other comorbidities:9%	
			Control: (N=30)	Waitlisting or no treatment	Age mean (years): 11.6 (Range 8-17) Males: 46% Caucasian: 100% Low income (<76,761.50): 46% High income (>$76761.50): 53% Dysthymia:13% Other comorbidities:3%	
Tillfors, 2011[134]	Sweden RCT Efficacy	SoP	Distance Therapy, (N=10)	Generic CBT Technology based Individual based	Age mean (years): 16.5 Male: 10%	0

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	Mental health clinic			Exposure 9 weekly modules with email feedback		
			Control, (N=9)	Waitlisting or no treatment	Age mean (years): 16.5 Male: 10%	
Vigerland, 2016[135, 136]	Sweden RCT Efficacy Outpatient	GAD, PD, SAD, SP, SoP	Distance Therapy, (N=46)	Generic CBT Exposure Relaxation Cognitive problem solving 11 modules over 10 weeks (at own pace) Delivered by psychologist and student	Age mean (years): 10.3 (range: 8-12) Male: 43% Less than high school or high school graduate(parent): 24% Some college(parent): 8% College graduate(parent): 60%	12
			Control, (N=47)	Waitlisting or no treatment	Age mean (years): 9.9 (range: 8-12) Male: 47% Less than high school or high school graduate: 16% Some college: 12% College graduate: 64%	
Wuthrich, 2012[137]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Distance Therapy, (N=24)	Cool Teens Technology based Individual based Exposure Cognitive problem solving 8 30-minute therapy modules plus 8 15-minute phone calls Delivered by therapist, computerized program	Age mean (years): 15.6 (range: 14-17) Males: 33.3% Caucasian: 87.5% Asian: 4.2% Other: 4.2% Low income (<$14,937)=5% Medium income ($14,937-$59,750)=35% High income (59,750) = 60%	12

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=19)	Waitlisting or no treatment	Age mean (years): 15.4 (range: 14-17) Males: 42.1% Caucasian: 84% Asian: 5.3% Other: 5.3% Low income (<$14,937)=5.3% Medium income ($14,937-$59,750)=36.8% High income (>$59,750) = 57.9%	

ADHD: attention deficit hyperactivity disorder, BRAVE: body signs, relaxation, active helpful thoughts, victory over your fears, enjoy! reward yourself. CBT: cognitive behavioral therapy, CGI: clinical global impression scale, EMDR: eye movement desensitization and reprocessing, GAD: generalized anxiety disorder, ODD: oppositional defiant disorder, PD: panic disorder, PTSD: posttraumatic stress disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia.

Table E.11. Characteristics of studies comparing different components of distance therapy

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Lyneham, 2006[131]	Australia RCT Efficacy Outpatient	GAD, PD (agoraphobia is not specified), SAD, SP, SoP	Distance Therapy, (N=28)	Other: Client initiated Individual based Contact as needed by phone/email over 12 weeks work Delivered by a Masters level clinician	Age mean (years): 9.42 (Range 6-12) Male: 49% Caucasian; 96% Asian: 1% Other: 3% Low income: n= 26 Medium income: n= 42 High income: n= 26	12
			Distance Therapy, (N=21)	Other: Telephone CBT Technology based Individual based 9 scheduled telephone calls; weekly sessions for the first 6 weeks and bi-weekly for the final 6 weeks Delivered by a Masters level clinician		
			Distance Therapy, (N=29)	Other: Email Psychotherapy, Technology based Individual based 9 scheduled emails, plus ad hoc replies; weekly sessions for the first 6 weeks and bi-weekly for the final 6 weeks Delivered by a Masters level clinician		
			Control, (N=22)	Waitlisting or no treatment		
Spence, 2017[133]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Distance Therapy: (N=48)	BRAVE online Exposure Relaxation Cognitive problem solving Individual based Delivered by doctoral level psychologists 10, 60min weekly sessions, 5-6 parent sessions	Age mean (years): 11.02 (Range 8-17) Males:46% Caucasian: 92% African Americans: 4% Asian: 4% Low income (<76,761.50): 58% High income (>$76761.50): 37.5% Other comorbidities: 10%	26
			Distance Therapy:	Other Therapy Exposure	Age mean (years): 11.34 (Range 8-17)	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			(N=47)	Relaxation Cognitive problem solving Individual based Delivered by doctoral level psychologists 10, 60min weekly sessions, 5-6 parent sessions	Males: 30% Caucasian: 98% Asian: 2% Low income (<76,761.50): 5% High income (>$76761.50): 36% Dysthymia:11% Other comorbidities:9%	
			Control: (N=30)	Waitlisting or no treatment	Age mean (years): 11.6 (Range 8-17) Males: 46% Caucasian: 100% Low income (<76,761.50): 46% High income (>$76761.50): 53% Dysthymia:13% Other comorbidities:3%	

BRAVE: body signs, relaxation, active helpful thoughts, victory over your fears, enjoy! reward yourself. CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, PD: panic disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia

Table E.12. Characteristics of studies comparing attention bias modification versus wait listing or pill placebo

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Eldar, 2012[138]	Israel RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	ABM plus therapy, (N=15)	Attention bias modification plus therapy Individual based Attention bias modification 4 weekly sessions	Age mean (years): 9.5 (range: 8-14)	NR
			Control, (N=15)	Attention control or treatment as usual ABM placebo ABM stimuli without attention training 4 weekly sessions	Age mean (years): 9.8 (range: 8-14)	
			Control, (N=10)	Attention control or treatment as usual ABM placebo ABM neutral (only neutral stimuli) 4 weekly sessions	Age mean (years): 10.5 (range: 8-14)	
Waters, 2015[139]	Australia RCT Efficacy	GAD, SAD, SoP, SP	ABM, (N=31)	Attention bias modification Technology based Individual based 12 weekly sessions, at home	Age mean (years): 9 Male: 39%	26
			Control, (N=28)	Waitlisting or no treatment	Age mean (years): 8.5 Male: 47%	

ABM: attention bias modification ,GAD: Generalized anxiety disorder, RCT: randomized control trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia.

Table E.13. Characteristics of studies comparing combined attention bias modification intervention and other therapy versus other therapy

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Britton, 2013 [140]	United States RCT Effectiveness Mental health clinic	GAD, SAD, SoP, SP	ABM + CBT, (N=18)	Other CBT Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist 8 weekly sessions	Age mean (years): 11.4 (range: 8-17) Males: 33% Depression: 5.5%	0
			ABM control + CBT, (N=18)	Therapy placebo, Other CBT Exposure Relaxation Cognitive problem solving(8 weekly sessions	Age mean (years): 10.9 (range: 8-17) Males: 33% Depression: 5.5%	
Pergamin-Hight, 2016 [141]	Israel RCT Efficacy Outpatient	Anxiety disorder (Social Anxiety Disorder)	ABM (N=36)	ABM Individual based 8, bi weekly sessions	Age mean (years): 12.71	12
			Control (N=31)	Attention control or treatment as usual ABM placebo	Age mean (years): 12.2	
Waters, 2014 [142]	Australia RCT Efficacy Outpatient	SP	ABM + OST , (N=19)	Exposure Individual based Delivered by student/trainee One 3hr session, 15 min attention bias modification training	Age mean (years): 10.06 (range: 6-17) Males: 58% High income (>$59,750): 85% College graduate (parent): 53%	12
			ABM control + OST, (N=18)	Exposure, Individual based Delivered by student/trainee One 3hr session	Age mean (years): 11.05 (range: 6-17)\ Males: 72% High income (>$59,750): 88% College graduate (parent) : 72%	

ABM: attention bias modification, CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, OST: one session treatment, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia.

Table E.14. Characteristics of studies comparing mindfulness based CBT to waitlisting

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Ebrahimineja d, 2016[143]	Iran RCT Effectiveness School	SoP	Mindfulness Based CBT : (N=15)	Cognitive problem solving Group based Delivered by Masters level clinician 8, 120min weekly sessions	Age mean (years): 14.5 (Range: 12-18) Males: 0% Other Race: 100% Medium income (middle class): 100%	NR
			Control: (N=15)	Waitlisting or no treatment	Age mean (years): 14.3 (Range: 12-18) Males: 0% Other Race: 100% Medium income (middle class): 100%	

CGI: clinical global impression scale, RCT: randomized controlled trial, SoP: social anxiety

Table E.15. Characteristics of studies comparing acceptance and commitment therapy versus waitlist or no treatment

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Azadeh, 2015[144]	Iran RCT Effectiveness Mental health clinic	SoP	(ACT), (N=NR)	Acceptance and commitment therapy Group based 10 sessions, 90 minute sessions, weekly	Total number of patients: 30 Age mean (years): 15.3 (range :15-16) Male: 0%	0
			Control, N=NR)	Waitlisting or no treatment		
Hancock, 2016 [44]	Australia RCT Effectiveness Mental health clinic	GAD, SAD	ACT, (N=68)	Acceptance and commitment therapy (ACT) Group based Relaxation 10 sessions, 90-minute weekly sessions Delivered by doctoral level psychologist	Age mean (years): 11.15 (range: 7-17) Male: 45.5% Caucasian: 87%, Asian: 3%, Other: 10% ADHD: 6%, Depression, 18%, OCD: 7.3% Treatment naïve: 27.9%	13
			Child and parent together CBT, (N=63)	Cool Kids Group based Exposure Cognitive problem solving 10 sessions, 90-minute weekly sessions Delivered by doctoral level psychologist	Age mean (years): 10.81 (range: 7-17) Male: 39.6% Caucasian: 94.4%, Other: 5.6% ADHD: 10%, Depression, 13%, OCD: 3% Treatment naïve: 22.2%	
			Control, (N=62)	Waitlisting or no treatment	Age mean (years): 11.66 (range: 7-17) Male: 41.9% Caucasian: 84%, Other: 16% Depression: 24%, OCD: 8% Treatment naïve: 70.9	

ABM: attention bias modification, ACT: acceptance and commitment therapy, CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety.

Table E.16. Characteristics of studies comparing non-CBT psychoanalysis versus wait listing

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Gottken, 2014[145]	Germany RCT Efficacy Mental health clinic	GAD, PD, PD with agoraphobia, SoP, SP	Non-CBT psychoanalysis, (N=18)	Short term psychoanalytic child therapy Individual based 20-25 weekly sessions Delivered by psychologist, psychiatrist	Age mean (years) (years): 7.07 (range: 4-10) Males: 61.1% Less than high school or high school graduate (parent): 37.5% Some college (parent): 31.3% College graduate (parent): 31.3% Depression: 44.5%	6
			Control, (N=12)	Waitlisting or no treatment	Age mean (years): 7.06 (range: 4-10) Males: 58.3% Less than high school or high school graduate (parent): 60% Some college (parent): 10% College graduate (parent): 30% Depression: 41.7% Selective mutism: 8.3%	

CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, PD: panic disorder, RCT: randomized controlled trial, SoP: social anxiety, SP: specific phobia.

Table E.17. Characteristics of studies comparing other therapy versus waitlisting or attention control or treatment as usual

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Abbasi, 2016 [27]	Iran RCT Efficacy Outpatient	SAD	Child CBT (N=15)	Modular CBT Individual based Exposure Cognitive problem solving 4-20 sessions, 1 hour sessions, with	Age range : 6-7 years Male: 53%	13
			Other Therapy, (N=15)	Child parent relationship training Individual based, 10 weekly, 1 hour sessions	Age range : 6-7 years Male: 33.3%	
			Control, (N=16)	Waitlisting or no treatment	Age range : 6-7 years Male: 48%	
Cornwall, 1996 [146]	Australia RCT Effectiveness Mental health clinic	SP (simple phobia	Other Therapy, (N=NR)	Reciprocal inhibition Emotive imagery treatment condition Individual based 6 40-minute weekly sessions Delivered by Masters level clinicians.	Age range: 7-10 years	13
			Control, (N=NR)	Waitlisting or no treatment		
Elkins, 2016[147]	United States RCT Efficacy Mental health clinic	PD	Other Therapy, (N=37)	Panic control treatment Single intensive CBT Exposure Cognitive problem solving 8 daily intensive sessions	Age mean (years): 15.04 Male: 45.5%	6
			Control, (N=17)	Waitlisting or no treatment	Age mean (years): 15.82 Male:35.2	
Goldbeck, 2012[148]	Germany RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Other therapy, (N=18)	Music therapy Relaxation 3 individual sessions (60mins), 9 group sessions (100mins), 2 parent sessions (50mins) over 17 weeks	Age mean (years): 9.94 (range: 8-12) Males: 33.3% Caucasian: 100% Less than high school or high school graduate (parent): 100% ADHD:5.5% Depression:5.5% Selective mutism:5.5%	16

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=18)	Attention control or treatment as usual	Age mean (years): 9.94 (8-12) Males: 66.6% Caucasian: 94.4% Other: 5.5% Less than high school or high school graduate (parent): 100% Depression: 5.5% Encopresis: 5.5%	
Joormann, 2002[149]	Germany RCT Efficacy Mental health clinic	SoP	Other Therapy, (N=9)	Generic CBT Group based Two sessions per week for 8 weeks	Age mean (years): 13.9 (range: 11-15) Male: 45%	52
			Control, (N=9)	Waitlisting or no treatment	Age mean (years): 11.33 (range: 8-15) Male: 45%	
Klein, 2015[150]	Netherlands RCT efficacy Mental health clinic	GAD, SAD, SoP.	Other Therapy, (N=44)	Other Therapy. Individual based 15 sessions over 2 weeks	Age mean (years): 9.1	2
			Control, (N=43)	Attention control or treatment as usual Therapy Placebo	Age mean (years): 9.4	
Lee, 2016[151]	United States RCT Efficacy Mental health clinic	GAD,SAD, SoP	Other Therapy, (N=37)	Friends Combines CBT only and CBT plus parenting Group based Exposure Relaxation Cognitive problem solving 9 sessions, plus 2 booster sessions; half of group also received 9 concurrent parent sessions	Caucasian: 97%	156
			Control, (N=24)	Waitlisting or no treatment		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Yoosefi Looyeh, 2014 [152]	Iran RCT Efficacy School	SoP	Other Therapy, (N=12)	Other: Narrative group therapy Group based Delivered by parent and teacher 14 sessions 90 minute sessions, twice per week Delivered by parent and teacher	Age range: (10-11) years Male: 100%	0
			Control, (N=12)	Pill Placebo		
Miller, 1972 [58, 59]	United States RCT Efficacy Outpatient	SP	Child CBT, (N=NR)	Reciprocal inhibition: Individual-based relaxation exposure Delivered by doctoral psychologist 60 min session 3 times per week for 8 weeks	Age mean (years): 10.8 (range: 6-14) Male: 55% Caucasian: 95.5%, African American: 4.5% Socioeconomic status: Lower: 7% Middle:75% High: 8%	104
			Other therapy, (N=NR)	Individual, play psychotherapy directed toward inner experiences 60 min session 3 times per week for 8 weeks		
			Control, (N=NR)	Waitlisting or no treatment 60 min session 3 times per week for 8 weeks		

ADHD: attention deficit hyperactivity disorder, CBT: cognitive behavioral therapy, CGI: clinical global impression scale, GAD: generalized anxiety disorder, NR: not reported, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia

Table E.18. Characteristics of studies comparing different non-CBT psychotherapies

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Muris, 1998 [153]	Netherland RCT Outpatient	SP	Other therapy, (N=9)	EMDR Delivered by psychotherapist 1,150min session	Age mean (years): 12.58 (range: 8-17) Caucasian: 100% Medium income: 100%	0
			Child CBT, (N=9)	Generic CBT Exposure Individual- delivered by behavioral scientist 1,150min session		
			Distance therapy, (N=8)	Generic CBT Exposure Individual-based exposure cognitive strategies Delivered by behavioral scientist 1,150min session		
Muris, 2002 [154]	Netherlands RCT Efficacy Mental health clinic	GAD,SAD SoP	Non-CBT (EMDR), (N=11)	Generic CBT Cognitive problem solving Group-based Delivered by student/trainee Weekly for 6 weeks, 50 min	Age mean (years): 9.3 (range: 8-12) Males: 37.5% Caucasian: 83% Asian: 17% Low income (Dutch Bureau of Statistics): 20.8% Medium income (Dutch Bureau of Statistics): 62.5% High income (Dutch Bureau of Statistics): 16.7%	0
			Other therapy, N=13)	Emotional disclosure Group based Weekly for 6 weeks, 50 min		
Parr, 2009[155]	United Kingdom RCT Efficacy Mental health clinic	SAD, SoP	Other therapy, (N=18)	Other therapy Video feedback, Individual based Delivered by psychology student One session	Age mean (years): 15.7 (range 13-17) male: 55.5%	NR

			Other therapy, (N=18)	Other therapy no video feedback Individual-based Delivered by psychology student. one session	Age mean (years): 14.3 (range 13-17) Male: 72%	

CBT: cognitive behavioral therapy, CGI: clinical global impression scale, EMDR: eye movement desensitization and reprocessing, GAD: generalized anxiety disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety.

