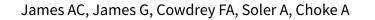


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# Cognitive behavioural therapy for anxiety disorders in children and adolescents (Review)



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# TABLE OF CONTENTS

ABSTRACT
PLAIN LANGUAGE SUMMARY
SUMMARY OF FINDINGS
BACKGROUND
OBJECTIVES
METHODS
Figure 1
Figure 2
Figure 3
RESULTS
Figure 4
Figure 5
DISCUSSION
AUTHORS' CONCLUSIONS
ACKNOWLEDGEMENTS
REFERENCES
CHARACTERISTICS OF STUDIES
DATA AND ANALYSES
Analysis 1.1. Comparison 1: CBT versus wait-list, Outcome 1: Remission of anxiety diagnoses (ITT analysis)
Analysis 1.2. Comparison 1: CBT versus wait-list, Outcome 2: Acceptability -participants lost to follow-up
Analysis 1.3. Comparison 1: CBT versus wait-list, Outcome 3: Reduction in anxiety symptoms
Analysis 1.4. Comparison 1: CBT versus wait-list, Outcome 4: Remission of anxiety diagnoses: long term follow-up
Analysis 1.5. Comparison 1: CBT versus wait-list, Outcome 5: Reduction in anxiety symptoms: long term follow-up
Analysis 1.6. Comparison 1: CBT versus wait-list, Outcome 6: Sensitivity analysis: Remission of anxiety diagnoses (completers only analysis)
Analysis 2.1. Comparison 2: CBT versus active controls, Outcome 1: Remission of anxiety diagnoses (ITT analysis)
Analysis 2.2. Comparison 2: CBT versus active controls, Outcome 2: Acceptability -participants lost to follow-up
Analysis 2.3. Comparison 2: CBT versus active controls, Outcome 3: Reduction in anxiety symptoms
Analysis 2.4. Comparison 2: CBT versus active controls, Outcome 4: Remission of anxiety diagnoses: long term follow-up (ITT
analysis)
Analysis 2.5. Comparison 2: CBT versus active controls, Outcome 5: Reduction in anxiety symptoms: long term follow-up
Analysis 2.6. Comparison 2: CBT versus active controls, Outcome 6: Sensitivity analysis: remission of anxiety diagnoses (completers only analysis)
Analysis 3.1. Comparison 3: CBT versus treatment as usual (TAU), Outcome 1: Remission of anxiety diagnoses (ITT analysis)
Analysis 3.2. Comparison 3: CBT versus treatment as usual (TAU), Outcome 2: Acceptability -participants lost to follow-up
Analysis 3.3. Comparison 3: CBT versus treatment as usual (TAU), Outcome 3: Reduction of anxiety symptoms
Analysis 3.4. Comparison 3: CBT versus treatment as usual (TAU), Outcome 4: Sensitivity analysis: remission of anxiety diagnoses (completers only analysis)
ADDITIONAL TABLES
APPENDICES
FEEDBACK
WHAT'S NEW
HISTORY
CONTRIBUTIONS OF AUTHORS
DECLARATIONS OF INTEREST
SOURCES OF SUPPORT
DIFFERENCES BETWEEN PROTOCOL AND REVIEW
INDEX TERMS



# [Intervention Review]

# Cognitive behavioural therapy for anxiety disorders in children and adolescents

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#### **ABSTRACT**

#### **Background**

A new Cochrane Review entitled 'Cognitive behavioural therapy for anxiety disorders in children and adolescents' was published on 16 November 2020 which supersedes this publication.

Citation: James AC, Reardon T, Soler A, James G, Creswell C. Cognitive behavioural therapy for anxiety disorders in children and adolescents. Cochrane Database of Systematic Reviews 2020, Issue 11. Art. No.: CD013162. DOI: 10.1002/14651858.CD013162.pub2.

A previous Cochrane review (James 2005) showed that cognitive behavioural therapy (CBT) was effective in treating childhood anxiety disorders; however, questions remain regarding (1) the relative efficacy of CBT versus non-CBT active treatments; (2) the relative efficacy of CBT versus medication and the combination of CBT and medication versus placebo; and (3) the long-term effects of CBT.

# **Objectives**

To examine (1) whether CBT is an effective treatment for childhood and adolescent anxiety disorders in comparison with (a) wait-list controls; (b) active non-CBT treatments (i.e. psychological placebo, bibliotherapy and treatment as usual (TAU)); and (c) medication and the combination of medication and CBT versus placebo; and (2) the long-term effects of CBT.

# Search methods

Searches for this review included the Cochrane Central Register of Controlled Trials (CENTRAL) and the Cochrane Depression, Anxiety and Neurosis Group Register, which consists of relevant randomised controlled trials from the bibliographic databases—*The Cochrane Library* (1970 to July 2012), EMBASE, (1970 to July 2012) MEDLINE (1970 to July 2012) and PsycINFO (1970 to July 2012).

# **Selection criteria**

All randomised controlled trials (RCTs) of CBT versus waiting list, active control conditions, TAU or medication were reviewed. All participants must have met the criteria of the *Diagnostic and Statistical Manual* (DSM) or the *International Classification of Diseases* (ICD) for an anxiety diagnosis, excluding simple phobia, obsessive-compulsive disorder, post-traumatic stress disorder and elective mutism.

# Data collection and analysis

The methodological quality of included trials was assessed by three reviewers independently. For the dichotomous outcome of remission of anxiety diagnosis, the odds ratio (OR) with 95% confidence interval (CI) based on the random-effects model, with pooling of data via



the inverse variance method of weighting, was used. Significance was set at P < 0.05. Continuous data on each child's anxiety symptoms were pooled using the standardised mean difference (SMD).

#### **Main results**

Forty-one studies consisting of 1806 participants were included in the analyses. The studies involved children and adolescents with anxiety of mild to moderate severity in university and community clinics and school settings. For the primary outcome of remission of any anxiety diagnosis for CBT versus waiting list controls, intention-to-treat (ITT) analyses with 26 studies and 1350 participants showed an OR of 7.85 (95% CI 5.31 to 11.60, Z = 10.34, P < 0.0001), but with evidence of moderate heterogeneity (P = 0.05, P = 0.05). The number needed to treat (NNT) was 3.0 (95% CI 1.75 to 3.03). No difference in outcome was noted between individual, group and family/parental formats. ITT analyses revealed that CBT was no more effective than non-CBT active control treatments (six studies, 426 participants) or TAU in reducing anxiety diagnoses (two studies, 88 participants). The few controlled follow-up studies (P = 0.05) indicate that treatment gains in the remission of anxiety diagnosis are not statistically significant.

#### **Authors' conclusions**

Cognitive behavioural therapy is an effective treatment for childhood and adolescent anxiety disorders; however, the evidence suggesting that CBT is more effective than active controls or TAU or medication at follow-up, is limited and inconclusive.

#### PLAIN LANGUAGE SUMMARY

#### Cognitive behavioural therapy for anxiety in children and young people

#### Why is this review important?

Many children and young people suffer from anxiety. Children and young people with anxiety are more likely to have difficulty with friendships, family life and school. Treatments for children and young people with anxiety can help to prevent them from developing mental health problems or drug and alcohol misuse in later life. Talking therapies such as cognitive behavioural therapy (CBT) can help children and young people to deal with anxiety by using new ways of thinking. Many parents and children prefer to try talking therapies rather than medication such as antidepressants.

#### Who will be interested in this review?

Parents, children and young people; people working in education; professionals working in mental health services for children and young people; and general practitioners.

#### What questions does this review aim to answer?

This review is an update of a previous Cochrane review from 2005, which showed that CBT is an effective treatment for children and young people with anxiety.

This update aims to answer the following questions:

- Is CBT more effective than no therapy (waiting list)?
- Is CBT more effective than other 'active' therapies such as self-help books aimed at children and young people?
- Is CBT more effective than medication?
- Does CBT help to reduce symptoms of anxiety for children and young people in the longer term?

# Which studies were included in the review?

Search databases were used to find all high-quality studies of CBT for anxiety in children and young people published between 1970 and July 2012. To be included in the review, studies had to be randomised controlled trials and had to include children and young people with a clear diagnosis of anxiety.

Forty-one studies with a total of 1806 participants were included in the review. The review authors rated the overall quality of the studies as 'moderate'.

# What does the evidence from the review tell us?

CBT is significantly more effective than no therapy in reducing symptoms of anxiety in children and young people.

No clear evidence indicates that one way of providing CBT is more effective than another (e.g. in a group, individually, with parents).

CBT is no more effective than other 'active therapies' such as self-help books.



The small number of studies meant the review authors could not compare CBT with medication.

Only four studies looked at longer-term outcomes after CBT. No clear evidence showed maintained improvement in symptoms of anxiety among children and young people.

# What should happen next?

The review authors recommend that future research should look in greater detail at what makes CBT work best for children and young people, how CBT can be provided in the most cost-effective way, and how CBT can be adapted for different age groups.



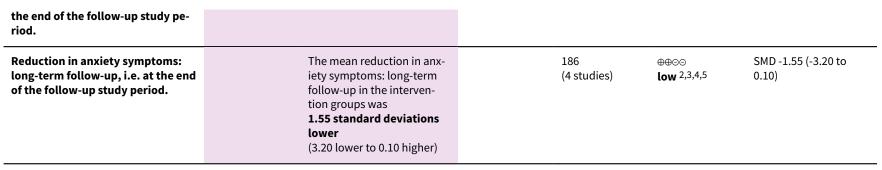
# Summary of findings 1. CBT compared to wait-list for children and adolescents with anxiety disorders

# CBT compared to wait-list for children and adolescents with anxiety disorders

Patient or population: children and adolescents with anxiety disorders

**Settings:** outpatient **Intervention:** CBT **Comparison:** wait-list

Outcomes	Illustrative com	parative risks* (95% CI)	Relative effect (95% CI)	No of Partici- pants	Quality of the evidence	Comments
	Assumed risk	Assumed risk Corresponding risk		(studies)	(GRADE)	
	Wait-list	СВТ				
Remission of anxiety diagnoses (ITT analysis) i.e. no longer meet- ing criteria for DSM or ICD anxiety diagnosis at the end of the trial.	161 per 1000	<b>600 per 1000</b> (504 to 689)	<b>OR 7.85</b> (5.31 to 11.6)	1350 (26 studies)	⊕⊕⊕⊝ moderate ¹	
Participants lost to follow-up	104 per 1000	<b>97 per 1000</b> (63 to 148)	<b>OR 0.94</b> (0.58 to 1.51)	1297 (26 studies)	⊕⊕⊙⊝ low <sup>2,3</sup>	
Reduction in anxiety symptoms at the end of the trial		The mean reduction in anxiety symptoms in the intervention groups was  0.98 standard deviations lower  (1.21 to 0.74 lower)		1394 (30 studies)	⊕⊕©⊝ low <sup>2</sup> ,4	SMD -0.98 (-1.21 to -0.74) standardised mean difference. [SMD (difference in means/ pooled standard deviation) of 0.2 standard deviation units is to be considered a small difference between intervention groups, 0.5 a moderate difference, and 0.8 a large difference (Cohen 1988).]
Remission of anxiety diagnoses: long-term follow-up i.e. no longer meeting criteria for DSM or ICD anxiety diagnosis at	516 per 1000	<b>775 per 1000</b> (506 to 920)	<b>OR 3.22</b> (0.96 to 10.75)	124 (3 studies)	⊕⊕⊙⊝ low <sup>1,5</sup>	



<sup>\*</sup>The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence:

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

- <sup>1</sup> Moderate heterogeneity present.
- <sup>2</sup> Large variation in treatment effects.
- <sup>3</sup> Very wide confidence intervals.
- $^{\rm 4}$  Significant heterogeneity present.
- <sup>5</sup> Small sample size.

# Summary of findings 2. CBT compared to active controls for children and adolescents with anxiety disorder

# CBT compared to active controls for children and adolescents with anxiety disorders

Patient or population: children and adolescents with anxiety disorders

Settings: outpatient Intervention: CBT

**Comparison:** active controls

Outcomes	Illustrative comparative risks* (95% CI)	Relative effect (95% CI)	No of Partici-	Quality of the evidence	Comments
	Assumed risk Corresponding risk	(33 % Ci)	(studies)	(GRADE)	
	Active controls CBT				

Remission of anxiety diagnoses (ITT) analysis i.e. no longer meet- ing criteria for DSM or ICD anxiety diagnosis at the end of the trial.	372 per 1000	<b>472 per 1000</b> (313 to 637)	<b>OR 1.51</b> (0.77 to 2.96)	426 (6 studies)	⊕⊕⊕⊝ moderate ¹	
Reduction in anxiety symptoms at the end of the trial		The mean reduction in anxiety symptoms in the intervention groups was <b>0.5 standard deviations lower</b> (1.09 lower to 0.09 higher)		411 (8 studies)	⊕⊕⊕⊝ moderate <sup>2</sup>	SMD -0.5 (-1.09 to 0.09) stan- dardised mean difference

<sup>\*</sup>The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence:

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

<sup>1</sup> Widely differing estimates of the treatment effect.

<sup>2</sup> Significant heterogeneity (introduced by one study).

# Summary of findings 3. CBT compared to treatment as usual (TAU) for children and adolescents with anxiety disorder

# CBT compared to treatment as usual (TAU) for children and adolescents with anxiety disorders

Patient or population: children and adolescents with anxiety disorders

**Settings:** outpatient **Intervention:** CBT

**Comparison:** treatment as usual (TAU)

Outcomes	Illustrative comp	parative risks* (95% CI)	Relative effect (95% CI)	No of Partici- pants	Quality of the evidence	Comments
	Assumed risk	Corresponding risk	(35 % 6.1)	(studies)	(GRADE)	
	Treatment as usual (TAU)	СВТ				
Remission of anxiety diagnoses (ITT analysis) i.e. no longer meet-	556 per 1000	<b>398 per 1000</b> (223 to 610)	<b>OR 0.53</b> (0.23 to 1.25)	88 (2 studies)	⊕⊕⊕⊝ moderate <sup>1</sup>	

ing criteria for DSM or ICD anxiety diagnosis at the end of the trial.				
Reduction of anxiety symptoms at the end of the trial	The mean reduction in anxiety symptoms in the intervention groups was <b>0.19 standard deviations lower</b> (0.79 lower to 0.4 higher)	98 (3 studies)	⊕⊕⊕⊝ moderate <sup>1,2</sup>	SMD -0.19 (-0.79 to 0.4) stan- dardised mean difference

<sup>\*</sup>The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence:

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

<sup>&</sup>lt;sup>1</sup> Small sample size.

<sup>&</sup>lt;sup>2</sup> Moderate heterogeneity present.



# BACKGROUND

# **Description of the condition**

Anxiety disorders are amongst the most common psychiatric disorders, occurring in 5% to 19% of all children and adolescents (Costello 2004). In children younger than 12, prevalence varies between 2.6% and 5.2%, and separation anxiety is the most common disorder (Costello 2004; Ford 2003).

One of the diagnostic challenges in this age group involves distinguishing normal, developmentally appropriate worries, fears and shyness from anxiety disorders. Distinguishing features of pathological anxiety include severity, persistence and associated impairment. An understanding of the developmental patterns of various anxieties is also important. School-age children commonly have worries about injury and natural events, whereas older children and adolescents typically have worries and fears related to school performance, social competence and health issues.

The presentation of anxiety disorders varies with age. Young children can present with undifferentiated worries and fears and multiple somatic complaints - muscle tension, headache or stomachache - and sometimes angry outbursts. The latter may be misdiagnosed as oppositional defiant disorder (ODD), as the child tries to avoid anxiety-provoking situations. Social anxiety disorder typically presents after puberty. Anxiety disorders with an onset in childhood often persist into adolescence (Last 1996) and early adulthood (Last 1997), and yet they often remain untreated, with many cases of social phobia (SOP) first diagnosed more than 20 years after onset (Schneier 1992).

The International Classification of Diseases (ICD) and Diagnostic and Statistical Manual (DSM) diagnostic systems distinguish various types of anxiety disorders, including generalized anxiety disorder (GAD), panic disorder (PD), social anxiety disorder (SAD) and specific phobias. These anxiety disorders are often associated with significant impairment in personal, social and academic functioning (Pine 2009). Comorbidities are common and include depression (Kovacs 1989), substance abuse (Kushner 1990) and subsequent adolescent anxiety disorders, social phobia (SOP), attention-deficit/hyperactivity disorder (ADHD), conduct disorder (Bittner 2007), suicidal behaviours and suicide (Hill 2011), Social anxiety disorder (SAD) which peaks in adolescence, is associated with more malignant depression later on (Beesdo 2007). It is clear that anxiety disorders in this age group present serious health issues; therefore effective and readily accessible treatments are needed.

# **Description of the intervention**

Current treatments for anxiety disorders in this age group include behavioural therapy, particularly for simple phobias, cognitive behavioural therapy (CBT) and/or medication. No specific guidelines on the indications for psychological treatment versus medication have been put forth, although given the prevalence of these disorders, the age of onset and public views on the acceptability of psychological treatments, these are often preferred as first-line therapy. CBT is a collaborative psychological treatment that can be delivered in various formats—individual, child or adolescent, group, parents or family. CBT for anxiety disorders in children and adolescents usually takes nine to twenty sessions.

One of the first manualised CBT programmes was Coping Cat (Kendall 1994), which consisted of education, modification of negative cognitions, exposure, social competence training, coping behaviour and self-reinforcement sessions. Others have followed, including the Cool Kids programme (http://education.qld.gov.au/studentservices/protection/sel/cool-kids.html), the Coping Koala programme (Barrett 1996), Skills for Academic and Social Success (SASS) (Masia-Warner 2007), ACTION (Waters 2009), Intervention With Adolescents With Social Phobia (IAFS) (Sánchez-García 2009), the TAPS (Masia-Warner 2011) and Building Confidence programme (Galla 2012). Some programmes have been specifically adapted for children with autism spectrum disorders (ASDs), including the Multimodal Anxiety and Social Skills Intervention (MASSI) programme (White 2012), TAFF (Schneider 2011) and Facing Your Fears (FYF) (Reaven 2012).