Table E.19. Characteristics of studies comparing CBT versus other psychotherapy

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Abbasi, 2016[27]	Iran RCT Efficacy Outpatient	SAD	Child CBT, (N=15)	Modular CBT Individual-based Exposure cognitive problem solving, 4-20 1 hour sessions.	Age range : 6-7 years Male: 53%	13
			Other therapy, (N=15)	Other: Child parent relationship training. One session a week for 10 weeks	Age range : 6-7 years Male: 33.3%	
			Control, (N=16)	Waitlisting or no treatment	Age range : 6-7 years Male: 48%	
Chavira, 2014 [156]	United States RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Child CBT, (N=24)	Cool Kids Exposure Cognitive problem solving Individual based Delivered by primary care physicians 10 sessions over 12 weeks, 60-90mins each	Age mean (years): 9.75 (range: 8-13) Males: 42% Caucasian: 83.3% Hispanic: 8.3% Other: 12.5% Less than high school or high school graduate (parent): 16.7% Some college (parent): 16.7% College graduate (parent): 33% OCD: 16.7% Depression: 12.5% Disruptive Behavior Disorders: 12.5% Autism: 4.2%	12
			Distance Therapy, (N=24)	Cool Kids Exposure Cognitive problem solving 10 sessions over 12 weeks, 60-90mins each	Age mean (years): 9.5 (range: 8-13) Males: 46% Caucasian: 62.5% Hispanic: 12.5% Other: 20.8% Less than high school or high school graduate (parent): 12.5% Some college (parent): 25.0%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					College graduate (parent): 45.8% OCD: 8.3% Depression: 4.2% Disruptive Behavior Disorders: 25% Autism: 4.2%	
Cobham, 2012 [36]	Australia RCT Efficacy Mental health clinic	GAD, PD, PD with agoraphobia, SAD, SoP, SP	Child CBT plus separate parent intervention, (N=23)	Do as I do Individual-based Exposure Cognitive problem solving 6 90-minutes sessions for parent and 6 60-minutes for child, weekly Delivered by Masters level clinicians	Age mean (years): 9.70 (range: 7-14) Males: 50% Caucasian 92% Asian: 8% PTSD: 4% ADHD: 7% Dysthymia: 4% Enuresis: 4%	26
			Distance Therapy, (N=20)	Do as I do "Do as I Do" and "Facing your Fears" bibliotherapy programs Exposure Cognitive problem solving 2 hour parent group, every other week 12 min phone calls for 12 weeks Delivered by parent and therapist	Age mean (years): 10.20 (range: 7-14) Males: 55% Caucasian 92% Asian: 8% ADHD: 5% PTSD: 5% Dysthymia: 5% Sleep terrors: 5%	
			Control, (N=12)	Waitlisting or no treatment	Age mean (years): 9.83 (range: 7-14) Males: 57% Caucasian 92% Asian: 8% PTSD: 4%	
Dewis, 2001[37]	Australia RCT Efficacy Mental health	SP	Child CBT, (N=9)	Generic CBT Live graded exposure Child CBT- (parents included < 20%) Individual based	Male: 35.7% Caucasian: 100% Age mean (years): 12.3 (Range 10-17)	4

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	clinic			Exposure Three 45-min treatment sessions every 3–4 days Provided by clinical psychologists		
			Distance Therapy, (N=10)	Other: Computer-aided vicarious exposure Individual computer based Exposure Three 45-min treatment sessions every 3–4 days	Male: 35.7% Caucasian: 100% Age mean (years): 13.8 (Range 10-17)	
			Control, (N=9)	Waitlisting or no treatment	Male: 35.7% Caucasian: 100% Age mean (years): 13.3 (Range 10 – 17)	
Hancock, 2016 [44]	Australia RCT Effectiveness Mental health clinic	GAD, SAD	ACT, (N=68)	Acceptance and commitment therapy (ACT) Group based Relaxation 10 sessions, 90-minute weekly sessions Delivered by doctoral level psychologist	Age mean (years): 11.15 (range: 7-17) Male: 45.5% Caucasian: 87%, Asian: 3%, Other: 10% ADHD: 6%, Depression, 18%, OCD: 7.3% Treatment naïve: 27.9%	13
			Child and parent together CBT, (N=63)	Cool Kids Group based Exposure Cognitive problem solving 10 sessions, 90-minute weekly sessions Delivered by doctoral level psychologist	Age mean (years): 10.81 (range: 7-17) Male: 39.6% Caucasian: 94.4%, Other: 5.6% ADHD: 10%, Depression, 13%, OCD: 3% Treatment naïve: 22.2%	
			Control, (N=62)	Waitlisting or no treatment	Age mean (years): 11.66 (range: 7-17) Male: 41.9% Caucasian: 84%, Other: 16% Depression: 24%, OCD: 8%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					Treatment naïve: 70.9	
Karbasi, 2010[157]	Iran RCT Efficacy Mental health clinic	Anxiety disorder	Child CBT plus parent involvement, (N=22)	Being Brave Exposure, relaxation, Cognitive Problem Solving Group-based 8, 75min weekly sessions	Age mean (years): 14.2 (range: 12-17)	3
			Distance therapy, (N=22)	Being Brave Exposure Relaxation Cognitive problem solving Individual Based 4, 75min weekly sessions, 4 sessions via CD	Age mean (years): 15.1 (range: 12-17)	
Khanna, 2010[102]	United States RCT Efficacy Mental health clinic	GAD, PD, SAD, SoP, SP	Child CBT, (N=17)	Coping Cat Exposure Relaxation Cognitive problem solving Individual-based Delivered by psychologist, student/ trainee Weekly for 12 weeks, 50 minute sessions	Age mean (years): 10.1 (range: 7-13) Males: 67% Caucasian: 83% African American: 14% Hispanic: 2% ADHD: 16% ODD:4% Tic disorder: 2%	13
			Distance, (N=16)	Camp cope a lot Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist, student/ trainee Weekly for 12 weeks,		
			Control, (N=16)	Attention control or treatment as usual Individual-based Technology-based Delivered by psychologist, student/		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				trainee Weekly for 12 weeks, 60 minute sessions. 30 minutes of support and 30 minutes of computer.		
Leong,2009[158]	Australia Efficacy RCT	GAD, SAD, SoP,SP	Child CBT plus parent Intervention, (N=15)	Do as I Do Exposure Cognitive problem solving Individual based Weekly for 12 weeks	Total population: 27 Age mean (years): 9.26 (range: 7-14) Males: 63% Caucasian: 100% Less than high school or high school graduate (parent); 40.7% College graduate (parent): 59.3% OCD: 4% Agoraphobia: 4%	20
			Distance therapy, (N=15)	Do as I Do Exposure Cognitive problem solving Delivered by parents Weekly for 12 weeks		
Mendlowitz, 1999 [56]	Canada RCT Efficacy Outpatient		Child CBT, (N=23)	Coping Bear Child CBT- (parents included < 20%) Group based Relaxation Cognitive problem solving 12 1.5-hour weekly sessions Delivered by 3 psychologists, 1 student/trainee, 1 youth worker	Age mean (years): 9.5 (Range 7-12) Male: 28.4%	NR
			Parent only intervention, (N=21)	Generic CBT Group based 12 1.5-hour weekly sessions Delivered by doctoral level psychologist, and student/trainee		
			Child CBT plus separate parent intervention, (N=18)	Coping Bear Group based Relaxation Cognitive problem solving 12 1.5-hour weekly sessions (one for kids, one for parents) Delivered by doctoral level		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				psychologist, student/trainee, youth worker		
			Control, (N=40)	Waitlisting or no treatment		
Miller, 1972[58, 59]	United States RCT Efficacy Outpatient	SP	Child CBT, (N=NR)	Reciprocal inhibition Individual-based Relaxation Exposure Delivered by doctoral psychologist 60 min session 3 times per week for 8 weeks	Age mean (years): 10.8 (range: 6-14) Male: 55% Caucasian: 95.5% African American: 4.5% Socioeconomic status: Low income: 7% Middle income:75% High income: 8%	104
			Other therapy, (N=NR)	Individual, play psychotherapy directed toward inner experiences 60 min session 3 times per week for 8 weeks		
			Control, (N=NR)	Waitlist: 60 min session 3 times per week for 8 weeks		
Monga, 2015[159]	Canada RCT Efficacy Outpatient	NR	Parent Only intervention, (N=32)	Taming sneaky fears Exposure Relaxation Cognitive problem solving Group based Delivered by psychologist, Masters level clinician, psychiatrist 60 min parents, 60 min child (attention placebo) Weekly for 11 weeks	Age mean (years): 7 (range: 5-7) Male: 40.6% Caucasian: 90.6%	52
			Child CBT + parent intervention, (N=45)	Taming sneaky fears Exposure Relaxation Cognitive problem solving Group Based Delivered by psychologist, Masters level clinician, psychiatrist 60min parents, 60min child(CBT)	Age mean (years): 6.6 (range: 5-7) Male: 35.6% Caucasian: 88.9%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				Weekly, 11 weeks		
Muris, 1998 [153]	Netherland RCT Efficacy Mental health clinic	SP	Other therapy, (N=9)	EMDR Delivered by psychotherapist 1,150min session	Age mean (years): 12.58 (range: 8-17) Caucasian: 100% Medium income: 100%	0
			Child CBT, (N=9)	Generic CBT Exposure Individual Delivered by behavioral scientist 1,150min session		
			Distance Therapy, (N=8)	Generic CBT Exposure Individual-based exposure cognitive strategies Delivered by behavioral scientist 1,150min session		
Rapee, 2006[69]	Australia RCT Efficacy Mental health clinic	GAD, PD (agoraphobia is not specified), SAD, SP, SoP.	Child and parent together CBT, (N=90)	Cool Kids Group based Exposure Cognitive problem solving 9 2-hour sessions over 12 weeks Delivered by student trainee.	Age mean (years): 9.475 (Range: 6 -12) Male: 66.6% Low income: n= 26 (<$30,000)	36
			Distance Therapy, (N=90)	Other: Bibliotherapy Individual based Exposure Relaxation Cognitive problem solving Treatment duration is 12 weeks at own pace	Age mean (years): 9.558 (Range: 6 – 12) Male: 64.44% Low income: n= 9 (<$30,000)	
			Control, (N=87)	Waitlisting or no treatment	Age mean (years): 9.5 (Range: 6 – 12) Male: 48.2% Low income: n= 15(<$30,000)	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Spence, 2006[81]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SP SoP	Child CBT plus separate parent intervention, (N=22)	Generic CBT Group based Exposure Relaxation Cognitive problem solving 10 60-minute weekly child sessions and 6 60-minute weekly parent sessions, plus booster sessions at 1 and 3 months Delivered by 5 doctoral level psychologists.	Age mean (years): 10.26 (Range 7-14) Male: 59%	12
			Distance Therapy, (N=27)	Generic CBT Internet CBT Group based Exposure Relaxation Cognitive problem solving 5 of the 10 child sessions plus the 3-month booster via Internet, with the remaining sessions being conducted in the clinic; 3 of the 6 parents sessions and the 3-month via Internet Delivered through the internet	Age mean (years): 9.8 (Range 7-14) Male: 59.2%	
			Control, (N=23)	Waitlisting or no treatment	Age mean (years): 9.8 (Range 7-14) Male: 56.5%	
Spence, 2011[82]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP, SP	Distance Therapy, (N=44)	Brave online Technology-based Individual based Exposure Relaxation Cognitive problem solving 10 adolescents weekly sessions and 5 parent sessions (60 minutes each)	Age mean (years): 13.98 (range: 12-18) Males: 41% High income(>$76,910): 47% College graduate (parent): 58% Depression: 2.6% ODD: 1.7% Dysthymic disorder: 9.7%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				over 12 weeks; 1 15-minute phone call, email feedback after each session Delivered by psychologist, Masters level clinician		
			Child CBT plus separate parent intervention, (N=44)	Individual based Exposure Relaxation Cognitive problem solving 10 adolescents weekly sessions and 5 parent sessions (60 minutes each) over 12 weeks Delivered by psychologist, Masters level clinician		
			Control, (N=27)	Waitlisting or no treatment		
Waters, 2009[86]	Australia RCT Efficacy Outpatient	GAD, SAD, SoP, SP	Child CBT plus separate parent intervention, (N=38)	Take action Group based Exposure Relaxation Cognitive problem solving 10 weekly 1-hour child and one hour parents sessions Delivered by psychologist	Age mean (years): 6.89 (range: 4-8) Males: 37% Caucasian: 97%	52
			Parent only intervention, (N=31)	Take action Group based Exposure Relaxation Cognitive problem solving 10 weekly 1-hour child and one hour parents sessions Delivered by psychologist	Age mean (years): 6.68 (range: 4-8) Males: 58% Caucasian: 97%	
			Control, (N=11)	Waitlisting or no treatment	Age mean (years): 6.79 (range 4-8)	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					Males: 55% Caucasian: 91%	
Waters, 2013[160]	Australia RCT Outpatient	GAD, SAD, SoP, SP	AMB, (N=18)	Attention bias modification training Individual based 4 sessions a week for 3 weeks	Age mean (years): 9.3 (range: 7-13) Males: 28% Caucasian: 100%	0
			CBT, (N=16)	4 sessions a week for 3 weeks	Age mean (years): 9.9 (range: 7-13) Males: 44% Caucasian: 100%	

ACT: acceptance and commitment therapy, ADHD: attention deficit hyperactivity disorder, BRAVE: body signs, relaxation, active helpful thoughts, victory over your fears, enjoy! reward yourself, CBT: cognitive behavioral therapy, CD: compact disc, CGI: clinical global impression, GAD: generalized anxiety disorder, NR: not reported, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, PD: panic disorder, PTSD: posttraumatic stress disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SoP: social anxiety, SP: specific phobia

Table E.20. Characteristics of studies comparing different CBTs

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Afshari, 2014 [29]	Iran RCT Efficacy Outpatient Mental health clinic	SAD	Child CBT, (N=12)	Coping Cat Exposure, Relaxation, Cognitive Problem Solving Group based Delivered by student/trainee 10, 60 min weekly sessions	Age mean (years): 10.4 (range: 9-13)	12
			Child CBT, (N=12)	Other CBT Cognitive problem solving Group based Delivered by student/trainee 12, 1hr weekly sessions	Age mean (years): 11 (range: 9-13)	
			Control, (N=10)	Waitlisting or no treatment	Age mean (years): 10.3 (range: 9-13)	
Amoros -Boix, 2011 [161]	Spain RCT Efficacy School	GAD,PD with agoraphobia, PD , SP	Child CBT, (N=25)	IAFS Exposure Cognitive problem zolving Group based 12, 90 min weekly sessions	Age mean (years): 14.88 Male: 16% depression: 8%, PTSD: 4%, Dysthymia: 4%	26
			Child CBT, (N=25)	IAFS Exposure Cognitive problem zolving Group based 12, 90 min weekly sessions	Age mean (years): 14.80 Male: 16% OCD: 4%	
Barrett, 1996 [32]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SoP	Child CBT, (N=28)	Coping Koala Individual based Exposure Relaxation Cognitive problem solving Delivered by doctoral level psychologists 12, 60 – 80 min weekly sessions	Age range: 7 – 14 years	52
			Child and Parent	Coping Koala Individual based		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			together CBT, (N=25)	Exposure Relaxation Cognitive problem solving Delivered by doctoral level psychologists 12, 30 min CBT, 40mins for family intervention weekly sessions		
			Control (N=26)	Waitlisting or no treatment		
Barrett, 1998 [33]	Australia RCT Efficacy Mental health clinic	GAD, SAD, SP, SoP.	Child CBT, (N=23)	Coping koala Group therapy, Exposure Relaxation Cognitive problem solving Delivered by 4 clinical psychologists. 1 session per week over 12 weeks.	Age range: 7 – 14 years Male: 53.3%	52
			Child and parent together CBT, (N=17)	Group-CBT and family management training. Group based Exposure Relaxation Cognitive problem solving Delivered by therapists 1 session per week.		
			Control, (N=20)	Waitlisting or no treatment		
Bodden, 2008 [162, 163]	Netherlands RCT Efficacy Mental health clinic	PD (agoraphobia is not specified), SAD, SP, SoP, GAD	Child CBT, (N=64)	Generic CBT Individual based, Exposure Cognitive problem solving Delivered by psychotherapists. 60 - 90 min session per week for 13 weeks	Age mean (years): 12.4 (range: 8-17) Males: 40.6% Caucasian: 100% ADHD: 8% Depression: 24% OCD: 5%	13

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Child CBT, (N=64)	Family CBT 60 - 90 min session per week. 13 session total; 3 sessions are with the child alone, 2 with child and parents, 5 with parents alone, and 3 involve the whole family, including siblings Delivered by therapists	ODD: 1% Conduct problems: 1% PTSD: 6%	
Chase, 2012[164]	United States Non-Randomized comparative studies Efficacy	PD with agoraphobia	Child CBT, (N=26)	Panic control treatment Exposure Relaxation, Cognitive problem solving Individual-based Delivered by doctoral psychologist 11, 50min sessions over 12 weeks	Age mean (years): 15.26 (range: 11-18) Male: 31.3% Caucasian: 98%, Hispanic: 2%	26
			Child CBT, (N=25)	Panic control treatment Exposure cognitive problem solving Group-based Delivered by doctoral psychologist 6 consecutive extended-length sessions over 8 days:3 sessions were (90min-120min long)2 were (360min-420min)		
Cobham, 1998 [165]	Australia RCT Effectiveness Mental health clinic	GAD, SAD, SP, SoP	Child CBT, (N=NR)	Coping Koala Exposure Relaxation Cognitive problem solving Group based Delivered by clinician 10, 90 min weekly sessions.	Age range: 7 – 14 years Male: n = 34	52
			Child CBT plus separate parent intervention, (N=NR)	Coping Koala Exposure Relaxation Cognitive problem solving Group based.		
Creswell,	United Kingdom	GAD,PD with	Child CBT	Cool Kids	Age mean (years): 9.94 (range:	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
2015[166]	RCT Efficacy Mental health clinic	agoraphobia, PD without agoraphobia, SAD, SoP, SP	plus separate parent intervention, (N=71)	Exposure Cognitive problem solving Individual-based Delivered by doctoral psychotherapist Mother: 60 min weekly sessions for 8 weeks Child CBT: 60 min weekly sessions for 8 weeks family health: 2 sessions for mother and 2 child and mother together - delivered over duration of 8 weeks	7-13) Male: 47.9% Caucasian: 96%, African: 2% , other :2%	
			Child CBT plus separate parent intervention, (N=69)	Cool Kids Exposure Cognitive problem solving Individual-based Delivered by doctoral psychotherapist Mother: CBT 8 sessions 60 min weekly sessions Child CBT 8, 60 min weekly sessions family health: 2 sessions for mother and 2 child and mother together delivered over duration of 16 weeks	Age mean (years): 9.89 (range: 6-12) Male: 50.7% Caucasian: 91%, Asian: 4.5% , other :4.5%	
			CBT, (N=71)	Cool Kids Exposure Cognitive problem solving Individual-based Delivered by doctoral psychotherapist Mother: Non - specific Intervention 2, 60 Min sessions, Child CBT: 8 s, 60 Min weekly sessions mother-child interaction - 10 sessions over 8	Age mean (years): 9.74 (range: 7-13) Male: 45.1% Caucasian: 91%, African: 1% , Asian : 3%, other : 5%	
De Groot, 2007[167]	Australia RCT	GAD, PD (agoraphobia is	Child CBT plus separate	Do as I Do Exposure	Age mean (years): 8.79 (Range 7 – 12)	36

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	Efficacy Mental health clinic	not specified), SP, SAD, SoP.	parent intervention, (N=14)	Relaxation Cognitive problem solving Individual-based Delivered by doctoral level psychologist 60-90 min weekly sessions for 6 weeks (parents and children)	Male: 64.2% Mean GCI: 6.93 (1.0)	
			Child CBT plus separate parent intervention, (N=15)	Exposure Relaxation Cognitive problem solving Delivered by doctoral level psychologist 60-90 minute weekly sessions for 6 weeks (parents and children)	Age mean (years): 8.93 (Range 7 -12) Male: 66.6% Mean GCI: 6.93 (0.8)	
Esbjorn, 2014[168]	Denmark RCT Effectiveness Mental health clinic	GAD, SAD, SoP, SP	Child CBT, (N=NR)	Individual based Delivered by therapists Weekly for 14 weeks	Total population: N= 54 Age mean (years): 9.59 (range: 7-12) Males: 52% Caucasian: 100% College graduate (parent): 35%	26
			Child CBT plus separate parent intervention, (N=NR)	Individual based Delivered by therapists Weekly for 14 weeks		
Flannery-Schroeder, 2000[39, 40]	United States RCT Efficacy Outpatient	GAD,SAD, SoP, SP	Child CBT, (N=18)	Coping Cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 18 sessions, 50-60 minute weekly sessions Delivered by Masters students	Male: 33.3% Caucasian: 94.4%, Other: 5.6% ADHD: 11%, Depression: 5.6%	13

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Child CBT, (N=13)	Coping Cat Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 18 sessions, 90 minute weekly sessions Delivered by Masters students	Male: 61.5% Caucasian: 84.6%, Other: 15.4% ADHD: 30.7%, Depression: 15.3%, ODD: 23%	
			Control, (N=14)	Waitlisting or no treatment	Male: 42.8% Caucasian: 92.8%, Other: 7.2% ADHD: 21.4%	
Garcia-Lopez, 2014[169]	Spain RCT Efficacy School	GAD, SAD, SoP, SP	Child CBT, (N=33)	IAFS Exposure Cognitive Problem Solving Group based Delivered by student/trainee 12, 90mins weekly sessions	Age mean (years): 15.42 (range: 13-18) Males: 34.6%	52
			Child CBT plus separate parent intervention, (N=27)	IAFS Exposure Cognitive Problem Solving Group based Delivered by psychologist, student/trainee 17 90min weekly sessions, and 5 120min parent sessions		
Gil-Bernal, 2009[43]	Mexico RCT Efficacy Public schools in low income district	SoP	Child CBT, (N=6)	IAFS Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving Nine 90-minutes sessions during 5 weeks Delivered by therapists	Age range: 7 – 12 years Male: 36.4%	36
			Child CBT	IAFS		

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			plus separate parent intervention, (N=5)	Combined therapy: IAFS + parent education Group based Exposure Relaxation Cognitive problem solving Nine 90-minutes sessions during 5 weeks Delivered by therapists		
			Control, (N=6)	Waitlisting or no treatment		
Herbert, 2009[97]	United States RCT Efficacy Mental health clinic	GAD , PD (agoraphobia is not specified), SAD, SP, SoP	Child CBT, (N=23)	Generic CBT Exposure Relaxation Cognitive Problem Solving Group based Delivered by Masters level clinicians 12, 120 min weekly sessions	Age mean (years): 14.6 (range 12 -17) Male : 56.5% Caucasian: 52%, African Americans: 39%, Asian: 8.6%	52
			Child CBT, (N=24)	Generic CBT Exposure Relaxation Cognitive Problem Solving Individual based Delivered by Masters level clinicians. 12, 60 min weekly sessions	Age mean (years): 14.3 (range 12 -17) Male: 25% Caucasian: 54.2%, African Americans: 45.8%	
			Control, (N=26)	Attention control or treatment as usual 12, 60 min weekly sessions	Age mean (years): 15.1 (range 12-17) Male: 53.8% Caucasian: 34.6%, African American: 50%, Hispanics: 7.69% Asians: 7.69%	
Hudson, 2014[170]	Australia RCT Efficacy Mental health	GAD, PD, SAD, SoP, SP anxiety	Child CBT, (N=94)	Cool Kids Exposure Cognitive problem solving Group-based	Age mean (years): 9.5	26

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	clinic			Delivered by psychologist, student/trainee 10, 2hr weekly sessions		
			Child CBT plus separate parent intervention, (N=95)	Exposure Cognitive problem solving Group-based Delivered by psychologist, student/trainee 10, 2hr weekly sessions, 5, 45 min parent sessions		
Ingul, 2014[99]	Norway RCT Efficacy Mental health clinic	SoP	Child CBT, (N=36)	Other CBT Exposure Cognitive problem solving Individual-based Delivered by psychologist and Masters level clinician 12, 50 min weekly sessions	Age mean (years): 14.98 (SD:0.94) Male: 43% ADHD: 14.29% Depression: 9.52% PTSD: 4.76%	52
			Child CBT, (N=58)	Cat Project Exposure Cognitive problem solving Group based 10, 90 min sessions	Age mean: 14.30(SD:0.89) Males: 40% ADHD: 5% Depression: 10%	
			Control, (N=34)	Attention control or treatment as usual 10, 90 min sessions	Age mean (years): 14.16 (SD:1.08) Male: 43% ADHD: 6.25% Depression: 6.25% OCD: 6.25% PTSD: 6.25%%	
Ishikawa, 2012[171]	Japan Non randomized comparative	GAD, SAD, SoP, SP	Child CBT, (N=NR)	Other CBT Exposure Cognitive problem solving Group-based	Total population= 33 Age mean (years): 11.24 (range:7-15) Male: 39%	12

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
	study Efficacy Outpatient			Delivered by psychologist, student/trainee 8, 90min weekly sessions	Depression: 18% Mutism: 3%	
			Child CBT, (N=NR)	Other Therapy Exposure Cognitive problem solving Individual-based Delivered by psychologist 8, 90min weekly sessions		
Kendall, 2008[100, 101]	United States RCT efficacy Mental health clinic	GAD, SAD, SoP	Child CBT, (N=25)	Coping Cat Exposure Relaxation Cognitive problem solving Individual based Delivered by doctoral level psychologists and Masters level clinicians 16, 60 min weekly sessions	Age mean (years): 10.1 (Range 7.8-13.8) Male: 62%	NR
			Child and parent together CBT, (N=25)	CC derivative Exposure Relaxation Cognitive problem solving Individual based Delivered by doctoral level psychologists and Masters level clinicians. 16, 60 min weekly sessions		
Liber, 2008[172, 173]	Netherlands RCT Efficacy Mental health clinic	GAD, SAD, SP, SoP.	Child CBT+ Parent Intervention, (N=65)	FRIENDS Dutch Exposure Relaxation Cognitive problem solving Individual based Delivered by a doctoral level psychiatrist and student/trainee 10, 90 min weekly sessions	Male: 53%	1

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			Child CBT + Parent Intervention, (N=62)	FRIENDS -Dutch Exposure Relaxation Cognitive problem solving Group based Delivered by a doctoral level psychiatrist and student/trainee 14, 90min weekly sessions	Male: 58%	
Manassis, 2002[174]	Canada RCT Efficacy Mental health clinic	GAD, PD (agoraphobia is not specified) SP, SAD, SoP	Child CBT + Parent Intervention, (N=37)	Coping bear Exposure Relaxation Cognitive problem solving Group based Delivered by primary care physician and student/trainee. 12, 90min weekly sessions	Age: 9.8 (Range 8 – 12) Caucasian : 84.6%	NR
			Child CBT + Parent Involvement, (N=41)	Coping bear Exposure Relaxation Cognitive problem solving Individual based Delivered by primary care physician and student/trainee 12, 90min weekly sessions		
Mendez, 2003 [55]	Spain RCT Efficacy Schools	SP	Child and Parent Together CBT (N=NR)	Emotive staging Exposure Individual based Delivered by psychologist Individual based 12, 30 min sessions over 3 weeks	Total number of patients: 64 Male: 50%	0
			Child and Parent Together CBT (N=NR)	Emotive staging Exposure Cognitive problem solving Individual based 12, 30 min sessions over 3 weeks		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=NR)	Waitlisting or no treatment		
Mendlowitz, 1999 [56]	Canada RCT Efficacy Outpatient	Anxiety disorder	Child CBT, (N=23)	Coping Bear Child CBT- (parents included < 20%) Group based Relaxation Cognitive problem solving 12 1.5-hour weekly sessions Delivered by 3 psychologists, 1 student/trainee, 1 youth worker	Age mean (years): 9.5 (Range 7-12) Male: 28.4%	NR
			Parent only intervention, (N=21)	Generic CBT Group based 12 1.5-hour weekly sessions Delivered by doctoral level psychologist, and student/trainee		
			Child CBT plus separate parent intervention, (N=18)	Coping Bear Group based Relaxation Cognitive problem solving 12 1.5-hour weekly sessions (one for kids, one for parents) Delivered by doctoral level psychologist, student/trainee, youth worker		
			Control, (N=40)	Waitlisting or no treatment		
Menzies, 1993[57]	Australia RCT Efficacy Outpatient	SP	Child CBT, (N=13)	In vivo exposure plus vicarious exposure Child CBT- (parents included < 20%) Individual based Delivered by student therapist 3 15-minute weekly session	Age mean (years): 5.5 (range:3-8) Male: 50.7% Caucasian: 96% Hispanic:4% Depression: 10% Treatment non responder: 100%	12