# How the intervention might work

CBT for anxiety disorders in children and adolescents involves helping the child to (1) recognise anxious feelings and bodily or somatic reactions to anxiety, (2) clarify thoughts or cognitions in anxiety-provoking situations (e.g. unrealistic or negative attributions and expectations), (3) develop coping skills (e.g. modifying anxious self-talk into coping self-talk) and (4) evaluate outcomes. Behavioural training strategies include modelling, reality exposure (in vivo exposure), role playing and relaxation training. Behavioural treatment is based on the premise that fear and anxiety are learnt responses (classically conditioned) that can be "unlearnt". A key CBT procedure is exposure (Silverman 1996). An element of treatment known as systematic desensitisation involves pairing anxiety stimuli, in vivo or by imagination, in a gradually increasing hierarchy with competing relaxing stimuli such as pleasant images and muscle relaxation.

Cognitive strategies are used, the most common of which are self-control strategies which rely on self-observation, self-modification, self-evaluation and self-reward. For instance, according to the STOP acronym (Silverman 1996), children and adolescents learn first to identify when they are feeling anxious or Scared (S), then to identify their anxious Thoughts (T). Next, they learn to modify or restructure their anxious thoughts by generating Other alternative coping thoughts and behaviours (O). Finally, they learn to reward or Praise themselves for confronting their fears (P).

CBT has been adapted to include family and parents. The main aspects of CBT parent/family treatment guidelines involve (1) modifying parents' beliefs about ways to help their anxious child and assisting parents to respond appropriately to the child's anxious and avoidant behaviours, and (2) assisting parents to manage their own anxiety.

CBT can be applied only after the child has reached a certain level of cognitive development. Kendall (Kendall 1990b) argued that the ability to measure a thought or belief against the notion of a rational standard and the ability to understand that a thought or belief can cause a person to behave and feel in a certain way were central to its proper use. The question arises: At what age does a child have the cognitive capacities to undertake these cognitive operations? A recent study (Hirshfeld-Becker 2010) reported positive effects in children younger than age 6; however, it is not clear whether children younger than 6 years of age are able to use de-centring techniques such as narratives or stories. In line with this, recent work suggests that young children may be more responsive to the



behavioural than the cognitive elements of this approach (Essau 2004). Recent work indicates that treatment of anxiety disorders in very young children may be effected by working directly with parents alone (Cartwright-Hatton 2011).

# Why it is important to do this review

Anxiety disorders in children and adolescents represent a considerable source of morbidity and are associated with later adult psychopathology. However, despite high prevalence and substantial morbidity, anxiety disorders in childhood remain under-recognised and under-treated (Esbjørn 2010) and as such represent an important public health issue. The evidence base for treatment of anxiety in children and adolescents is growing. Initial trials of CBT (Kendall 1994; Barrett 1996; Kendall 1997) were positive (Kendall 1997), and further randomised controlled trials (RCTs) and indeed reviews followed. What is needed now is synthesis of the growing body of evidence. This is an update of a previous Cochrane review of CBT for anxiety disorders in children and adolescents (James 2005), which found a positive response rate for the remission of anxiety diagnoses for CBT in 56% of cases. The current review was undertaken to provide comprehensive and up-to-date evidence on the efficacy of CBT in the treatment of anxiety disorders in children and adolescents, including the use of differing CBT formats—individual, group and family/parent. Further, this review will examine the efficacy of CBT relative to active treatments, such as educational support and treatment as usual (TAU). The question of the comparative efficacy of medication versus CBT and the combination of CBT and medication needs to be addressed. Last, this review will aim to assess whether treatment effects of CBT are maintained at long-term follow-up.

It is recognised that children and adolescents with autism spectrum disorders (ASDs) have high rates of anxiety disorders, particularly SOP (Settipani 2012); however, a recent review of CBT for anxiety disorders in ASD (Lang 2010) included only a few studies. Furthermore, it is unclear how anxiety disorders are recognised or, indeed, treated in those with intellectual impairments, indicating a pressing need for work in this particular area. Review of the efficacy of CBT in children and adolescents with ASD will be undertaken.

Recognition of the importance of anxiety disorders in childhood is increasing, as can be seen in several reviews on the treatment of anxiety in children and adolescents, including Cochrane reviews for post-traumatic stress disorder (PTSD) (Bisson 2007), obsessive-compulsive disorder (OCD) (O'Kearney 2006) and pharmacological treatments (Ipser 2009). These disorders will not be included in this review.

# **OBJECTIVES**

- To carry out a meta-analysis of identified studies to determine
  whether CBT leads to remission of childhood and adolescent
  anxiety disorders and/or a clinically significant reduction in
  anxiety symptoms in comparison with passive (waiting list—W/
  L) controls, active controls or treatment as usual (TAU).
- To carry out a subgroup analysis of different types of CBT according to format (individual, group and parent/family).
- To determine the comparative efficacy of CBT alone, and the combination of CBT and medication, versus placebo.
- To determine whether post-treatment gains of CBT are maintained at follow-up.

# **METHODS**

# Criteria for considering studies for this review

#### Types of studies

RCTs, including cross-over trials and cluster-randomised trials, of manualised and documented modular CBT of at least nine sessions, involving direct contact with the child, were included, as were follow-up data with comparators (W/L, active controls or TAU).

# **Types of participants**

#### Participant characteristics

Children and adolescents older than four years and younger than 19 years.

# **Diagnosis**

Participants meeting diagnostic criteria of the DSM (DSM III, III-R, IV and IV-TR) (APA 1980; APA 1987; APA 1994; APA 2000) or of ICD9 and ICD10 (WHO 1978, WHO 1992) for anxiety disorder, including one or more disorders of GAD, over-anxious disorder, SAD, SOP or PD, but excluding PTSD, simple phobias, elective mutism and OCD.

#### Comorbidity

All comorbidities allowable for anxiety disorders under the rules of DSM and ICD were included, such as ASD, intellectual impairment and physical disorders.

# Settings

All settings such as research settings (i.e. university outpatient clinics, inpatient services, community clinics, and schools) were included.

# **Exclusion criteria**

We excluded PTSD and OCDs because they are covered by separate Cochrane reviews (Bisson 2007; O'Kearney 2006). In line with other reviews (Reynolds 2012), simple phobias were excluded because established behavioural treatments necessarily involve cognitive interventions.

## Types of interventions

# **Experimental intervention**

Manualised CBT, or modular CBT, alone or in combination with medication was required. A documented, written protocol stating the specific treatment at each stage of at least nine sessions provided by trained therapists under regular supervision was required. The choice of nine sessions is arbitrary; nonetheless, all major published protocols consist of at least this number of sessions.

CBT had to be administered according to standard principles as a psychological model of treatment involving helping the child to (1) recognise anxious feelings and somatic reactions to anxiety, (2) clarify cognitions in anxiety-provoking situations, (3) develop coping skills that involve modification of these anxiety-provoking cognitions and (4) respond to behavioural training strategies with exposure in vivo or by imagination, usually in a gradual, hierarchical manner, and relaxation training. No concurrent medications for the treatment of anxiety were to be administered naturalistically.



CBT can be delivered individually, in a group format or with family or parental involvement. The latter spans a range of direct involvement such as (rarely) the whole family and (more usually) the parents for some conjoint or separate sessions. Family/parental CBT may include providing psycho-education for parents or even teaching parents to be co-therapists.

The control groups were W/L or TAU. Comparison of the latter group against CBT allows one to demonstrate any added effect or not of CBT over other active treatments, whereas the comparison of CBT against W/L yields a baseline or estimate of CBT versus no treatment.

# **Comparator interventions**

- Waiting list and no treatment for anxiety during that period.
- Psychological treatment that did not include CBT elements, or attention only (e.g. support but with no elements of CBT).
- TAU.
- Drug placebo.

# Types of outcome measures

# **Primary outcomes**

- Remission the absence of a diagnosis of an anxiety disorder, as diagnosed by reliable and valid structured interviews for DSM or ICD child and adolescent anxiety disorders, including:
  - Anxiety Disorder Interview Schedule for Parents (ADIS-P) (Silverman 1987).
  - Anxiety Disorder Interview Schedule for Children (ADIS-C) (Silverman 1987).
  - Diagnostic Interview Schedule for Children, Adolescents and Parents (DISCAP) (Holland 1995).

The diagnostic interviews were required to be carried out independently of the treatment team.

In addition we included non-specific rating scales such as the Clinical Global Impression scale (CGI-I) (Guy 1976), a validated seven-item scale used to assess treatment responders. Treatment response was deemed as a score of 1 (very much improved) or 2 (much improved) on the CGI-I.

 Acceptability, as determined by the numbers of participants who were lost to follow-up.

# Secondary outcomes

- Reduction in anxiety symptoms to be measured using psychometrically robust measures of anxiety symptoms (Myers 2002) that yield symptom scores on continuous scales, such as:
  - Revised Children's Manifest Anxiety Scale (RCMAS) (Reynolds 1985).
  - Fear Survey for Children—Revised (FSSC-R) (Ollendick 1998).
  - Social Phobia and Anxiety Inventory for Children (SPAI-C) (Beidel 1995).
  - Child Behaviour Checklist (CBCL) (Achenbach 1991).
  - Social Anxiety Scale for Adolescents (SAS-A) (La Greca 1998).

- State-Trait Anxiety Inventory for Children (STAI-C) (Spielberger 1973).
- Screen for Child Anxiety Related Emotional Disorders (SCARED) (Birmaher 1999).
- SCAS (Spence Child Anxiety Scale, Child and Parent Versions) (Spence 1997).

These scales are self-report or are completed by a parent or guardian or an independent rater. Where possible, the child's or adolescent's report was used. Often multiple measures were reported, and the most validated, best recognised, or most frequently used measures were included in the analysis.

A crucial issue is how well these measures discriminate between clinical and non-clinical levels of anxiety. A meta-analysis of 43 articles (Seligman 2004) found a large effect size for the measures RCMAS, STAI-C and CBCL in discriminating children and adolescents with anxiety disorders versus controls and those with externalising disorders, but not affective disorders. The RCMAS, STAI-C and CBCL were also moderately sensitive to treatment gains.

# Search methods for identification of studies

We identified all studies that might describe RCTs of CBT for anxiety disorders in children and adolescents from the Depression, Anxiety and Neurosis Cochrane Review Group Trials Registers (CCDANCTR) (most recent search, 01/05/2012).

# **Electronic searches**

# **CCDAN's Specialized Register (CCDANCTR)**

The Cochrane Depression, Anxiety and Neurosis Group (CCDAN) maintains two clinical trials registers at its editorial base in Bristol, UK: a references register and a studies-based register. The CCDANCTR-References Register contains more than 31,500 reports of trials in depression, anxiety and neurosis. Approximately 65% of these references have been tagged to individual, coded trials. The coded trials are held in the CCDANCTR-Studies Register, and records are linked between the two registers through the use of unique Study ID tags. Coding of trials is based on the EU-Psi coding manual. Please contact the CCDAN Trials Search Co-ordinator for further details. Reports of trials for inclusion in the Group's registers are collated from routine (weekly), generic searches of MEDLINE (1950-), EMBASE (1974-) and PsycINFO (1967-), from quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL) and from review-specific searches of additional databases. Reports of trials are also sourced from international trial registers c/o the World Health Organization's trials portal (ICTRP), as well as from drug companies and from the handsearching of key journals, conference proceedings and other (non-Cochrane) systematic reviews and meta-analyses.

Details of CCDAN's generic search strategies can be found on the Group's Website.

 The CCDANCTR-Studies register was searched using the following search strategy:

Condition = (anxiety or anxious or "phobic disorder\*" or "panic disorder\*" or "social phobia")

AND

Intervention = (behavior\* or behaviour\* or cognitive\*)
AND



Age = (child\* or adolescent\* or unclear or "not stated").

 The CCDANCTR-References register was searched using a more sensitive set of free-text terms to identify additional untagged/ uncoded reports of RCTs:

(CBT or cognitive\* or behavior\* or behaviour\*) and (anxiety or anxious or \*phobi\* or panic\*) and (child\* or adolesc\* or juvenil\* or school\* or pediatri\* or paediatri\* or teen\* or young or youth\*).

· Additional searches:

A complementary search of MEDLINE and MEDLINE In-Process was conducted in September 2009 when the CCDANCTR was out-of-date as the result of a changeover of staff at the editorial base (Appendix 1).

 The WHO Trials portal (ICTRP) and ClinicalTrials.gov were also searched to identify additional unpublished and/or ongoing studies.

# **Searching other resources**

• The following journals were handsearched up until 2004:

Cognitive Therapy and Research 1977-2004
Journal of Child Psychology and Psychiatry 1970-2004
British Journal of Psychiatry 1970-2004
Behavioural and Cognitive Psychotherapy 1970-2004
British Journal of Clinical Psychology 1970-2004
Psychological Medicine 1970-2004

Journal of the American Academy of Child and Adolescent Psychiatry 1970-2004

Journal of Consulting and Clinical Psychology 1970-2004 Journal of Clinical Child and Adolescent Psychology 1997-2004 Journal of Abnormal Psychology 1970-2004 Journal of Abnormal Child Psychology 1970-2004 Journal of Behaviour Therapy Experimental Psychiatry 1970-2004 Behaviour Research and Therapy 1970-2004 Behaviour Therapy 1970-2004

These journals are now available online; therefore it was not deemed necessary to handsearch for the years 2005 through to 2012.

# Reference lists

The reference lists of all identified studies were inspected for additional studies.

# • Personal communication

The lead author on all included studies and other experts in the field were approached to request details of any further published or unpublished studies.

# · Book chapters

Textbooks on child and adolescent psychiatry and anxiety disorders were searched for additional relevant studies.

# **Data collection and analysis**

#### **Selection of studies**

All citations identified by searching were separately inspected by four reviewers (ACJ, FAC, GJ and AS) to ensure reliability. All articles that possibly met our inclusion criteria were obtained so that the full text could be independently assessed as to whether they met review criteria. Authors were not blinded to the names of authors, institutions, journals of publication and results, when they applied the inclusion criteria. Any disagreement on the eligibility of a study was discussed with the other review authors, and, where necessary, the authors of the studies were contacted for further information.

# **Data extraction and management**

References were organised using Reference Manager. Data extraction forms were developed a priori and included information regarding study methods, participant details, treatment details and adherence to treatment protocol and outcome measures. Data were extracted and assessed by FAC, GJ and ACJ independently. Consensus was reached through discussion. In cases of disagreement, the other review authors were consulted. Any areas of remaining uncertainty were resolved by contacting the author of the study.

# **Main comparisons**

- CBT compared with waiting list controls.
- CBT compared with other active treatments.
- · CBT compared with TAU.
- CBT compared with medication or placebo.
- CBT and medication combination compared with placebo.

# Assessment of risk of bias in included studies

For each included study, three review authors (ACJ, FAC and GJ) independently assessed risk of bias using the seven domains set out below from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), with ratings of 'low risk', 'high risk' and 'unclear risk':

- · Sequence generation.
- Allocation concealment.
- Blinding of participants and personnel.
- Blinding of outcome assessors.
- Incomplete outcome data.
- · Selective outcome reporting.
- · Other bias: CBT non-manualisation.

Risk of bias was assessed using the Cochrane Risk of Bias tool, a summary of which is displayed in Figure 1 and Figure 2. Selection bias was identified by assessing the adequacy of the randomisation process in terms of the description of adequacy of sequence generation and the concealment of treatment group allocation. Given the nature of psychological interventions, blinding of either participants or personnel delivering the treatments was possible only in those studies involving CBT versus active controls or TAU; therefore performance bias was assessed only in those studies. Detection bias was assessed by identifying whether study personnel carrying out outcome assessments were blinded to the treatment status of participants. Attrition bias was assessed by



determining whether studies provided a description of withdrawals and dropouts (Figure 2).



Figure 1. Risk of bias summary: risk of bias item for each included study.

Blinding (performance bias and detection bias): All outcomes Incomplete outcome data (attrition bias): All outcomes Blinding of outcome assessment (detection bias): Random sequence generation (selection bias) Allocation concealment (selection bias) Selective reporting (reporting bias) Barrett 1996 Barrett 1998 Barrington 2005 Chalfant 2007 Cobham 2012 Dadds 1997 Dadds 1999 Flannery-Schroeder 2000 Galla 2012 Gil-Bernal 2009 Ginsburg 2002 Ginsburg 2012 Hayward 2000 Herbert 2009 Hirshfeld-Becker 2010 Hudson 2009 Kendall 1994 Kendall 1997 Kendall 2008 Lau 2010 Masia-Warner 2005 Masia-Warner 2007 Masia-Warner 2011 McNally Keehn 2012 Melfsen 2011 Mendlowitz 1999 1 /------- DOOD



Figure 1. (Continued)

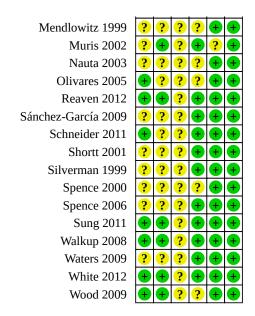
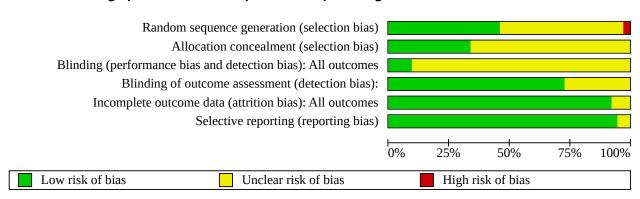


Figure 2. Risk of bias graph: risk of bias item presented as percentages across all included studies.