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=13)	Attention control or treatment as usual Only vicarious exposure 3 30-minute weekly session Delivered by student therapist		
			Child CBT, (N=13)	In vivo exposure Child CBT- (parents included < 20%) Individual based Exposure 3 30-minute weekly session Delivered by student		
			Control, (N=12)	Waitlisting or no treatment Assessment only		
Muris, 2001 [175]	Netherlands RCT Efficacy Outpatient	GAD,SAD, SoP	Child CBT, (N=19)	Coping koala Exposure Cognitive problem solving Group-based 12 30-40min twice weekly sessions	Age mean (years): 9.9 (range: 8-13) Male: 25% Caucasian: 97% Other: 3% ADHD: 3%	0
			Child CBT, (N=17)	Coping koala Exposure Cognitive problem solving Individual-based 12 30-40min twice weekly sessions		
Nauta, 2001[176]	Netherlands RCT Effectiveness Mental health clinic	GAD,SAD, SoP,	Child CBT, (N=9)	Coping Cat –Dutch Exposure Relaxation Cognitive problem solving Individual based Delivered by student/ trainee 12, 60min sessions	Age mean (years): 10.8 Male:77.7%	65
			Child CBT+ parent Intervention, (N=9)	Coping Cat - Dutch Exposure, Relaxation Cognitive problem solving Delivered by doctoral level psychologists 12, 60 min sessions and 7 parent	Age mean (years): 9.9 Male: 33.3%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				sessions.		
Nauta, 2003 [177]	Netherlands RCT Effectiveness Mental health clinic	GAD, PD without agoraphobia, SoP, SAD	Child CBT alone, N=37)	Coping Cat –Dutch Exposure Cognitive problem solving Individual based Delivered by doctoral level psychologist student/trainee 12, 60min sessions	Age mean (years): 11 Male: 51.3%	12
			Child CBT+ parent Intervention, (N=39)	Coping cat - Dutch Exposure, Cognitive problem solving Delivered by doctoral level psychologists and student/trainee 12, 60 min sessions and 7 parent sessions.		
Olivares, 2002[61]	Spain Non-Randomized comparative studies School	GAD, PD with agoraphobia, SoP,SP	Child CBT, (N=14)	SET-C Spanish Child CBT- (parents included < 20%) Exposure 29 treatment sessions over a period of 17 weeks, generally twice weekly	Age mean (years): 15.57 (range: 15-17) Male: 28.5% Depression: 35.7% OCD: 7% Substance abuse: 7% PTSD: 7% Avoidant personality disorder: 100% Selective mutism: 7%	52
			Child CBT, (N=15)	Group based Child CBT- (parents included < 20%) Exposure Cognitive problem solving 16 90-minute sessions over 14 weeks	Age mean (years): 16.07 (range: 15-17) Male: 35.7% Depression: 60% OCD: 6% Substance abuse: 6% PTSD: 6% Avoidant personality disorder: 94% Selective mutism: 12%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Child CBT, (N=15)	IAFS Child CBT- (parents included < 20%) Exposure Cognitive problem solving 12 90-minute weekly group sessions, and optional individual sessions	Age mean (years): 15.87 (range: 15-17) Male: 26.6% Depression: 40% OCD: 6% Substance abuse: 6% PTSD: 6% Avoidant personality disorder: 100% Selective mutism: 6%	
			Control, (N=15)	Waitlisting or no treatment	Age mean (years): 15.87 (range: 15-17) Male: 35.7% Depression: 46% OCD: 6% Substance abuse: 12% PTSD: 6% Avoidant personality disorder: 100% Selective mutism: 12%	
Olivares-Rodriguez, 2006[178]	Spain RCT Efficacy School	GAD, PD without agoraphobia, SoP.	Child CBT, (N=12)	IAFS Exposure Cognitive problem solving Group based 12, 90 min weekly sessions, and 6 individual sessions	Age mean (years): 15.33 Male: 33.33%	36
			Child CBT, (N=13)	IAFS Exposure Cognitive problem solving Group based Delivered by therapists. 12, 90 min weekly sessions	Age mean (years): 15.31 Male: 38.4%	
Olivares-Olivares,	Spain RCT Efficacy	GAD, PD with agoraphobia, PD (agoraphobia is	Child CBT, (N=18)	IAFS Exposure Cognitive problem solving	Age mean (years): 15.7 (range 14 -18) Male: 18.8%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
2008[179]	Mental health clinic	not specified), SP, SoP.		Group based Delivered by doctoral level psychologists 12, 90min weekly sessions		
			CBT, (N=20)	IAFS Exposure Cognitive problem solving, Group based,= Delivered by doctoral level psychologists 12,90min weekly sessions, 6 individual sessions	Age mean (years): 15.15 (Range 14 – 18) Male: 35%	
			Child CBT, (N= 19)	IAFS Exposure, Cognitive Problem Solving, Group based, Delivered by doctoral level psychologists 12,90min weekly sessions, 12 individual sessions	Age mean (years): 15.58 (Range 14 -18) Male: 36.8%	
Olivares, 2014[62]	Spain Efficacy Mental health clinic	SoP	Child CBT, (N=38)	IAFS Child CBT- (parents included < 20%) Group based Exposure Cognitive problem solving Delivered by experienced psychologist12 90-minute weekly sessions	Age mean (years): 15.58 (SD: 0.76) Males: 36.81%	52
			Child CBT, (N=37)	IAFS Child CBT- (parents included < 20%) Delivered by inexperienced psychologist Group based Exposure Cognitive problem solving 12 90-minute weekly sessions	Age mean (years): 15.30 (SD: 0.81) Males: 29.74%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Control, (N=35)	Waitlisting or no treatment	Age mean (years): 15.23 (SD: 1.26) Males: 37.1%	
Ollendick Thomas, 2015[180]	United States RCT Outpatient	SP	Child CBT, (N=46)	OST Exposure Individual based Delivered by Masters level clinicians. 1 180 min session	Age mean (years): 8.79 (range: 6-15) Male:52.1% Caucasian: 82.6% parental over-protection:15.2	26
			Child and Parent together CBT, (N=51)	OST Exposure Individual based Delivered by Masters level clinicians 1 180min session	Age mean (years): 8.93 (range: 6-15) Male: 45% Caucasian: 86.2% parental over-protection: 13.7%	
Ost, 2001[66]	Sweden RCT Efficacy Mental health clinic	GAD,SAD, SoP, SP	Child CBT, (N=21)	OST Exposure Individual-based Delivered by doctoral level Psychologist 1, 180 min session	Age mean (years): 11.7 (range: 7-17) Male: 33	52
			Child and Parent together CBT, (N=20)	OST Exposure Individual based Delivered by doctoral level Psychologist 1, 180min session	Age mean (years): 11.7 (range: 7-17) Male: 45%	
			Control, (N=19)	Waitlisting or no treatment	Age mean (years): 11.7 (range: 7-17) Male: 36%	
Ost, 2015[67]	Sweden RCT Efficacy Mental health clinic	GAD, PD, SAD, SP	Child CBT, (N=16)	SET-C Exposure Delivered by psychologist 12 weekly group sessions and 12 individual sessions	Age mean (years): 11.6 (range: 8-14) Depression: 15% OCD: 5% ODD: 2%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
			Child and Parent together CBT, (N=16)	SET-C Exposure Delivered by psychologist 24 children, 8 parent sessions over 12 weeks	Neurodevelopmental Disorder:9%	
			Control, (N=23)	Waitlist/no treatment		
Rosa-Alcazar , 2013[181]	Spain RCT Efficacy School	GAD, PD, PD with agoraphobia, SP	Child CBT, (N=25)	IAFS Exposure Relaxation Cognitive problem solving Group based 12, 90min weekly sessions	Age mean (years): 14.80 (range: 13-17) Males: 24% Depression: 4% PTSD: 4% Dysthymia: 4%	6
			Child CBT, (N=25)	IAFS Exposure Group based 12, 90min weekly sessions	Age mean (years): 14.40 (range: 13-17) Males: 28% Depression: 8% PTSD: 4% Dysthymia: 4%	
Sánchez-García, 2009 [75]	Spain RCT Efficacy schools	SAD	Child CBT, (N=28)	IAFS Exposure Cognitive problem solving Group based Delivered by practicing clinician 12, 90min weekly sessions	Age mean (years): 11.91 Male: 38% White: 82%	52
			Child CBT, (N=29)	IAFS Exposure Group based Delivered by Practicing clinician 12, 90min weekly sessions		
			Control, (N=25)	Waitlisting or no treatment		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Schneider, 2013[182]	Germany RCT Efficacy Mental health clinic	SAD	Child and Parent together CBT, (N=31)	Other therapy Exposure Cognitive problem solving Individual based Delivered by psychologist, Masters level clinicians 16, 50min weekly sessions	Age mean (years): 10.36 (range: 8-13) Males: 48%	52
			Child CBT, (N=33)	Coping cat Exposure Relaxation Cognitive problem aolving Individual based Delivered by psychologist, Masters level clinicians 16, 50min weekly sessions		
Siqueland, 2005[183]	United States RCT Efficacy Outpatient	GAD, PD (agoraphobia is not specified) SP, SoP.	Child and parent together CBT, (N=5)	Other Therapy Exposure Relaxation, Cognitive problem solving Individual based, Delivered by doctoral level psychologists, Masters level psychologists, and graduate students 16 weekly sessions.	Age mean (years): 14.9 (Range 12 - 17) Male: 72.7% Caucasians: 90% Africans:9%	9
			Child CBT, (N=6)	Coping Cat Exposure Relaxation Cognitive problem solving Individual based, Delivered by doctoral level psychologists, Masters level psychologists, and Masters level students		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				16 weekly sessions.		
Silverman, 2009[184]	United States RCT Efficacy Mental health clinic	GAD, PD agoraphobia, SAD, SP, SoP	Child and parent together CBT, (N=59)	Generic CBT Exposure Cognitive problem solving Individual based Delivered by doctoral level psychologists 12-14, 60 min weekly sessions	Age mean (years): 9.93 (range: 7 – 16)/ No SD Male: 40% White: 40%, Hispanic 73%, other: 6% Mean household income: $34,312 Low income <20,000 n = 33	52
			Child CBT, (N=60)	Generic CBT Exposure Cognitive problem solving Individual-based Delivered by doctoral level psychologists 12-14, 60 min weekly sessions		
Spence, 2000[80]	Australia RCT Effectiveness Mental health clinic	GAD, SAD, SP, SoP	Child CBT + parent Intervention, (N=17)	Generic CBT Exposure Relaxation Cognitive problem solving Group based Delivered by doctoral level psychologist. 12 weekly sessions	Age mean (years): 10.49 (range: 7-14) Males: 59% ODD: 12% ADHD: ^%	52
			Child CBT, (N=19)	Generic CBT Exposure Relaxation Cognitive problem solving Group based Delivered by doctoral level psychologist. 12 weekly sessions	Age mean (years): 11 (range: 7-14) Males: 53% ODD: 10% Dysthymia: 5%	
			Control, (N=14)	Waitlisting or no treatment	Age mean (years): 9.93 (range: 7-14)	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					Males: 79% Dysthymia: 7%	
St-Jacques, 2010[185]	Canada RCT Efficacy Mental health clinic	SP	Child CBT, (N=17)	Other Therapy Exposure Individual-based 60 min session once a week for 4 weeks	Age mean (years): 10.16 (range:8-15) Males: 16%	36
			Child CBT, (N=14)	Generic CBT Exposure Individual-based 60 min weekly sessions for 4 weeks		
Suveg, 2009[114]	United States RCT Outpatient	GAD, SAD, SoP, SP	Child CBT, (N=55)	Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist, Masters level clinician 16, 60 min weekly sessions	Age range: 7-14 years ADHD: 32% Depression: 11% ODD: 14% Conduct disorder: 1%	52
			Child and parent together CBT, (N=56)	Exposure Relaxation Cognitive problem solving Individual based Delivered by psychologist, Masters level clinician 16, 60 min weekly		
			Control, (N=50)	Attention control or treatment as usual Weekly for 16 weeks		

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Wergeland, 2014[88, 89]	Norway RCT Efficacy Outpatient	GAD, SAD, SoP	Child CBT, (N=91)	Friends Child CBT- (parents included < 20%) Individual based Exposure Relaxation Cognitive problem solving 10 weekly sessions, lasting 60 min (ICBT), plus 2 parent only sessions Delivered by psychologist, Masters level clinician	Age mean (years): 11.4 (range: 8-15) Males: 48% Caucasian: 76% Hispanic: 0.5% Asian: 3% ADHD: 5% Depression: 8% ODD: 9% Tic disorder: 7%	52
			Child CBT, (N=88)	Friends Child CBT- (parents included < 20%) Group based Exposure Relaxation Cognitive problem solving 10 weekly sessions, lasting 90 minutes, plus 2 parents sessions Delivered by psychologist, Masters level clinician	Age mean (years): 11.7 (range: 8-15) Males: 45% Caucasian: 76% Hispanic: 0.5% Asian: 3% ADHD: 6% Depression: 16% ODD: 2% Tic disorder: 7%	
			Control, (N=38)	Waitlisting or no treatment	Age mean (years): 11.4 (range: 8-15) Males: 50% Caucasian: 76% Hispanic: 0.5% Asian: 3% ADHD: 3% Depression: 11% ODD: 8% Tic disorder: 5%	
Whiteside, 2015[186]	United States RCT Effectiveness Mental health clinic	GAD, PD, SAD, SoP, SP	Child CBT, (N=7)	Anxiety management strategies Relaxation Cognitive problem solving Individual based Delivered by psychologist and	Age mean (years): 9.71 (range: 7-14) Male: 29% Depression: 14% College Graduate(parent): 100%	52

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				masters level clinicians 6, 50-60 min weekly sessions		
			Child and parent together CBT, (N=7)	Parent coached exposure therapy Exposure Delivered by psychologist and Masters level clinicians	Age mean (years): 10.71 (range: 7-14) Male: 29% Depression: 14% College Graduate(parent): 100%	
Wood, 2006[187]	RCT Efficacy Mental health clinic	GAD, SAD, SP, SoP.	Child CBT, (N=20)	Coping Cat Exposure Relaxation Cognitive problem solving Individual based Delivered by student trainee, doctoral level psychologist and clinical psychologist 12-16, 60-80 min sessions.	Age mean (years): 9.83 (Range 6 – 13) Male: 65% Caucasian: 65% African American: 5% Hispanic: 15% Other: 15%	NR
			Child and parent together CBT, (N=20)	Building confidence Exposure Relaxation Cognitive problem solving Individual based Delivered by student trainee, doctoral level psychologist and clinical psychologist. 12-16, 60-80 min sessions	Age mean (years): 9.83 (Range 6 – 13) Male: 55% Caucasian: 55% Hispanic:5% Asian: 5% Others: 30%	
Walczak, 2016[188]	Denmark RCT Efficacy Mental health xlinic	GAD SAD SoP SP	Child CBT plus separate parent intervention: (N=28)	Generic CBT Individual based Delivered by Masters level clinician 14 sessions: two family, 2 child, 6 parent	Age mean (years): 13.95 (Range: 11-17) Depression: 4% ODD: 4%	156
			Child CBT: (N=26)	Generic CBT Individual based Delivered by Masters level clinician 14 sessions, two family and 12 child	Age mean (years): 13.95 (Range: 11-17) Depression:4% OCD: 4%	

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
				only	ODD: 4% PTSD: 4%	
Warner, 2016[116]	United States RCT Efficacy Outpatient	GAD, PD, SAD, SP, SoP	Child CBT, (N=46)	SASS: Group-based exposure cognitive problem solving (Skills for academic and social success provided by psychologists) Delivered by doctoral level psychologist 12 in school group sessions (ranged from 50- 90 mints)	Age mean (years): 15.5 Male: 30.4% Caucasian: 74%, African American :4% , Hispanic: 4%, Asian: 12%, Other: 4% Mean income: 94.155	20
			Child CBT, (N=47)	SASS: Group-based Exposure Cognitive problem solving Delivered by doctoral level psychologist 12 in school group sessions (ranged from 50- 90 mints)	Age mean (years): 15.34 Male: 29.7% Caucasian: 75%, African American :8% , Hispanic: 5%, Asian: 6%, Other: 6%	
			Control, (N=43)	Attention control or treatment as usual Relaxation Cognitive problem solving A nonspecific counseling program, SFL, controlled for the attention and group involvement.	Age mean (years): 15.37 Male: 37% Caucasian: 67%, African American :2% , Hispanic: 14%, Asian: 7%, Other: 9%	

ADHD: attention deficit hyperactivity disorder, CBT: cognitive behavioral therapy, CC: coping cat, CGI: clinical global impression, FRIENDS: feeling worried?; relax and feel good; inner thoughts; explore plans; nice work so reward yourself; don't forget to practice; and stay calm, GAD: generalized anxiety disorder, ICBT: individualized cognitive behavioral therapy, IAFS: intervencion en adolescents con fobia social (Treatment for adolescents with social phobia), NR: not reported, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, OST: one session treatment, PD: panic disorder, PTSD: posttraumatic stress disorder, RCT: randomized controlled trial, SAD: separation anxiety disorder, SET-C: social effectiveness therapy, SoP: social anxiety, SP: specific phobia.

Table E.21. Characteristics of single-cohort observational studies with adverse events

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
Biederman, 1987[189]	United States Case series/case report Outpatient	GAD, PD with agoraphobia, PD without agoraphobia, SAD, SoP	Clonazepam, (N=3)	1 mg/day	Age mean (years): 10 (range: 8-11) Males: 66.6% Caucasian: 100%	21.5-156
Birmaher, 1994[190]	United States Case series Outpatient	SAD, SoP	SSRI: Fluoxetine, (N=21)	Mean dose of 25.7 mg/day for up to 43 weeks	Age Range: (11- 17) years Male: 55% CGI>=6: 91%	0
Chavira, 2002[191]	United States Case series/case report Outpatient	SoP, SP	SSRI: Citalopram, (N=12)	100-40 mg/day for 12 weeks	Age mean (years): 13.42 (range: 8-17) Males: 33.3% Caucasian: 6% African American: 8% Hispanic: 16.6% Others:25% Mean CGI-S=4.82	0
Chutko, 2011[192]	Kazakhstan Case series Outpatient	GAD	SNRI: Adaptol, (N=32)	1000 mg/day for 4 weeks	Age range: 7-14 years	0
Compton, 2001[193]	United States RCT Outpatient	SoP	SRI, SSRI: Sertraline, (N=14)	Maximum of 200 mg/day for 8 weeks	Age Range: (10-17) years Males: 57%	0
dAmato, 1962[194]	United States Case series/case report Outpatient	SP	Benzodiazepine: Chlordiazepoxide: (N=9)	10-30mg/day for 1-4 weeks	Age range: 8-11 years Males: 44%	0
Dummit, 1996[195]	United States Case series/case report Outpatient	GAD, SAD, SoP, SP	SSRI: Fluoxetine (N=21)	20-60 mg/day for 9 weeks	Age mean (years): 8.2 (range: 8-14) Males: 24% Caucasian: 90% Asian: 9.5% ODD: 5% Learning disabilities: 14%	0

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
					Enuresis: 5% Trichotillomania: 5%	
Fairbanks, 1997[196]	United States Case series/case report Outpatient	GAD, PD, PD with agoraphobia, SAD, SoP	SSRI: Fluoxetine (N=18)	Oral, 20- 40mg/day (children) or 20-80mg/day (adolescents) for 9 weeks.	Age mean (years): 11.9 (range: 9-17) Caucasian: 55% African American: 5% Hispanic: 5% Other: 5% Body Dysmorphic Disorder: 5%	0
Isolan, 2007[197]	Brazil Case series Mental health clinic	GAD, SAD, SP, SoP.	SSRI: Escitalopram (N= 20)	10-20 mg/day for 12 weeks.	Age mean (years): 15 (Range 10 - 17) Male: 30%	0
Karabekiroglu, 2011[198]	Turkey Case series Outpatient	GAD,SAD, SoP, SP	SSRI: Fluoxetine: (N=40)	12 weeks of treatment.	Age mean (years): 10.08 (range: 7-17) Male: 57% ADHD: 7.5%, OCD : 2.5%, selective mutism: 2.5%	0
Lepola, 1996[199]	Finland Case series Outpatient	PD with agoraphobia	SSRI: Citalopram, (N=3)	20mg/day for 34-64 weeks	Age range: 9-16 years Males: 66.6%	52
Mancini, 1999[200]	Canada Case series/ case report Outpatient	SoP	SSRI: Paroxetine, (N=5)	40 - 80 mg/day for 5-24 weeks	Age Range: 7-18 years Males: 20% OCD: 40% Dysthymia: 40%	0
			SNRI: Nefazodone, (N=1)	350 mg/day for 20 weeks	Age: 15 Males: 0%	
			SSRI: Sertraline, (N=1)	175 mg/day,	Age: 17 Males: 0% Depression: 100% Dysthymia: 100%	
Masi, 2001[201]	Italy Case series Outpatient	GAD, PD with agoraphobia, PD without	SSRI: paroxetine, (N=18)	Average 23.9 mg/day Daily for 2-24 weeks	Age mean (years): 12.3 (range: 7-16) Males: 66.6%	0

Author, Year	Study Country, Study Design, Type of Study (Efficacy/ Effectiveness), Study Settings	Type of Anxiety/Severity (CGI)	Intervention and Comparisons (N of Patients)	Characteristics of Interventions (Psychotherapy: Components, Delivery Model)/Pharm: Drug) Intensity, Duration (Weeks))	Patient Characteristics Mean Age (Range) , Male (%), Race/Ethnicity, Comorbidity, Household Income, Parent Education, Family Dysfunction/Stressor, Treatment Sequence, Insurance, History of Maltreatment)	Length of Follow up (Weeks)
		agoraphobia, SAD, SoP, SP			Depression: 22% OCD: 22% Tic Disorder: 11%	
Mrakotsky, 2008[202]	United States Open-label pilot Outpatient	SoP	Tetracyclic Antidepressant: Mirtazapine, (N=18)	15-45 mg/day for 8 weeks	Age mean (years): 12.06 (range: 8-17) Males: 50% ODD: 5% Depression: 10%	0
Renaud, 1999[203]	United States Case series Outpatient	GAD, PD, SAD, SoP, SP	SSRI, (N=12)	9 received Fluoxetine (34.4 mg/day) 2 received Paroxetine (20 mg/day) 1 received of Sertraline (125 mg/day)	Age mean (years): 12 (range: 7-17) Males: 42% Depression: 66.6% Substance abuse: 8% OCD: 8%	26
Simeon, 1987[204]	Canada Cross over study Outpatient	GAD	Benzodiazepine: Alprazolam, (N=12)	0.5 mg to 1.5 mg/day	Age mean (years):11.5 (Range: 8-14) Males: 90% Caucasian: 100%	4
Simeon, 1994[205]	Canada Case series Outpatient	GAD, SAD	Buspirone: (N=15)	NR	Age mean (years): 10 (range: (6-14) Males: 66.6% ADHD: 27% Avoidant disorder: 7%	0
Zwier, 1993[206]	United States Case series/case report Inpatient	SoP	Buspirone: (N=1)	20 mg/day for 52 weeks	Age: 16 Males: 100% Caucasian 100%	0

ADHD: attention deficit hyperactivity disorder, CGI: clinical global impression scale, GAD: generalized anxiety disorder, NR: not reported, OCD: obsessive compulsive disorder, ODD: oppositional defiant disorder, PD: panic disorder, SAD: separation anxiety disorder, SNRI: serotonin–norepinephrine reuptake inhibitor, SoP: social anxiety, SP: specific phobia, SRI: serotonin reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor.

Appendix F. Risk of Bias

Table F.1. Risk of bias for randomized controlled trials (Cochrane Risk of Bias tool)[207]

Author, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Overall Risk of Bias
Abbasi, 2016 [27]	Low	Unclear	High	High	Unclear	Unclear	High
Abikoff, 2005 [1]	Unclear	Unclear	Unclear	Unclear	High	Unclear	Unclear
Adler Nevo, 2014[28]	Low	Low	Unclear	Low	Low	Unclear	Moderate
Afshari, 2014 [29]	Low	Unclear	High	High	High	Low	High
Alfano, 2007 [2]	Unclear	Unclear	Low	Low	Unclear	Low	Unclear
Amoros -Boix, 2011[161]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Arendt, 2015 [30]	Low	Low	High	Low	Low	Low	High
Azadeh, 2015[144]	Unclear	Unclear	High	High	Unclear	High	High
Baer, 2005 [31]	Low	High	High	High	Low	Low	High
Barrett, 1996 [32]	Low	Unclear	High	Low	Low	Low	High
Barrett, 1998 [33]	Low	Unclear	High	High	Low	Low	High
Beidel, 2000 [92]	Unclear	Unclear	Unclear	Unclear	High	Low	Unclear
Beidel, 2007 [3]	Low	Unclear	High	High	High	Low	High
Bernstein, 2000 [118]	High	Unclear	Low	Low	Low	Low	High
Birmaher, 2003 [5]	Unclear	Unclear	Unclear	Unclear	High	Unclear	Unclear
Black, 1994 [4]	Unclear	Unclear	Low	Unclear	Low	Low	Unclear
Bodden, 2008 [162, 163]	Unclear	Low	Low	Unclear	Low	Low	Unclear
Britton, 2013 [140]	Unclear	Unclear	High	Low	High	Low	High
Cartwright-Hatton, 2011 [122]	Low	Unclear	High	High	Low	Unclear	High
Chalfant, 2007 [34]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Chavira, 2014 [156]	Low	Unclear	High	High	High	Low	High
Chiu, 2013 [35]	Low	Unclear	High	Low	Low	Low	High
Cobham, 1998 [165]	Unclear	High	High	High	Unclear	Low	High
Cobham, 2012 [36]	Low	Unclear	High	Unclear	Low	Low	High
Cornwall, 1996 [146]	Unclear	Unclear	High	High	Unclear	Unclear	High
Creswell, 2015[166]	Low	Low	High	High	High	Low	High
da Costa, 2013[6]	Low	Unclear	Low	Unclear	Low	High	Unclear
De Groot, 2007[167]	Low	Unclear	Low	Unclear	Low	Low	Unclear
Dewis, 2001[37]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Donovan, 2014[129]	Low	High	High	High	Low	Low	High
Donovan, 2015[38]	High	Unclear	High	High	High	Low	High

Author, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Overall Risk of Bias
Ebrahiminejad, 2016[143]	Unclear	Unclear	High	High	Low	Unclear	High
Eldar, 2012[138]	Low	Unclear	Low	Unclear	Low	Low	Unclear
Elkins, 2016[147]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Esbjorn, 2014[168]	Unclear	Unclear	High	High	Unclear	Low	High
Flannery-Schroeder, 2000[39, 40]	Low	Unclear	High	High	Low	Low	High
Fujii, 2013[93]	Low	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Gallagher, 2004[41]	Low	Unclear	High	High	Unclear	Low	High
Gallo, 2012[42]	Low	Unclear	High	High	Unclear	Low	High
Garcia-Lopez, 2014[169]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Geller, 2007[7]	Low	Low	Low	Low	High	Unclear	Unclear
Gil-Bernal, 2009[43]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Ginsburg, 2002[94]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Ginsburg, 2012[95]	Low	High	High	Low	Low	Low	High
Gittelman-Klein, 1973[8]	Unclear	Unclear	Low	Low	Low	Low	Unclear
Goldbeck, 2012[148]	High	Unclear	High	High	Low	Low	High
Gottken, 2014[145]	High	High	High	High	High	Low	High
Graae, 1994[9]	Unclear	Unclear	Low	Low	Low	Low	Unclear
Halldorsdottir, 2016[96]	Unclear	Unclear	High	High	High	Low	High
Hancock, 2016 [44]	Low	Unclear	High	High	High	Low	High
Hayward, 2000[45]	Low	Unclear	High	Low	Low	Low	High
Herbert, 2009[97]	Low	Unclear	High	High	High	Low	High
Hiller, 2016[128]	Low	Unclear	Low	High	High	Low	High
Hirshfeld-Becker, 2010[47]	Low	Unclear	High	High	Low	High	High
Holmes, 2014[46]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Hudson, 2009[98]	Low	Unclear	High	High	Low	Low	High
Hudson, 2014[170]	Low	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Infantino, 2016[130]	Low	Unclear	High	High	Low	Low	High
Ingul, 2014[99]	Low	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Joormann, 2002[149]	Unclear	Unclear	High	High	Low	Low	High
Karbasi, 2010[157]	Low	Unclear	High	High	Low	Low	High
Kendall, 1995[48]	Low	Unclear	High	High	Unclear	Low	High
Kendall, 1997 [49]	Unclear	Unclear	High	High	High	Low	High

Author, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Overall Risk of Bias
Kendall, 2008[100, 101]	Unclear	Unclear	High	High	High	Low	High
Khanna, 2010[102]	Low	High	High	High	Low	Low	High
Klein, 1992[120]	Unclear	Unclear	Low	Unclear	Low	Unclear	Unclear
Klein, 2015[150]	Unclear	Unclear	Low	Low	Unclear	Unclear	Unclear
Last, 1998[103]	Unclear	Unclear	High	High	High	Low	High
Lee, 2016[151]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Leong,2009[158]	Low	Unclear	High	High	Low	Low	High
Leutgeb, 2011[50]	Unclear	Unclear	High	High	Low	Low	High
Liber, 2008[172, 173]	Unclear	Unclear	High	High	Low	Low	High
Lyneham, 2006[131]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Manassis, 2002[174]	Unclear	Unclear	High	High	Low	Low	High
March, 2007[10]	Low	Low	Low	Unclear	High	Low	Unclear
March, 2009[132]	Low	Unclear	High	High	Low	Low	High
Masia-Warner, 2005[51]	Low	Unclear	High	High	Low	Low	High
Masia-Warner, 2007 [104]	Low	Unclear	High	Low	High	Low	High
McConachie, 2014[52]	Low	Low	High	Low	Low	Low	High
McNally Keehn, 2013[53]	Low	Unclear	High	High	Low	Low	High
Melfsen, 2011[54]	Low	Unclear	High	High	High	Low	High
Melvin, 2016[121]	Unclear	Unclear	High	High	Unclear	Unclear	High
Mendez, 2003[55]	Unclear	Unclear	High	Unclear	Unclear	Unclear	High
Mendlowitz, 1999 [56]	Unclear	Unclear	High	High	Low	Low	High
Menzies, 1993[57]	Low	Unclear	High	High	Low	Unclear	High
Miller, 1972[58, 59]	Low	Low	High	High	Low	Low	High
Monga, 2015[159]	Low	Low	High	Low	Low	Low	High
Muris, 1998 [153]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Muris, 2001 [175]	Unclear	Unclear	Unclear	Unclear	High	High	Unclear
Muris, 2002 [154]	Low	Unclear	High	High	Low	Low	High
Muris, 2002 [105]	Unclear	Unclear	High	High	Low	Low	High
Nauta, 2001[176]	Unclear	High	High	High	Low	Low	High
Nauta, 2003 [177]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
O'Brien, 2007[106]	Unclear	Unclear	Low	Unclear	High	Low	Unclear