We did not exclude studies from meta-analysis on the basis of the 'risk of bias' assessment. We conducted a sensitivity analysis for the primary outcome, excluding trials with 'no' or 'unclear' ratings for allocation concealment if appropriate. We reported on the remainder of the risk of bias assessments for these trials and include discussion of this assessment in the Results and Discussion sections.

# **Measures of treatment effect**

Post-treatment outcomes were assessed using dichotomous data on remission of anxiety symptoms and continuous data on anxiety symptoms, with the use of standardised measures. These measures were also used to assess the maintenance of treatment effects versus W/L controls at follow-up. For dichotomous data, the review used odds ratio (OR) and 95% confidence interval (CI), with pooling of data via the inverse variance method of weighting. Continuous data, measured in different ways across studies but conceptually the same (i.e. measuring anxiety), were pooled using the standardised mean difference (SMD). For both dichotomous

and continuous data, a random-effects model was used and significance was set at P < 0.05. Completer and intent-to-treat (ITT) analyses were undertaken. However, for symptoms, last observation carried forward (LOCF) analyses were not performed as we did not have access to raw data.

# **Unit of analysis issues**

# Cluster-randomised trials

Cluster-randomised controlled trials based in schools were included. Cluster-randomised trials may, in principle, be combined with individually randomised trials in the same meta-analysis (Higgins 2011). We did not estimate that there would be many cluster-randomised trials; therefore identified cluster-randomised trials will be included in the meta-analyses and sensitivity analyses undertaken to investigate the robustness of any conclusions drawn. To correct the influence of any cluster trials, an average intraclass correlation coefficient of 0.02 was used (Health Services Research Unit 2004).



The effective sample size of a single intervention group in a cluster-randomised trial is its original sample size divided by the 'design effect'. The design effect is 1 + (M-1) ICC, where M is the average cluster size and ICC is the intracluster correlation coefficient (Rao 1992). For dichotomous data, both the number of participants and the number experiencing the event were divided by the same design effect. For continuous data, only the sample size was reduced; means and standard deviations were not altered.

#### Cross-over trials

For any cross-over trials, paired analysis was to be undertaken if data were presented.

# Studies with multiple treatment groups

Studies with more than two intervention arms can pose analytical problems in pair-wise meta-analysis. Where studies had two or more active treatment arms to be compared against TAU, data were managed in this review as follows:

#### Continuous data

The control group was divided equally into two and the means and SDs of these groups compared against the means and SDs of the two treatment arms.

#### Dichotomous data

For trials with two or more active treatment arms and a control group, participants in the control arm group were split equally between the active treatment arm.

#### Dealing with missing data

# **Missing statistics**

In the first instance, attempts were made to contact the original researchers for any missing data. If only standard errors (SEs) were reported, standard deviations (SDs) were calculated.

# **Missing participants**

ITT analyses were undertaken. For the analysis of dichotomous data, it was assumed that all non-completers in the CBT group were treatment failures and non-completers in the control group were treatment successes, thereby yielding the most conservative treatment estimate. LOCF analysis for symptoms was not performed.

# **Assessment of heterogeneity**

Clinical heterogeneity was assessed by comparing differences in the distribution of important participant factors between trials (e.g. age, gender, specific diagnosis, duration and severity of disorder, associated comorbidities). We assessed methodological heterogeneity by comparing trial factors (randomisation, concealment, blinding of outcome assessment, losses to follow-up). The Chi² test and the I² statistic were used to assess heterogeneity. Significance was set at P < 0.1. The Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011) recommends using a range for I² and a guide to interpretation. For this review, if either moderate heterogeneity (I² in the range of 30% to 60%) or substantial heterogeneity (I² in the range of 50% to 90%) was found, subgroup and sensitivity analyses were used, with meta-regression analyses (STATA 2009).

#### **Assessment of reporting biases**

Publication bias was investigated using funnel plots, and any asymmetry found was subjected to statistical investigation using the Egger's test (STATA 2009).

# **Data synthesis**

#### Dichotomous data

The review used ORs and 95% CIs based on the random-effects model, with pooling of data via the inverse variance method of weighting. Significance was set at P < 0.05. Where available, data from an interview with the child or adolescent were used; otherwise data from interviews with the parents were used. Where both endpoint and change data were available for the same outcome, the endpoint was presented. The number needed to treat (NNT) with 95% CIs was calculated (STATA 2009). For each comparison, a summary statistic of all those responding to treatment was calculated as a percentage of the total number of participants.

#### Continuous data

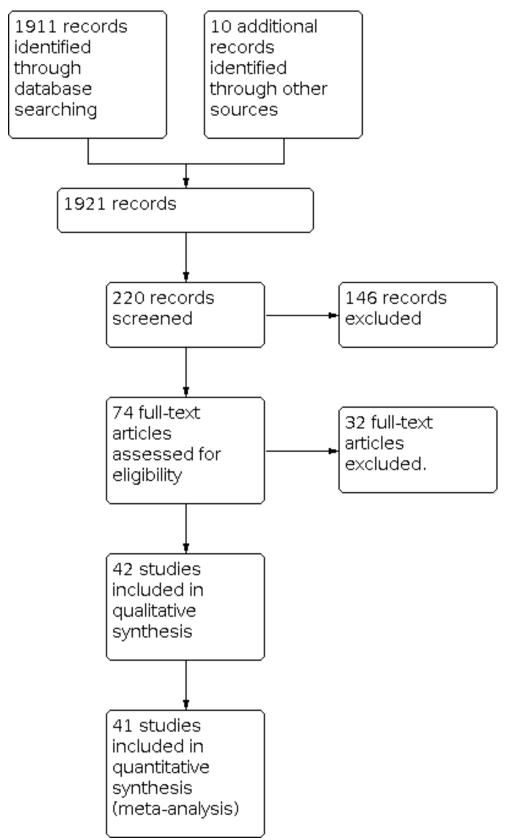
For those completing trials, analysis of continuous data, based on the random-effects model, was conducted. Continuous data, measured in different ways across studies but conceptually the same (i.e. measuring anxiety), were pooled using the SMD. Where possible, the child's or adolescent's own measures were used; otherwise parental or clinician reports of anxiety were used. Where both endpoint and change data were available for the same outcome, the endpoint was presented. Significance was set at P < 0.05. Pretreatment data were used to assess the influence of severity on outcome using meta-regression (STATA 2009).

# **Tables and figures**

Data were entered into the Review Manager programme and were presented graphically, so that the area to the left of the line of no effect indicated a favourable outcome for CBT. Tables were used to display characteristics of the studies included. Excluded studies were presented in a table with reasons for exclusion. A figure was used to summarise the risk of bias in the included studies (Figure 1 and Figure 2), and a PRISMA flow chart (Moher 2009; Figure 3) was included.



Figure 3. PRISMA Study flow diagram.





# Subgroup analysis and investigation of heterogeneity

- A subgroup analysis was undertaken to examine differences between individual, group and family/parental CBT formats.
- A second analysis was carried out to identify whether CBT was more effective than other active treatments, with subgroups of active controls and TAU.
- Last, maintenance of treatment gains was assessed using followup data of treatment versus W/L follow-up controls and CBT versus active controls.

The  $\text{Chi}^2$  test and the  $\text{I}^2$  statistic were used to assess statistical heterogeneity for all analyses and between groups. Significance was set at P < 0.1.

# **Sensitivity analysis**

Sensitivity analysis is the study of how the uncertainty in the output of an analysis can be apportioned to different sources of uncertainty in its inputs. Sensitivity analyses can therefore be carried out to test the robustness of decisions made in the review process. Sensitivity analyses were carried out where there was evidence of the following:

- Significant heterogeneity: Forest plots were inspected and each study in turn was examined to determine the source of any significant heterogeneity.
- Selection bias: Those studies judged to be at high risk of bias for selection bias were excluded from the main analysis.
- Allocation concealment: Those studies judged to be at high risk of bias for allocation concealment were excluded from the main analysis.
- We also undertook all of the above for the completer analyses (Analysis 1.6; Analysis 2.6; Analysis 3.4).

# RESULTS

# **Description of studies**

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

All studies were RCTs, and one was a school-based cluster-RCT (Dadds 1997). The active controls or the psychological placebo consisted of psycho-education (Herbert 2009; Kendall 2008; Masia-Warner 2007), bibliotherapy (Cobham 2012) and therapist and peer support (Ginsburg 2002).

# Results of the search

We found 1921 citations using the search strategy run in July 2012, of which 220 were abstracts of potential interest. Among the retrieved articles, 74 studies were relevant for further assessment, and 42 of these were included (Figure 3).

In cases where clarification or further data were needed, the trial authors were contacted. We contacted 20 trialists, and 16 replied with the relevant data.