Author, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Overall Risk of Bias
Obler, 1970[60]	Unclear	Unclear	High	High	Low	Low	High
Olivares, 2014[62]	High	Unclear	Unclear	Unclear	Unclear	Unclear	High
Olivares-Olivares, 2008[179]	Low	Unclear	High	Unclear	Low	Low	High
Olivares-Rodriguez, 2006[178]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Ollendick, 2009[63]	Low	Low	High	High	Low	Low	High
Ollendick Thomas, 2015[180]	Unclear	Unclear	High	High	High	Unclear	High
Ortbandt, 2009[64, 65]	Unclear	Unclear	High	High	Low	Low	High
Ost, 2001[66]	Low	Unclear	High	High	High	Unclear	High
Ost, 2015[67]	Low	Low	High	Low	Low	Low	High
Ozyurt, 2015[123]	Low	Low	High	Low	High	Low	High
Parr, 2009[155]	High	Unclear	High	High	Low	Low	High
Pergamin-Hight, 2016[141]	Low	Low	Low	Unclear	Low	Unclear	Low
Pincus, 2010[107]	High	Unclear	Unclear	Unclear	Low	Unclear	High
Pine, 2001 [11, 12]	Unclear	Unclear	Low	Low	High	Low	Unclear
Rapee, 2006[69]	Low	Unclear	High	High	High	Low	High
Reaven, 2009[70]	High	High	High	High	Low	Low	High
Reigada, 2015[108]	Low	High	High	High	Low	Low	High
Reinblatt, 2009[13]	Low	Unclear	Low	Low	Low	Unclear	Unclear
Ritter, 1968[71]	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Rodriguez, 2005[73]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Rosa-Alcazar, 2007[109]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Rosa-Alcazar, 2009[72]	High	Low	Unclear	Unclear	Unclear	High	High
Rosa-Alcazar Ana, 2013[181]	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Rynn, 2001[14]	Unclear	Unclear	Low	Low	Low	Low	Unclear
Rynn, 2007[15]	Unclear	Unclear	Low	Low	High	Low	Unclear
Sanchez-Garcia, 2009 [74]	Unclear	Unclear	Unclear	Unclear	High	Low	Unclear
Sánchez-García, 2009 [75]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Santacruz, 2006[124]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear

Author, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Overall Risk of Bias
Santucci, 2013[76]	Low	Unclear	High	High	Low	Low	High
Scharfstein, 2011[16]	Unclear	Low	Low	Low	Low	Low	Unclear
Schneider, 2011[77]	Low	Low	High	High	Low	Unclear	High
Schneider, 2013[182]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Shortt, 2001[78]	Unclear	Unclear	Low	Low	High	Low	Unclear
Silk, 2016 [111]	Low	Unclear	Unclear	Unclear	High	High	High
Silverman, 1999 [79]	Unclear	Unclear	High	Low	High	Low	Unclear
Silverman, 2009[184]	Low	Unclear	Unclear	Unclear	High	Low	Unclear
Siqueland, 2005[183]	High	High	Unclear	Unclear	Low	Low	High
Smith, 2014[125]	Low	Unclear	High	Unclear	Low	Low	High
Southam-Gerow, 2010[110]	Unclear	Unclear	Low	Unclear	High	Low	Unclear
Spence, 2000[80]	Low	Unclear	High	High	Low	Low	High
Spence, 2006[81]	Low	Unclear	High	High	Low	Low	High
Spence, 2011[82]	Unclear	Unclear	High	High	High	Low	High
Spence, 2017[133]	Low	Unclear	High	High	Unclear	Unclear	High
St-Jacques, 2010[185]	Low	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Storch, 2013[113]	Low	Low	High	Low	Low	Low	High
Storch, 2015[112]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Strawn, 2015[17]	Unclear	Unclear	Low	Low	High	Low	Unclear
Suveg, 2009[114]	Unclear	High	High	High	Unclear	Low	High
Thirlwall, 2013[126, 127]	Low	Low	Unclear	Unclear	High	Low	Unclear
Tillfors, 2011[134]	Unclear	Unclear	High	High	Low	Low	High
Treadwell, 1996[83]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Valles-Arandiga, 2014 [84]	High	Unclear	Unclear	Unclear	Low	Unclear	High
Van Steensel, 2014[115]	Low	Unclear	High	High	Low	Low	High
Vigerland, 2016[135, 136]	Unclear	Unclear	High	High	Low	Low	High
Wagner, 2004[18]	Low	Low	Low	Unclear	Low	Low	Unclear
Walczak, 2016[188]	Unclear	Unclear	High	High	Low	Unclear	High
Walkup, 2002[19]	Low	Unclear	High	High	High	Low	High
Walkup, 2008[20-26]	Low	Low	High	Low	Low	Low	Moderate

Author, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Overall Risk of Bias
Warner, 2011[87]	Low	Unclear	High	High	Low	Low	High
Warner, 2016[116]	Low	Unclear	Low	Low	Low	Low	Low
Waters, 2009[86]	Low	Unclear	High	High	High	Low	High
Waters, 2013[160]	Low	Unclear	Low	Low	High	Low	Unclear
Waters, 2014[142]	Low	Unclear	High	Low	Low	Low	High
Waters, 2015[139]	Unclear	Unclear	High	High	Low	Low	High
Wergeland, 2014[88, 89]	Low	Unclear	High	Unclear	Low	Low	High
White, 2013[90]	Low	Unclear	High	Unclear	Unclear	Low	High
Whiteside, 2015[186]	Low	Unclear	Unclear	Unclear	High	Low	Unclear
Wood, 2006[187]	Low	Low	High	High	Low	Low	High
Wood, 2009 [91]	Low	Low	Low	Unclear	Low	Unclear	Unclear
Wuthrich, 2012[137]	Low	Unclear	High	High	Low	Low	High
Yoosefi Looyeh, 2014[152]	Low	Unclear	High	High	Low	Low	High

Low: low risk of bias; Moderate: moderate risk of bias; High: high risk of bias; Unclear: unclear risk of bias

Table F.2. Risk of bias for non-randomized comparative studies (Newcastle-Ottawa Quality Assessment Scale)[208]

Author, Year	Representativeness of the Population	Selection of the Cohort	Ascertainment of Exposure	Ascertainment of Outcome	Adequacy of Follow Up	Possible Conflicts of Interest	Overall Risk of Bias
Chase, 2012[164]	Moderate	High	Low	High	Low	Unclear	High
Eichstedt, 2011[119]	Low	Low	Low	High	High	Low	High
Ishikawa, 2012[171]	Moderate	Unclear	Low	High	Low	Low	High
Olivares, 2002[61]	Moderate	Low	Low	High	Low	Unclear	High
Rapee, 2000[68]	Moderate	Low	Low	High	Low	Low	High
van Steensel, 2015[85]	High	High	Low	Low	Moderate	Unclear	Moderate
Yen, 2014[117]	Moderate	Low	Low	Low	Unclear	Unclear	Moderate

Low: low risk of bias; Moderate: moderate risk of bias; High: high risk of bias; Unclear: unclear risk of bias

Appendix G. Subgroup Analysis

Table G.1. Subgroup analysis – age

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Age	CBT vs. attention control or treatment as usual	Primary anxiety, child report	7-12 years	SMD: -1.05; 95% CI: -1.99 to -0.11; I^2= N/A[105]
			13-18 years	SMD: -1.04; 95% CI: -1.65 to -0.42; I^2= 60.7%[94, 104]
	CBT vs. waitlisting or no treatment	Primary anxiety, clinician report	7-12 years	SMD: -0.82; 95% CI: -1.34 to -0.30; I^2= 58.9%[38, 41]
			13-18 years	SMD: -1.19; 95% CI: -1.87 to -0.52; I^2= 0.0%[31, 61]
		Primary anxiety, child report	7-12 years	SMD: -0.37; 95% CI: -1.17 to 0.43; I^2= 0.0%[38, 41, 56]
			13-18 years	SMD: -1.22; 95% CI: -1.89 to -0.55; I^2= 0.0%[31, 61]
		Function	7-12 years	SMD: -0.48; 95% CI: -1.00 to 0.04; I^2= 88.7%[38, 41]
			13-18 years	SMD: -1.65; 95% CI: -2.50 to -0.80; I^2= N/A[61]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, SMD: standardized mean difference

Table G.2. Subgroup analysis – comorbidity

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Comorbidity	CBT vs. attention control or treatment as usual	Primary anxiety, child report	Comorbidity	SMD: -0.31; 95% CI: -0.84 to 0.23; I^2= N/A[103]
			No comorbidity	SMD: -0.53; 95% CI: -1.49 to 0.44; I^2= 74.7%[99, 102, 104, 116]
	CBT vs. Pill Placebo	Function	Comorbidity	SMD: 0.02; 95% CI: -0.59 to 0.63; I^2= N/A[121]
			No comorbidity	SMD: -0.60; 95% CI: -0.84 to -0.36; I^2= 90.5%[3, 20-26]
		Secondary measure	Comorbidity	SMD: 0.30; 95% CI: -0.32 to 0.91; I^2= N/A[121]
			No comorbidity	SMD: -1.02; 95% CI: -1.45 to -0.58; I^2= N/A[3]
	CBT vs. waitlisting or no treatment	Primary anxiety, clinician report	Comorbidity	SMD: -1.25; 95% CI: -1.79 to -0.70; I^2= 93.2%[90, 91]
			No comorbidity	SMD: -0.83; 95% CI: -1.85 to 0.20; I^2= 88.8%[30, 31, 36, 38, 41, 44, 46, 81, 82, 88, 89, 209]
		Primary anxiety, child report	Comorbidity	SMD: -0.85; 95% CI: -2.82 to 1.12; I^2= 90.0%[34, 53, 70, 91]
			No comorbidity	SMD: -0.42; 95% CI: -0.78 to -0.07; I^2= 74.4%[30, 31, 36, 38-41, 44, 46, 48, 49, 81, 82, 88, 89, 209]
		Primary anxiety, parent report	Comorbidity	SMD: -1.82; 95% CI: -4.44 to 0.80; I^2= 0.90.5%[34, 53, 70, 91]
			No comorbidity	SMD: -0.63; 95% CI: -1.15 to -0.12; I^2= 76.7%[30, 38-40, 46, 48, 49, 81, 82, 88, 89]
		Function	Comorbidity	SMD: -0.62; 95% CI: -1.19 to -0.05; I^2= 75.8%[53, 210]
			No comorbidity	SMD: -0.20; 95% CI: -1.07 to 0.67; I^2= 91.9%[30, 38, 41, 44, 46, 82]
		Secondary measure	Comorbidity	SMD: -0.33; 95% CI: -0.92 to 0.25; I^2= N/A[34]
			No comorbidity	SMD: 0.24; 95% CI: -0.54 to 1.02; I^2= 94.5%[39, 40, 44, 46, 48, 49, 209]
		Response	Comorbidity	RR: 12.69; 95% CI: 0.81 to 198.10; I^2= N/A[53]
			No comorbidity	RR: 10.16; 95% CI: 2.98 to 34.66; I^2=0.0%[39, 40, 46, 49, 209]
	Fluvoxamine vs. pill placebo	Primary anxiety, clinician report	Comorbidity	SMD: -0.30; 95% CI: -1.11 to 0.51; I^2= N/A[1]
			No comorbidity	SMD: -1.11; 95% CI: -1.49 to -0.74; I^2=

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
				N/A[11]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.3. Subgroup analysis – ADHD

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
ADHD	Fluvoxamine vs. pill placebo	Primary anxiety, clinician report	ADHD	SMD: -0.30; 95% CI: -1.11 to 0.51; I^2= N/A[1]
			No ADHD	SMD: -1.11; 95% CI: -1.49 to -0.74; I^2= N/A [11]

ADHD: attention deficit hyperactivity disorder, CI: confidence interval, N/A: not applicable, SMD: standardized mean difference

Table G.4. Subgroup analysis – autism

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Autism	CBT vs. waitlisting or no treatment	Primary anxiety, clinician report	Autism	SMD: -1.25; 95% CI: -1.79 to -0.70; I^2= 93.2%[91, 210]
			No Autism	SMD: -0.83; 95% CI: -1.85 to 0.20; I^2= 88.8%[30, 31, 36, 38, 41, 46, 81, 82, 88]
		Primary anxiety, child report	Autism	SMD: -0.85; 95% CI: -2.82 to 1.12; I^2= 90.0%[34, 53, 70, 91]
			No Autism	SMD: -0.42; 95% CI: -0.78 to -0.07; I^2= 74.4%[30, 31, 34, 36, 38-41, 44, 46, 48, 49, 81, 82, 88, 89, 209]
		Primary anxiety, parent report	Autism	SMD: -1.82; 95% CI: -4.44 to 0.80; I^2= 90.5%[34, 53, 70, 91]
			No Autism	SMD: -0.62; 95% CI: -1.14 to -0.10; I^2=74.4%[30, 34, 38-40, 46, 48, 49, 81, 82, 88, 89]
		Function	Autism	SMD: -0.62; 95% CI: -1.19 to -0.05; I^2= 75.8%[53, 210]
			No Autism	SMD: -0.20; 95% CI: -1.07 to 0.67; I^2= 91.9%[30, 38, 41, 44, 46, 82]
		Response	Autism	RR: 12.69; 95% CI: 0.81 to 198.10; I^2= N/A[53]
			No Autism	RR: 9.91; 95% CI: 2.25 to 43.65; I^2= 0.0%[39, 40, 46, 49, 209]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.5. Subgroup analysis – school refusal

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
School Refusal	CBT vs. attention control or treatment as usual	Primary anxiety, child report	School refusal	SMD: -0.31; 95% CI: -0.84 to 0.23; I^2= N/A[103]
			No School refusal	SMD: -0.53; 95% CI: -1.49 to 0.44; I^2= 74.7%[99, 102, 104, 116]
	CBT vs. pill placebo	Secondary measure	School refusal	SMD: 0.30; 95% CI: -0.32 to 0.91; I^2= N/A[121]
			No School refusal	SMD: -1.02; 95% CI: -1.45 to -0.58; I^2= N/A[3]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, SMD: standardized mean difference

Table G.6. Subgroup analysis – diagnosis

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Diagnosis	CBT vs. attention control or yreatment as usual	Primary anxiety, clinician report	Panic Disorder	SMD: -0.97; 95% CI: -1.79 to -0.15; I^2= N/A[107]
			Social Anxiety Disorder	SMD: -0.44; 95% CI: -1.95 to 1.08; I^2= 73.9%[72, 97, 116]
			Specific Phobias	SMD: -0.00; 95% CI: -0.36 to 0.35; I^2= 87.8% [96, 110]
		Primary anxiety, child report	Panic Disorder	SMD: -0.24; 95% CI: -1.02 to 0.53; I^2= N/A [107]
			Social Anxiety Disorder	SMD: -0.70; 95% CI: -1.34 to -0.05 ; I^2= 66.4%[72, 99, 104, 109, 116]
		Primary anxiety, parent report	Social Anxiety Disorder	SMD: -0.65; 95% CI: -2.67 to 1.38; I^2= 90.3%[72, 97, 104, 116]
			Specific Phobias	SMD: 0.11; 95% CI: -0.45 to 0.68; I^2= N/A[110]
		Secondary measure	Panic Disorder	SMD: -0.50; 95% CI: -1.28 to 0.29; I^2= N/A[107]
			Social Anxiety Disorder	SMD: -1.71; 95% CI: -2.46 to -0.96; I^2= N/A[72]
	CBT vs. waitlisting or no treatment	Primary anxiety, clinician report	Generalized Anxiety	SMD: -2.42; 95% CI: -3.23 to -1.62; I^2= N/A[46]
			Panic Disorder	SMD: -1.09; 95% CI: -1.71 to -0.47; I^2= N/A[42]
			Social Anxiety Disorder	SMD: -1.59; 95% CI: -2.38 to -0.80; I^2= 81.0%[31, 38, 41, 45, 51, 54, 61, 67, 74, 80, 178]
			Specific Phobias	SMD: -1.01; 95% CI: -1.35 to -0.68; I^2= 83.2%[58, 63]
		Primary anxiety, Child report	Generalized Anxiety	SMD: -0.30; 95% CI: -0.91 to 0.31; I^2= N/A[46]
			Separation Anxiety	SMD: -0.29; 95% CI: -0.89 to 0.32; I^2= N/A[77]
			Social Anxiety Disorder	SMD: -1.21; 95% CI: -1.91 to -0.52; I^2= 87.4%[31, 38, 41, 45, 51, 54, 61, 62, 67, 74, 80, 178]
			Specific Phobias	SMD: -0.08; 95% CI: -0.93 to 0.77; I^2= 9.4%[50, 63, 66, 124]
		Primary anxiety, parent report	Generalized Anxiety	SMD: -0.14; 95% CI: -0.75 to 0.47; I^2= N/A[46]
			Separation Anxiety	SMD: -1.27; 95% CI: -1.90 to -0.65; I^2= 50.0%[27, 77]
			Social Anxiety Disorder	SMD: -0.89; 95% CI: -1.66 to -0.13; I^2= 72.9%[38, 51, 62, 65, 67]

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
			Specific Phobias	SMD: -0.83; 95% CI: -1.45 to -0.21; I^2= N/A[58]
		Function	Generalized Anxiety	SMD: -0.30; 95% CI: -0.91 to 0.31; I^2= N/A[46]
			Separation Anxiety	SMD: 1.41; 95% CI: 0.74 to 2.08; I2= N/A[77]
			Social Anxiety Disorder	SMD: -1.00; 95% CI: -1.74 to -0.26; I^2= 83.7%[38, 41, 51, 54, 61, 62, 67, 178]
		Secondary measure	Generalized Anxiety	SMD: -0.38; 95% CI: -0.99 to 0.23; I^2=N/A[46]
			Social Anxiety Disorder	SMD: -0.57; 95% CI: -1.53 to 0.38; I^2= 94.2%[61, 62, 74, 178, 209]
			Specific Phobias	SMD: 1.18; 95% CI: -3.99 to 6.34; I^2= 93.8%[50, 63, 66]
		Social function	Generalized Anxiety	SMD: -0.61; 95% CI: -1.24 to 0.01; I^2= N/A[46]
			Social Anxiety Disorder	SMD: 0.15; 95% CI: -1.27 to 1.56; I^2= 90.6%[38, 41, 61, 80, 178]
		Remission	Generalized Anxiety	RR: 7.67; 95% CI: 0.42 to 139.83; I^2= N/A[46]
			Social Anxiety Disorder	RR: 11.38; 95% CI: 1.56 to 83.22; I^2= 0.0%[43, 62]
		Response	Generalized Anxiety	RR: 20.81; 95% CI: 1.29 to 335.97; I^2= N/A[46]
			Social Anxiety Disorder	RR: 8.42; 95% CI: 3.88 to 18.25; I^2= 0.0%[45, 51, 67, 80, 178]
			Specific Phobias	RR: 22.67; 95% CI: 3.24 to 158.60; I^2= N/A[63]
	Venlafaxine vs. pill placebo	Primary anxiety, child report	Generalized Anxiety	SMD: -0.52; 95% CI: -0.84 to -0.19; I^2= N/A[15]
			Social Anxiety Disorder	SMD: -0.47; 95% CI: -0.70 to -0.24; I^2= N/A[10]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.7. Subgroup analysis – treatment settings

Subgroup	Comparison	outcome	Subgroup Variable	Conclusion
Treatment Settings (School, Mental Health Clinic, Outpatient primary care)	CBT vs. attention control or treatment as usual	Primary anxiety, clinician report	Mental health clinic	SMD: -0.11; 95% CI: -0.55 to 0.33; I^2= 55.2%[96-98, 101, 106, 110]
			School	SMD: -0.24; 95% CI: -2.46 to 1.98; I^2= 84.7%[72, 95, 116]
		Primary anxiety, child report	Mental health clinic	SMD: -0.32; 95% CI: -0.66 to 0.01; I^2= 54.2%[98-101, 103, 107, 108, 117, 154]
			School	SMD: -0.49; 95% CI: -1.16 to 0.17; I^2= 66.2%[34, 72, 95, 109, 116]
		Primary anxiety, parent report	Mental health clinic	SMD: 0.08; 95% CI: -0.20 to 0.37; I^2= 0.0% [97, 98, 100, 101, 110, 117]
			School	SMD: -0.68; 95% CI: -2.66 to 1.30; I^2= 89.6[72, 95, 104, 116]
		Function	Mental health clinic	SMD: -0.30; 95% CI: -1.26 to 0.66; I^2= 61.9%[99, 101, 114]
			School	SMD: -1.18; 95% CI: -3.42 to 1.05; I^2= 79.2%[72, 104, 109]
		Secondary measure	Mental health clinic	SMD: -0.50; 95% CI: -1.28 to 0.29; I^2= N/A[100, 101, 107]
			School	SMD: -1.71; 95% CI: -2.46 to -0.96; I^2= N/A[72, 109]
		Social function	Mental health clinic	SMD: -0.36; 95% CI: -1.02 to 0.30; I^2= 15.7%[97, 114, 117]
			School	SMD: -0.34; 95% CI: -0.72 to 0.03; I^2= 82.6%[109, 116, 211]
		Remission	Mental health clinic	RR: 1.53; 95% CI: 1.11 to 2.11; I^2= 0.0%[98, 111]
			School	RR: 2.68; 95% CI: 0.11 to 64.50; I^2= 64.3%[72, 95, 116]
		Response	Mental health clinic	RR: 1.50; 95% CI: 1.07 to 2.11; I^2= 0.0%[98, 100, 101]
			School	RR: 1.95; 95% CI: 0.28 to 13.39; I^2= 79.1%[95, 104, 116]
	CBT vs. Waitlisting or No Treatment	Primary anxiety, clinician report	Mental health clinic	SMD: -1.07; 95% CI: -1.66 to -0.47; I^2= 84.8%[30-32, 36, 38, 41, 42, 44-47, 52, 54, 58, 59, 63, 67, 69, 79-82, 86-88, 90, 91]
			School	SMD: -1.97; 95% CI: -3.26 to -0.68; I^2= 89.5%[35, 51, 61, 74, 151, 178]
		Primary anxiety, child report	Mental health clinic	SMD: -0.58; 95% CI: -0.88 to -0.28; I^2= 83.7%[29-34, 36, 38, 39, 41, 44-46, 48-50, 52-54, 56, 62, 63, 66-70, 77-82, 88, 91]

Subgroup	Comparison	outcome	Subgroup Variable	Conclusion
			School	SMD: -1.32; 95% CI: -2.43 to -0.21; I^2= 91.4%[35, 61, 74, 151, 178]
		Primary anxiety, parent report	Mental health clinic	SMD: -0.86; 95% CI: -1.23 to -0.48; I^2= 81.1%[27, 29, 30, 34, 38, 39, 46-49, 52, 53, 58, 59, 62, 65, 67, 69, 70, 77, 79, 81, 82, 88, 91]
			School	SMD: -0.50; 95% CI: -1.24 to 0.24; I^2= 0.0%[35, 51, 151]
		Function	Mental health clinic	SMD: -0.64; 95% CI: -1.41 to 0.14; I^2= 92.6%[30, 32, 38, 41, 44, 46, 53, 54, 59, 62, 67, 77, 82, 87, 90]
			School	SMD: -1.27; 95% CI: -3.09 to 0.55; I^2= 74.2%[51, 61, 178]
		Secondary measure	Mental health clinic	SMD: 0.05; 95% CI: -0.44 to 0.55; I^2= 93.5%[32, 34, 39, 44, 46-50, 56, 62, 63, 66, 69, 80]
			School	SMD: -0.14; 95% CI: -1.87 to 1.59; I^2=94.7% [61, 74, 178]
		Social function	Mental Health Clinic	SMD: -0.07; 95% CI: -0.69 to 0.55; I2= 74.8%[38, 39, 41, 44, 46, 48, 80]
			School	SMD: 0.10; 95% CI: -4.66 to 4.86; I^2= 95.1%[61, 178]
		Remission	Mental health clinic	RR: 2.78; 95% CI: 0.24 to 31.98; I^2= 76.1%[32, 46, 62, 86]
			School	RR: 5.74; 95% CI: 2.17 to 15.20; I^2= 0.0%[35, 46]
		Response	Mental health clinic	RR: 3.60; 95% CI: 1.77 to 7.32; I^2= 83.0%[45-49, 52, 53, 63, 67, 79, 80, 86, 87]
			School	RR: 14.45; 95% CI: 2.94 to 71.01; I^2= 0.0%[51, 178]
	Fluvoxamine vs. pill placebo	Primary anxiety, clinician report	Mental health clinic	SMD: -0.30; 95% CI: -1.11 to 0.51; I^2= N/A[1]
			Outpatient primary care	SMD: -1.11; 95% CI: -1.49 to -0.74; I^2= N/A[11]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.8. Subgroup analysis – follow up less than 6 months

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Follow up (less than 6 months)	Benzodiazepine vs. pill placebo	Primary anxiety, clinician report	Less than 6 months	SMD: -0.40; 95% CI: -1.43 to 0.63; I^2=N/A[9]
	CBT vs. attention control or treatment as usual	Primary anxiety, clinician report	Less than 6 months	SMD: -0.11; 95% CI: -0.52 to 0.30; I^2=49.9% [95-98, 101, 106, 116]
		Primary anxiety, child report	Less than 6 months	SMD: -0.41; 95% CI: -0.88 to 0.07; I^2= 54.2%[95, 98, 101, 104, 108, 109, 116]
		Primary anxiety, parent report	Less than 6 months	SMD: 0.16; 95% CI: -0.53 to 0.85; I^2=76.7%[95, 97, 98, 106, 116]
		Function	Less than 6 months	SMD: -0.87; 95% CI: -2.98 to 1.23; I^2=79.5%[101, 109, 116]
		Social Function	Less than 6 months	SMD: 0.62; 95% CI: -1.03 to 2.26; I^2=82.0%[97, 109, 116]
		Remission	Less than 6 months	RR: 1.52; 95% CI: 0.22 to 10.48; I^2=74.9%[95, 98, 116]
		Response	Less than 6 months	RR:1.70; 95% CI: 0.34 to 8.53; I^2=77.9%[95, 98, 116]
	CBT vs. waitlisting or no treatment	Primary anxiety, clinician report	Less than 6 months	SMD: -1.02; 95% CI: -1.65 to -0.38; I^2=86.1%[32, 41, 46, 58, 59, 63, 72, 74, 76, 151, 178]
		Primary anxiety, child report	Less than 6 months	SMD: -1.43; 95% CI: -2.72 to -0.14; I^2=94.4%[29, 32, 41, 46, 63, 72, 74, 76, 151, 178]
		Primary anxiety, parent report	Less than 6 months	SMD: -0.93; 95% CI: -2.98 to 1.13; I^2=85.1%[29, 46, 58, 59, 72, 76, 151]
		Function	Less than 6 months	SMD: -0.52, 95% CI: -1.28 to 0.23; I^2=73.0%[32, 41, 59, 72, 76, 178]
		Social function	Less than 6 months	SMD: -1.60; 95% CI: -11.13 to 7.92; I^2=96.1%[41, 46, 84, 178]
		Remission	Less than 6 months	RR: 4.38; 95% CI: 0.03 to 598.20; I^2=78.2%[32, 46, 72]
		Response	Less than 6 months	RR: 1.50; 95% CI: 0.71 to 3.17; I^2=N/A[178]
	Clonazepam vs. pill placebo	Primary anxiety, clinician report	Less than 6 months	SMD: -0.40; 95% CI: -1.43 to 0.63; I^2=N/A[9]
	Fluoxetine plus CBT vs. CBT	Function	Less than 6 months	SMD: -0.53; 95% CI: -0.10 to 1.15; I^2=N/A[121]
		Secondary aeasure	Less than 6 months	SMD: 0.39; 95% CI: -0.23 to 1.01; I^2=N/A[121]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.9. Subgroup analysis – follow up longer than 6 months

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Follow up (longer than 6 months)	CBT vs. attention control or treatment as usual	Primary anxiety, clinician report	Longer than 6 months	SMD: -0.06; 95% CI: -0.50 to 0.38; I^2=N/A[96]
		Primary anxiety, child report	Longer than 6 months	SMD: -0.20; 95% CI: -0.48 to -0.09; I^2=83.5%[99-101]
		Function	Longer than 6 months	SMD: -0.31; 95% CI: -0.59 to -0.02; I^2=89.7%[99, 114]
		Social function	Longer than 6 months	SMD: -0.09; 95% CI: -0.47 to 0.29; I^2=N/A[114]
		Remission	Longer than 6 months	RR: 1.26; 95% CI: 0.99 to 1.60; I^2=N/A[111]
		Response	Longer than 6 months	RR: 1.40; 95% CI: 0.97 to 2.04; I^2=N/A[100, 101]
	CBT vs. waitlisting or no treatment	Primary anxiety, clinician report	Longer than 6 months	SMD: -0.59; 95% CI: -1.31 to -0.13; I^2=0.0%[32, 72, 151]
		Primary anxiety, child report	Longer than 6 months	SMD: -0.08; 95% CI: -0.56 to 0.39; I^2=0.0%[32, 45, 72, 151]
		Primary anxiety, parent report	Longer than 6 months	SMD: -1.55; 95% CI: -8.38 to 5.28; I^2=96.1%[59, 72, 151]
		Function	Longer than 6 months	SMD: -0.36, 95% CI; -2.39 to 1.67; I^2=85.1%[32, 59, 72]
		Remission	Longer than 6 months	RR: 0.71; 95% CI: 0.57 to 1.03; I^2=N/A[32]
	Fluoxetine plus CBT vs. CBT	Function	Longer than 6 months	SMD: -0.64; 95% CI: -1.26 to -0.01; I^2=N/A[121]
		Secondary measure	Longer than 6 months	SMD: 0.65; 95% CI: 0.02 to 1.27; I^2=N/A[121]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.10. Subgroup analysis – therapy components

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
CBT with cognitive strategies	CBT without cognitive strategies vs. CBT with cognitive strategies	Primary anxiety, clinician report	No cognitive vs. cognitive	SMD: -0.30; 95% CI: -1.44 to 0.83; I^2=41.3%[74, 181, 186]
		Primary anxiety, child report	No cognitive vs. cognitive	SMD: 0.09; 95% CI: -2.25 to 2.44; I^2= 87.0%[74, 181, 186]
		Primary anxiety, parent report	No cognitive vs. cognitive	SMD: -1.29; 95% CI: -2.46 to -0.13; I^2= N/A[186]
		Function	No cognitive vs. cognitive	SMD: 0.09; 95% CI: -0.42 to 0.59; I^2= 82.4%[181, 186]
		Secondary measure	No cognitive vs. cognitive	SMD: -0.27; 95% CI: -0.83 to 0.29; I^2= N/A[186]
		Social function	No cognitive vs. cognitive	SMD: -0.36; 95% CI: -0.92 to 0.20; I^2= N/A[181]
		Response	No cognitive vs. cognitive	RR: 0.62; 95% CI: 0.31 to 1.22; I^2= N/A[181]
CBT with exposure sessions	CBT without exposure sessions vs. CBT with exposure sessions	Primary anxiety, clinician report	No exposure vs. exposure	SMD: 0.13; 95% CI: -0.74 to 1.37; I^2= N/A[186]
		Primary anxiety, child report	No exposure vs. exposure	SMD: 0.62; 95% CI: -0.46 to 1.70; I^2= N/A[186]
		Primary anxiety, parent report	No exposure vs. exposure	SMD: 1.29; 95% CI: 0.13 to 2.46; I^2= N/A[186]
CBT with relaxation strategies	CBT without relaxation strategies vs. CBT with relaxation strategies	Primary anxiety, clinician report	No relaxation vs. relaxation	SMD: -0.15; 95% CI: -0.64 to 0.33; I^2= 0.0%[164, 186]
		Primary anxiety, child report	No relaxation vs. relaxation	SMD: -0.16; 95% CI: -1.08 to 0.75; I^2= 48.4%[46, 164, 182, 186]
		Primary anxiety, parent report	No relaxation vs. Relaxation	SMD: -0.16; 95% CI: -2.37 to 2.05; I^2= 65.3%[46, 186]
		Function	No relaxation vs. relaxation	SMD: -0.01; 95% CI: -0.46 to 0.44; I^2= 78.3%[182, 186]
		Secondary measure	No relaxation vs. relaxation	SMD: 0.41; 95% CI: -0.14 to 0.97; I^2= N/A[164, 186]
		Social function	No relaxation vs. relaxation	SMD: 0.88; 95% CI: -0.38 to 2.13; I^2= N/A[46]
		Remission	No relaxation vs. relaxation	RR: 1.25; 95% CI: 0.33 to 4.77; I^2= N/A[46]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.11. Subgroup analysis – CBT delivery mode