# **Included studies**

Forty-one studies met the inclusion criteria for the main analysis of this review (Barrett 1996; Barrett 1998; Barrington 2005; Chalfant 2007; Cobham 2012; Dadds 1997; Dadds 1999; Flannery-Schroeder 2000; Galla 2012; Gil-Bernal 2009; Ginsburg 2002; Ginsburg 2012;

Hayward 2000; Herbert 2009; Hirshfeld-Becker 2010; Hudson 2009; Kendall 1994; Kendall 1997; Kendall 2008; Lau 2010; McNally Keehn 2012; Melfsen 2011; Mendlowitz 1999; Muris 2002; Nauta 2003; Olivares 2005; Reaven 2012; Sánchez-García 2009; Schneider 2011; Shortt 2001; Silverman 1999; Spence 2000; Spence 2006; Sung 2011; Walkup 2008; Waters 2009; Masia-Warner 2005; Masia-Warner 2007; Masia-Warner 2011; White 2012; Wood 2009).

#### Design

The studies were randomised controlled studies; some had three arms: one control group and two CBT formats (individual and group or family/parental). Two studies were pilot studies (Hayward 2000; Ginsburg 2002). One study tested a CBT protocol in very young children (4 to 7 years) (Hirshfeld-Becker 2010), and three studies included slightly older but still young children (Lau 2010; Waters 2009; Schneider 2011).

Eleven studies (Ginsburg 2002; Muris 2002; Barrington 2005; Masia-Warner 2007; Kendall 2008; Sánchez-García 2009; Herbert 2009; Hudson 2009; Sung 2011; Ginsburg 2012) were considered in the secondary analysis of the effectiveness of CBT compared with other active treatments or TAU. With regard to the comparison of CBT with medication, only one study (Walkup 2008) was included in this review; therefore no meta-analysis was possible.

Last, follow-up publications from studies involved in the main analysis were retained and included in a separate analysis. In total only four studies were eligible, involving waiting list controls at follow-up (Dadds 1999; Gil-Bernal 2009; Hayward 2000; Sánchez-García 2009). The follow-up period ranged from 6 months to 24 months (mean 13.5 months, SD 7.5). Other studies, which purported to show the persistence of the effects of CBT, did not include follow-up of controls.

# Sample sizes

The 41 studies involved 1034 participants and 921 controls. The numbers of participants in the studies are shown in Table 1.

# Settings

Most of the studies were initially conducted in research settings (i.e. university outpatient clinics); however, later studies were conducted in community clinics and inner city schools, and included various cultures such as Hong Kong Chinese (Lau 2010). No studies involved inpatients.

# **Participants**

Participants were recruited from the community via local advertisements or outpatient clinics. All met criteria for a psychiatric diagnosis of an anxiety disorder, ranging from mild to moderate, but not severe.

# **Conditions**

Anxiety disorders included in the studies were: separation anxiety disorder (SAD) 21; overanxious disorder (OAD) 6; social phobia (SOP) 20; panic disorder (PD) 4; generalised anxiety disorder (GAD) 17 and specific phobia (SP) 4.

Comorbid conditions were included and most often involved other secondary anxiety diagnoses: depression, conduct disorders (CDs) and oppositional defiant disorder (ODD) and attention-deficit/hyperactivity disorder (ADHD).



#### Interventions

The number of sessions varied, with a mean of 13.1 (SD 2.9) and a range of 9 to 20. Active controls included a psychological placebo such as educational and bibliotherapy/supportive work with no elements of CBT. TAU was described as including family therapy, play therapy, supportive psychotherapy, psychodynamic psychotherapy and non-CBT eclectic approaches. In this review the only medication included in a trial of CBT versus medication and in combination versus placebo was sertraline.

The 41 studies involved 1038 participants and 768 controls. Most of the studies were initially conducted in research settings (i.e. university outpatient clinics); however, later studies were undertaken in community clinics and inner city schools and included differing cultures such as Hong Kong Chinese (Lau 2010). No studies involved inpatients. Comorbid conditions were included and most often involved other secondary anxiety diagnoses: depression, CDs and ODD and ADHD. Participants were recruited from the community via local advertisements or outpatient clinics. All met criteria for a psychiatric diagnosis of anxiety disorder; the range was from mild to moderate, and severe cases were not included.

#### **Outcomes**

Valid and reliable assessment is regarded as essential to the successful application of CBT (Thyrer 1991). All studies used semistructured instruments to diagnose anxiety disorders: ADIS (the Anxiety Disorder Interview Schedule) (Barrett 1996; Barrett 1998; Barrington 2005; Dadds 1997; Flannery-Schroeder 2000; Ginsburg 2002; Ginsburg 2012; Hayward 2000; Herbert 2009; Hudson 2009; Kendall 1994; Kendall 1997; Kendall 2008; Lau 2010; Nauta 2003; Olivares 2005; Silverman 1999; Spence 2000; Spence 2006; Masia-Warner 2005; Masia-Warner 2007; Masia-Warner 2011; Reaven 2012; Sánchez-García 2009; Waters 2009; White 2012; Wood 2009); the Kiddie-Schedule for Affective Disorders and Schizophrenia (Hirshfeld-Becker 2010; Lau 2010); DISCAP (Diagnostic Interview Schedule for Children, Adolescents and Parents) (Shortt 2001; Mendlowitz 1999) or the Kinder-DIPS (Schneider 2011). Only one study did not use a structured interview (Sung 2011). ADIS is administered separately to parents and child, and results are then combined for an overall diagnosis; however, several studies used approaches different from this practice to determine diagnosis (parents only) (Shortt 2001; Spence 2000) (children only) (Olivares 2005) and treatment outcomes (parents only) (Flannery-Schroeder 2000; Kendall 1994; Kendall 1997; Shortt 2001; Spence 2000; Spence 2006).

Anxiety symptoms were assessed using a wide range of rating scales, making comparisons difficult; some rating scales were used in only one or two studies. Scales that were used frequently include the following: the Revised Children's Manifest Anxiety Scale (RCMAS) (Dadds 1997; Flannery-Schroeder 2000; Kendall 1994; Kendall 1997; Kendall 2008; Mendlowitz 1999; Shortt 2001; Silverman 1999; Spence 2000; Spence 2006); the Fear Survey for Children Revised (FSSC-R) (Barrett 1996; Barrett 1998; Kendall 1994; Nauta 2003; Silverman 1999); the Social Anxiety Scale for Adolescents (SAS-A) (Ginsburg 2002; Herbert 2009; Olivares 2005); the Social Phobia and Anxiety Inventory for Children (SPAI) (Hayward 2000; Herbert 2009; Olivares 2005); the Mood and Anxiety Symptom Scale (MASQ) (Kendall 2008); the Spence Child Anxiety Scale, child and parent versions (SCAS) (Hudson 2009; Lau

2010;; Nauta 2003; Spence 2000; Spence 2006); the Child Behavior Checklist (CBCL) (Barrett 1996; Barrett 1998; Dadds 1997; Flannery-Schroeder 2000; Gil-Bernal 2009; Kendall 1994; Kendall 2008; Nauta 2003; Shortt 2001; Silverman 1999; Spence 2006) and the Clinical Global Impressions scale (Herbert 2009; Hirshfeld-Becker 2010). All the measures used have been assessed as having reasonably good psychometric properties in terms of reliability, validity and efficacy in measuring internalising symptoms (Myers 2002). In view of poor agreement between child and parent reporting of anxiety symptoms (Grills 2003), child self-report ratings were preferred when data were entered into the meta-analysis. Data on the CBCL were presented in two forms—raw scores and transformed scores —which did not allow direct comparative analysis.

#### **Excluded studies**

Eleven studies were excluded (Blagg 1984; King 1998; Last 1998; Lowry-Webster 2003; Mifsud 2005; Olivares 2007; Ordeig 2004; Sofronoff 2005; Warren 1984) because some participants did not have verifiable anxiety diagnoses, or they did not provide a primary outcome measure. Four studies involved SOPs only or a large majority of simple phobias or participants with OCD, and the authors of these studies were unable to provide the data with these participants removed (Cornwall 1996; Menzies 1993; Silverman 1999b; Sofronoff 2005). Nine studies were primarily concerned with issues of comorbidity and/or presented data previously reported elsewhere or were preliminary studies or follow-up studies (Flannery-Schroeder 1998; Flannery-Schroeder 2005; Garcia-Lopez 2006; Forman 2007; Holmes 2006; Kendall 2001; Kendall 2009; Suveg 2009; Wood 2009b). In one foreign language study, cases were allocated on an alternating basis (Joorman 2002), and in another study an active but unspecified control treatment was administered (Beidel 2000). Two studies were excluded because the intervention (Social Effectiveness Therapy for Children and Adolescents) was primarily a behavioural treatment rather than CBT (Baer 2005; Beidel 2007).