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Individual-based CBT vs Group-based CBT	Individual-based CBT vs group-based CBT	Primary anxiety, clinician report	Individual vs group	SMD: -0.07; 95% CI: -0.35 to 0.22; I^2= 0.0%[88, 89, 97, 164, 167, 174]
		Primary anxiety, child report	Individual vs group	SMD: -0.1; 95% CI: -0.35 to 0.16; I^2= 0.0%[88, 89, 164, 167, 172, 174]
		Primary anxiety, parent report	Individual vs group	SMD: -0.03; 95% CI: -0.81 to 0.75; I^2= 49.9% [88, 89, 97, 174]
		Function	Individual vs group	SMD: -0.64; 95% CI: -1.10 to -0.19; I^2= N/A[174]
		Secondary measure	Individual vs group	SMD: -0.41; 95% CI: -0.97 to 0.14; I^2= N/A[164]
		Social function	Individual vs group	SMD: 0.28; 95% CI: -0.30 to 0.85; I^2= N/A[97]
		Remission	Individual vs group	RR: 0.81; 95% CI: 0.47 to 1.39; I^2= N/A [88, 89]
		Response	Individual vs group	RR: 0.93; 95% CI: 0.70 to 1.23; I^2= 0.0%[88, 89, 172, 173]

CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, RR: risk ratio, SMD: standardized mean difference

Table G.12. Subgroup analysis – CBT intensity

Subgroup	Comparison	Outcome	Subgroup Variable	Conclusion
Treatment Intensity (low, medium, and high)	CBT with low intensity vs. CBT with medium intensity CBT vs. CBT with high intensity	Primary anxiety, child report	Low intensity vs. medium	SMD: 0.22; 95% CI: -0.11 to 0.56; I^2= N/A[164, 166]
		Primary anxiety, parent report	Low intensity vs. medium	SMD: 0.18; 95% CI: -0.15 to 0.51; I^2= N/A[164, 166]
		Function	Low intensity vs. medium	SMD: -0.02; 95% CI: -0.35 to 0.31; I^2= N/A[166]
		Primary anxiety, clinician report	Medium intensity vs. high	SMD: 0.16; 95% CI: -0.24 to 0.56; I^2= 0.0%[166]
		Primary anxiety, child report	Medium intensity vs. high	SMD: 0.25; 95% CI: -0.03 to 0.54; I^2= 84.2%[166]
		Primary anxiety, parent report	Medium intensity vs. high	SMD: 0.04; 95% CI: -0.24 to 0.33; I^2= 35.2%[166]
		Function	Medium intensity vs. high	SMD: -0.12; 95% CI: -0.46 to 0.21; I2= N/A166
		Secondary measure	Medium intensity vs. high	SMD: -0.41; 95% CI: -0.97 to 0.14; I^2= N/A[166]

Intensity: low: less than 480 minutes in total sessions; medium: 480 minutes to 960 minutes in total sessions; high: greater than 960 minutes in total sessions. CBT: cognitive behavioral therapy, CI: confidence interval, N/A: not applicable, SMD: standardized mean difference

Appendix H. Figures

Figure H.1. Funnel plot CBT versus waitlisting or no treatment for primary anxiety symptoms, clinician report

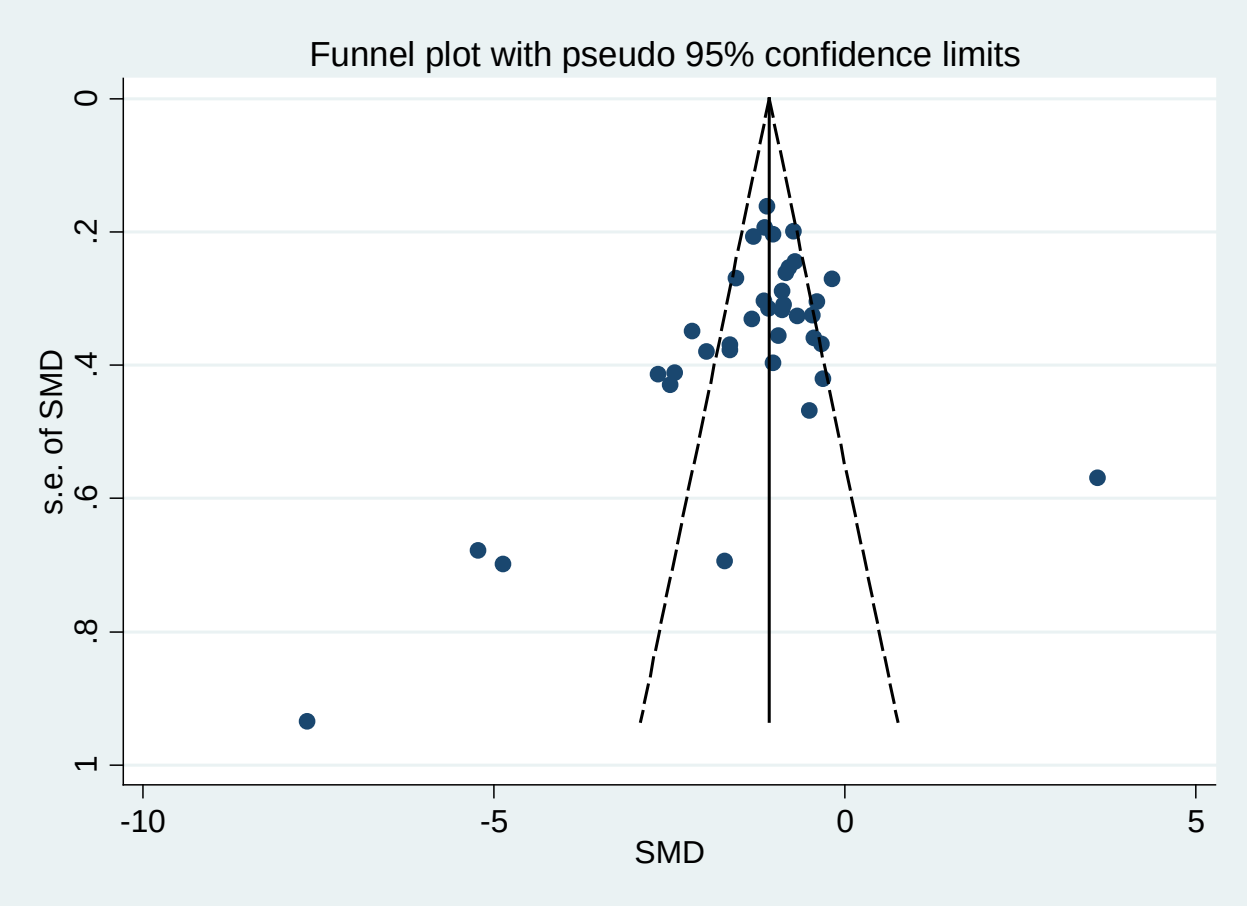


Figure H.2. Funnel plot CBT versus waitlisting or no treatment for primary anxiety symptoms,

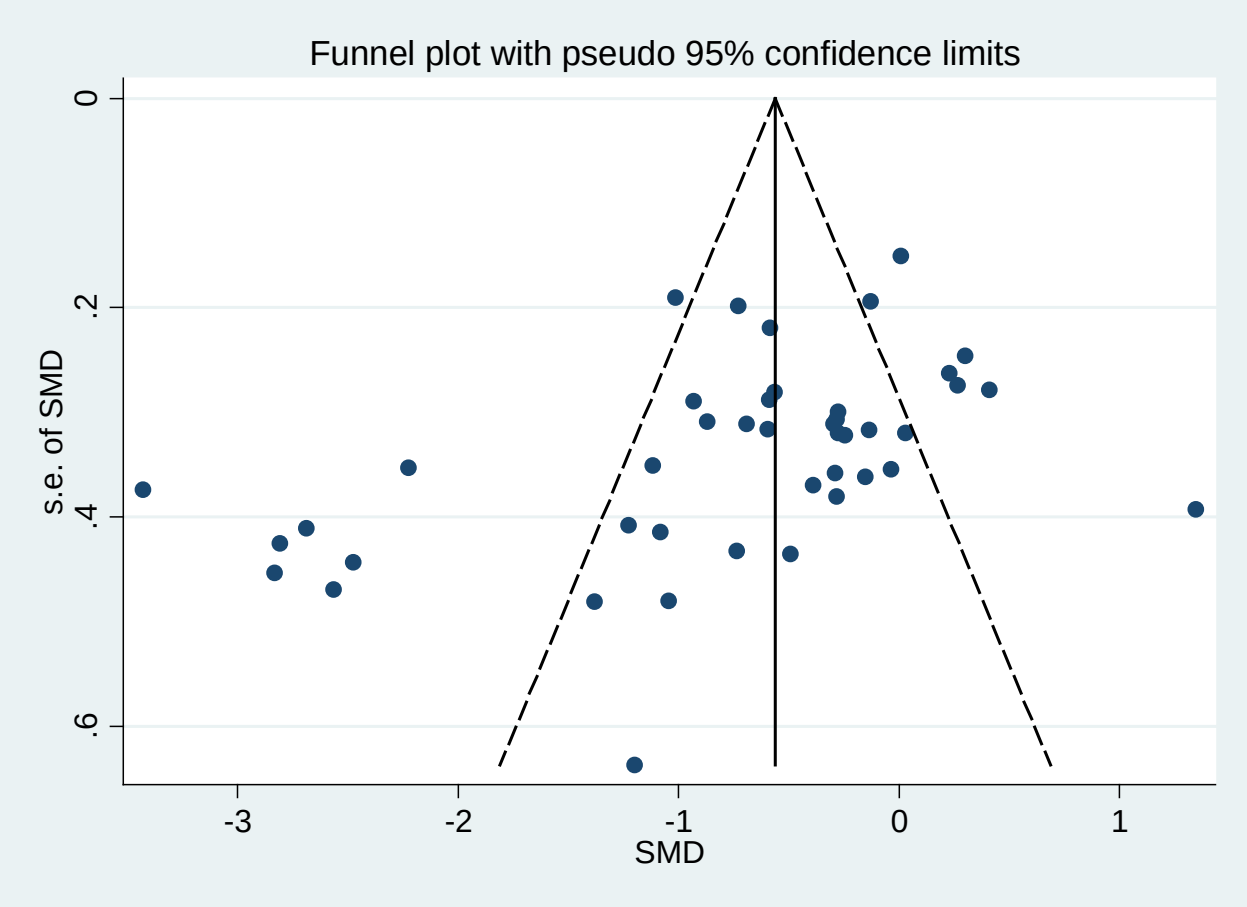
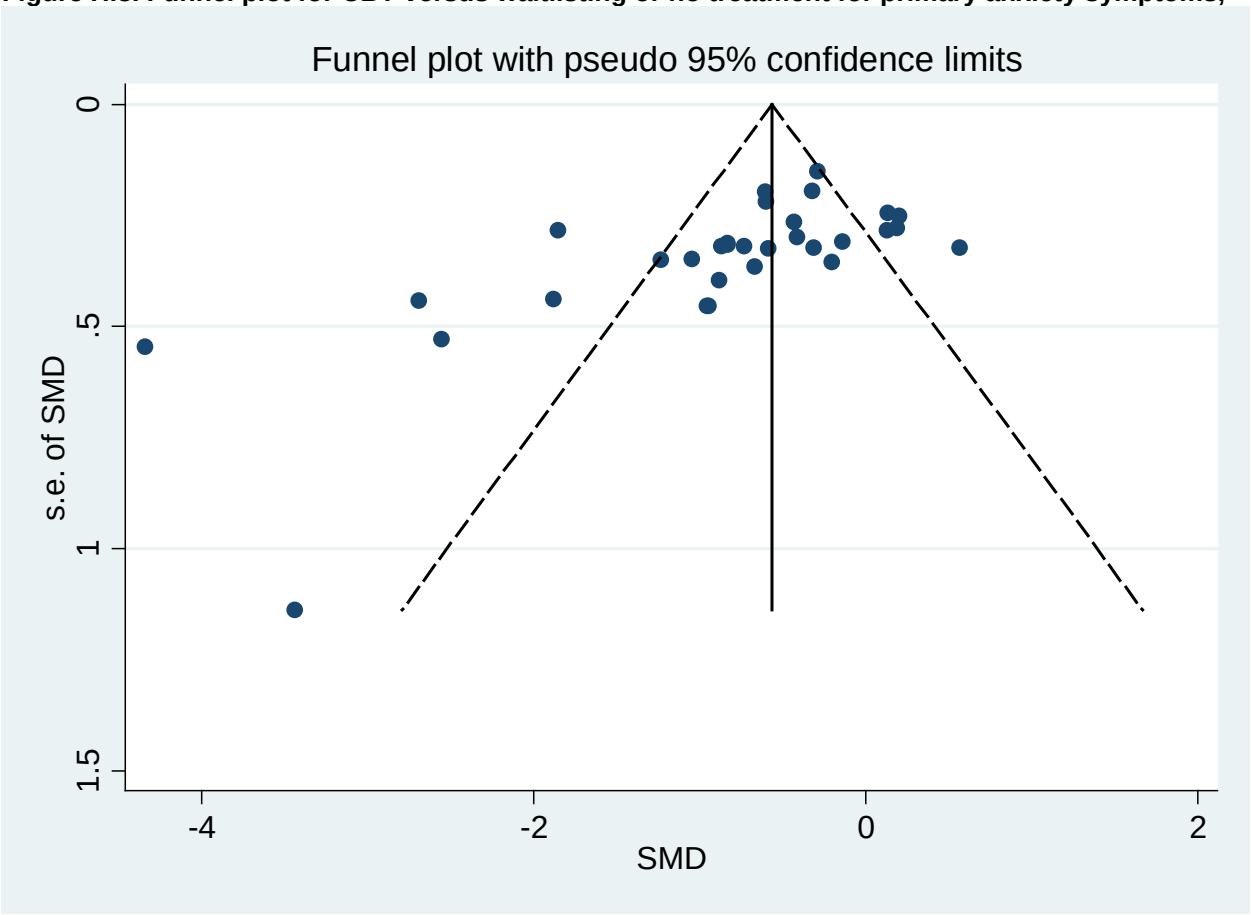


Figure H.3. Funnel plot for CBT versus waitlisting or no treatment for primary anxiety symptoms,



Appendix I. References for Appendixes

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