# Risk of bias in included studies

# Allocation

Ten studies provided a clear description of the process of adequate sequence generation (Walkup 2008; Masia-Warner 2011; Reaven 2012; White 2012; Ginsburg 2012; Ginsburg 2002; Hudson 2009; Kendall 2008 Spence 2006; Melfsen 2011). In six studies (Herbert 2009; Flannery-Schroeder 2000; Galla 2012; Schneider 2011; Sung 2011; Wood 2009), restricted randomisation was used, whereby participants were allocated in blocks. In the pilot study (Hayward 2000), participants were recruited to the control group following the process of randomisation, and the results were reported as from a single control group. One study used coin tossing as a means of randomising allocation (Spence 2006), and in another the process of randomisation involved picking numbers out of a box (White 2012). In other included studies, the process of sequence generation was unclear. A sensitivity analysis (not shown) for those studies reporting clear processes of randomisation showed similar direction of results as the main analysis with all studies included, with CBT being effective versus W/L controls for the remission of anxiety diagnoses (OR 0.1, 95% CI 0.05 to 0.18, Z = 7.48, P < 0.00001).

# **Blinding**

Thirty-two of the studies in the main analysis and the subanalyses had blinded outcome evaluations (Barrett 1996; Barrett



1998; Barrington 2005; Cobham 2012; Dadds 1997; Dadds 1999; Galla 2012: Ginsburg 2002; Hayward 2000; Herbert 2009; Hirshfeld-Becker 2010; Hudson 2009; Kendall 1994; Kendall 2008; Lau 2010; McNally Keehn 2012; Melfsen 2011; Muris 2002; Reaven 2012; Schneider 2011; Shortt 2001; Silverman 1999; Spence 2000; Spence 2006; Sánchez-García 2009; Sung 2011; Walkup 2008; Masia-Warner 2005; Masia-Warner 2007; Masia-Warner 2011; Waters 2009;; White 2012; Wood 2009). In the remainder of included studies, it was unclear whether outcome assessors were blinded to the treatment status of participants, leading to the possibility of a moderate to severe degree of detection bias in these studies.

Performance bias was assessed only in the trials of CBT versus active treatment or TAU, as plainly this was not possible or sensible in the case of CBT versus W/L controls. In the former studies, measures were taken and described to ensure comparability of treatments, so that non-specific confounders such as length of treatment, etc, did not influence the outcome in either arm of the trial.

# Incomplete outcome data

Overall accounting for participants was complete; however, a CONSORT flow diagram was used in only 11 studies (11/41 = 26.8%). No difference was noted with regard to withdrawals or dropouts between CBT and W/L controls (Z = 0.27, P = 0.78). No exclusions were reported, and a low but consistent rate of reported dropouts was described (CBT 10.8% vs W/L 10.3%).

# **Selective reporting**

Reporting bias, which refers to any systematic difference between reported and unreported findings, is regarded as one of the most substantial biases affecting results from individual studies (Chan 2005). Systematic examination revealed no cases of unreported findings in the studies included in this meta-analysis.

# Other potential sources of bias

#### **Treatment protocols**

Use of a protocol not only allows reproducibility—an important goal of research and, ultimately, for introduction into clinical practice—it should prevent unintentional differences or indeed 'drift', but not necessarily documented changes away from the core treatment design. In most of the studies, a defined, published protocol was used and supervision was included at various stages of treatment. In two studies (Barrett 1998; Kendall 1997), a small number of participants were treated flexibly, but the treatment delivered was in accord with a manual. Modular but documented CBT was delivered in three studies (Galla 2012; Ginsburg 2012; White 2012). Most of the therapists were post-doctorate psychologists.Individual, group and family formats

were included. Groups were often staged according to age, for instance, as older and younger children. Family formats differed and included some sessions with the child or adolescent; others involved sessions with parent(s) or guardian(s) separately. Considerable variation was noted in length of treatment (from 7.5 hours (Ginsburg 2002) to 27 hours (Flannery-Schroeder 2000)) and in the number of sessions (mean 13.2, SD 2.9, range 9 to 20). Five studies (Dadds 1997; Ginsburg 2002; Olivares 2005; Galla 2012; Ginsburg 2012) were school based, and others were clinic based. Controls were participants who either (1) remained on the waiting list without treatment for anxiety before they were offered CBT, or (2) received a form of treatment with a therapeutic element that was not CBT based (active control) or were given only attention or TAU.

#### **Effects of interventions**

See: Summary of findings 1 CBT compared to wait-list for children and adolescents with anxiety disorders; Summary of findings 2 CBT compared to active controls for children and adolescents with anxiety disorder; Summary of findings 3 CBT compared to treatment as usual (TAU) for children and adolescents with anxiety disorder

# Comparison one: CBT versus waiting list

# **Primary outcomes**

#### 1.1 Remission of anxiety diagnoses (ITT analysis)

Twenty-six studies (Barrett 1996; Barrett 1998; Chalfant 2007; Cobham 2012; Dadds 1997; Flannery-Schroeder 2000; Galla 2012; Gil-Bernal 2009; Hayward 2000; Hirshfeld-Becker 2010; Kendall 1994; Kendall 1997; Lau 2010; Melfsen 2011; McNally Keehn 2012; Nauta 2003; Olivares 2005; Schneider 2011; Shortt 2001; Silverman 1999; Spence 2000; Spence 2006; Masia-Warner 2005; Masia-Warner 2011; Waters 2009; Wood 2009) were included in the final analysis on remission of any anxiety diagnosis. The ITT analysis included 808 CBT participants and 542 controls, with a response rate for remission of any anxiety diagnosis of 58.9% for CBT versus 16 % for controls (OR 7.85, 95% CI 5.31 to 11.60) (Analysis 1.1). Most of the studies (72%,18 out of 25) reported findings in the direction of showing clear benefit for CBT (95% CI does not cross 1, indicating equivalence of response) (Analysis 1.1; Figure 4). Evidence of heterogeneity was found ( $I^2 = 30\%$ , Chi<sup>2</sup> = 44.58, d.f. = 31, P = 0.05). Heterogeneity was investigated using metaregression (STATA 2009), which showed that only modest variability was accounted for by participant age (1.06%), sex (5.32%), level of comorbidity (6.7%), initial level of anxiety (5.5%) or number of CBT sessions (0.23%). No difference in outcome was noted for the differing formats of CBT — individual, group and family (Chi<sup>2</sup> = 0.06, d.f. = 2; P = 0.97) — or for heterogeneity between formats ( $I^2 = 0\%$ ).



Figure 4. Forest plot of comparison: 1 CBT versus wait-list, outcome: 1.1 Remission of anxiety diagnoses (ITT analysis).

	CBT		Wait-li			Odds Ratio	Odds Ratio
Study or Subgroup	Events T	otal	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Individual CBT							
Barrett 1996	16	28	4	13	4.7%	3.00 [0.74, 12.11]	
Flannery-Schroeder 2000	7	18	0	7	1.5%	9.78 [0.48 , 197.85]	
Galla 2012	15	22	1	18	2.5%	36.43 [4.01 , 331.19]	
Kendall 1994	17	27	1	20	2.6%	32.30 [3.74, 279.31]	
Kendall 1997	32	60	11	43	7.4%	3.32 [1.42 , 7.80]	
McNally Keehn 2012	7	12	0	10	1.4%	28.64 [1.37 , 600.41]	
Nauta 2003	20	37	1	10	2.5%	10.59 [1.22, 92.25]	
Subtotal (95% CI)	20	204	-	121	22.6%	7.92 [3.37, 18.63]	
Total events:	114	204	18	121	22.070	7.52 [5.57 , 10.05]	_
Heterogeneity: Tau <sup>2</sup> = 0.42; (		6 (D – C		0/_			
Test for overall effect: $Z = 4$ .		•	).1/), I <sup>2</sup> – 34 <sup>3</sup>	/0			
1.1.2 Group CBT							
Barrett 1998	9	23	3	10	4.0%	1.50 [0.31 , 7.36]	
Chalfant 2007	20	28	0	19	1.5%	94.06 [5.08 , 1741.83]	<del></del>
Dadds 1997	35	46	27	48	7.2%	2.47 [1.02 , 6.00]	
Flannery-Schroeder 2000	7	13	0	7	1.4%	17.31 [0.82 , 365.21]	_
Gil-Bernal 2009	3	6	0	5	1.3%	11.00 [0.43 , 284.30]	<del></del>
Hayward 2000	6	12	1	22	2.3%		<del>                                     </del>
Lau 2010		24	0	21	1.5%	21.00 [2.10 , 210.14]	<del></del>
	16					83.47 [4.49 , 1552.94]	
Masia-Warner 2005	12	21	4	21	4.7%	5.67 [1.41 , 22.76]	
Melfsen 2011	7	21	1	23	2.5%	11.00 [1.22 , 99.26]	<del></del>
Olivares 2005	10	17	0	17	1.5%	49.00 [2.53 , 948.62]	
Silverman 1999	16	37	5	19	5.5%	2.13 [0.64 , 7.16]	+-
Spence 2000	23	36	0	7	1.5%	26.11 [1.38 , 493.87]	<del></del>
Spence 2006	13	20	3	23	4.2%	12.38 [2.70 , 56.73]	_ <del>-</del>
Subtotal (95% CI)		304		242	39.2%	7.86 [3.83 , 16.12]	•
Total events:	177		44				
Heterogeneity: $Tau^2 = 0.68$ ; C Test for overall effect: $Z = 5$ .		,	= 0.04); I <sup>2</sup> = 4	15%			
1.1.3 Family/Parental CBT							
Barrett 1996	21	25	5	13	4.1%	8.40 [1.79, 39.44]	
Barrett 1998	7	17	3	10	3.7%	1.63 [0.31, 8.61]	
Cobham 2012	18	23	0	12	1.5%	84.09 [4.26 , 1659.99]	
Gil-Bernal 2009	2	6	0	5	1.3%	6.11 [0.23 , 162.73]	
Hirshfeld-Becker 2010	16	30	5	29	5.5%	5.49 [1.65 , 18.23]	
Masia-Warner 2011	11	20	1	20	2.5%	23.22 [2.59 , 208.61]	
Nauta 2003	23	39	1	10	2.5%	12.94 [1.49 , 112.44]	
Schneider 2011	16	21	3	22	4.0%	20.27 [4.18 , 98.23]	
Shortt 2001	33	54	2	17	4.0%	11.79 [2.44, 56.85]	
Spence 2000	15	17	0	7	1.3%	93.00 [3.95 , 2189.96]	
Waters 2009	14	31	2	11	3.7%	3.71 [0.69, 20.04]	
Wood 2009	9	17	3	23	4.1%	7.50 [1.60 , 35.07]	
Subtotal (95% CI)	Э	300	J	179	38.3%	8.65 [5.01, 14.92]	
Total events:	185	300	25	1/9	JU.J 70	0.05 [5.01 , 14.92]	▼
Heterogeneity: Tau <sup>2</sup> = 0.08; (		- 11 (D -		00/_			
Test for overall effect: $Z = 7$ .		,	- v.svj, r S	70			
Total (95% CI)		808		542	100.0%	7.85 [5.31 , 11.60]	
Total events:	476	-55	87		, , ,	[, 11.00]	•
Total events:							



# Figure 4. (Continued)

Heterogeneity:  $1au^2 = 0.54$ ;  $CnI^2 = 44.58$ , CnI = 31 (P = 0.05);  $I^2 = 30\%$  Test for overall effect: Z = 10.34 (P < 0.00001) Test for subgroup differences:  $Chi^2 = 0.06$ , df = 2 (P = 0.97),  $I^2 = 0\%$ 

#### 1.2 Acceptability: participants lost to follow-up

No difference was reported between CBT and W/L controls in terms of the rate of those lost to follow-up (Analysis 1.2), indicating a similar degree of acceptability. In the CBT group, the rate of loss to follow-up was 10.6% (82 out of 771) versus 10.6% (56 out of 550) in the control group (OR 0.94, 95% CI 0.58 to 1.51). Test for overall effect: Z = 0.27. P = 0.79.

#### Secondary outcomes

#### 1.3 Reduction in anxiety symptoms

Thirty studies (Barrett 1996; Barrett 1998; Chalfant 2007; Cobham 2012; Dadds 1997; Gil-Bernal 2009; Flannery-Schroeder 2000; Galla 2012; Hayward 2000; Hirshfeld-Becker 2010; Kendall 1994; Kendall 1997; Lau 2010; Melfsen 2011; McNally Keehn 2012; Mendlowitz 1999; Nauta 2003; Olivares 2005; Sánchez-García 2009; Schneider 2011; Shortt 2001; Silverman 1999; Spence 2000; Spence 2006; Masia-Warner 2005; Masia-Warner 2011; Muris 2002; Waters 2009; White 2012; Wood 2009) were included in the final analysis on reduction of anxiety symptoms. The standard mean difference (SMD) was -0.98 (95% CI -1.21 to -0.74, Z = 8.21, P < 0.00001) with significant heterogeneity ( $I^2 = 75\%$ , Chi<sup>2</sup> = 140.07, d.f. = 35, P < 0.00001) (Analysis 1.3). Heterogeneity was investigated using meta-regression (STATA 2009), but no significant results were found for the covariates of age, sex, and length of treatment. Evidence revealed a significant subgroup difference between individual, group and family/parental formats of CBT (Chi<sup>2</sup> = 7.48 d.f. = 2, P = 0.02), with considerable heterogeneity ( $I^2 = 73.3\%$ ). Inspection of the forest plot and of the summary statistics for each subgroup suggests that both group and family/parental formats of CBT produce greater reduction of symptoms than is produced by individual CBT.

# 1.4 Remission of anxiety diagnoses - long-term follow-up

Three studies examined CBT participants and control follow-ups (Dadds 1999; Gil-Bernal 2009; Hayward 2000) at 24, 6 and 12 months, respectively (mean 13.5 months, SD 7.5). In terms of remission of anxiety diagnoses, a non-significant effect was noted (OR 3.22, 95% CI 0.96 to 10.75, Z = 1.90, P = 0.06) ( $I^2 = 38\%$ ) (Analysis 1.4).

# 1.5 Reduction in anxiety symptoms—long-term follow-up

With just four studies, a non-significant effect was noted in the reduction of symptoms (SMD = -1.55, 95% CI -3.22 to 0.11, Z = 1.83, P = 0.07) with great heterogeneity (Chi<sup>2</sup> = 49.69, d.f. 3, P = 0.00001,  $I^2 = 94\%$ ) (Analysis 1.5).

#### Comparison two: CBT versus active controls

#### **Primary outcomes**

#### 2.1 Remission of anxiety diagnoses (ITT analysis)

Six studies examined CBT versus active controls with respect to remission of anxiety diagnoses, which were non-significant (OR 1.51,95% CI 0.77 to 2.96, Z = 1.21, P = 0.23) (Analysis 2.1).

#### 2.2 Acceptability: participants lost to follow-up

Five studies examined CBT versus active controls with respect to participants lost to follow-up, which were significant, favouring CBT over active controls (OR 0.52, 95% CI 0.31 to 0.91, Z = 2.28, P = 0.02) (Analysis 2.2).

#### Secondary outcomes

#### 2.3 Reduction in anxiety symptoms

Eight studies examined reduction in anxiety symptoms (SMD = -0.50, 95% CI -1.09 to 0.09); findings were non-significant (Z = 1.66, P = 0.1) (Analysis 2.3). The significant heterogeneity (I<sup>2</sup> = 86%, P < 0.00001) was reduced to 3% with the removal of one study (Masia-Warner 2007).

# 2.4 Remission of anxiety diagnoses—long-term follow-up

Two studies examined CBT versus active controls with respect to remission of anxiety diagnoses at follow-up; findings were significant, favouring CBT over active controls (OR 2.03, 95% CI 1.22 to 3.36, Z = 2.74, P = 0.006) (Analysis 2.4).

# 2.5 Reduction in anxiety symptoms - long-term follow-up

Four studies examined CBT versus active controls with respect to remission of anxiety symptoms at follow-up; findings were non-significant (SMD -0.92, 95% CI -2.12 to 0.29, Z = 1.49, P = 0.14) ( Analysis 2.5). The significant heterogeneity ( $I^2 = 96\%$ , P < 0.00001) was reduced to 0% with the removal of one study (Hudson 2009).

# Comparison three: CBT versus treatment as usual (TAU)

# **Primary outcomes**

# 3.1 Remission of anxiety diagnoses (ITT analysis)

Only two studies examined CBT versus TAU with respect to remission of anxiety diagnoses; findings were non-significant (OR 0.53, 95% CI 0.23 to 1.25, Z = 1.03, P = 0.3) (Analysis 3.1).

# 3.2 Acceptability: participants lost to follow-up

Two studies examined CBT versus TAU with respect to participants lost to follow-up; findings were non-significant (OR 1.01, 95% CI 0.31 to 3.31, Z = 0.02, P = 0.98) (Analysis 3.2).



# Secondary outcomes

#### 3.3 Reduction in anxiety symptoms

Three studies examined reduction in anxiety symptoms; findings were non-significant (SMD = -0.19, 95% CI -0.79 to 0.40, Z = 0.64, P = 0.52) (Analysis 3.3).

#### 3.x Remission of anxiety diagnoses - long-term follow-up

No data were available.

# 3.x Reduction in anxiety symptoms - long-term follow-up

No data were available.

# Comparisons four and five: CBT versus medication and combination versus placebo

Only one study was available (Walkup 2008), so no meta-analysis was possible. This large multi-centre comparative study of CBT versus medication with more than 400 participants showed that both CBT and sertraline—a selective serotonin re-uptake inhibitor (SSRI) antidepressant—were more effective than placebo in treating paediatric anxiety disorders, and that the combination of CBT with medication was more effective than CBT or medication alone.

#### Sensitivity analyses

# CBT versus waiting list: completers-only analysis

#### 1.6 Remission of anxiety diagnoses

Twenty-six studies examined CBT versus waiting list with respect to remission of anxiety diagnoses; findings were highly significant (OR 11.09, 95% CI 7.47 to 16.45, Z = 12.24, P = < 0.0001) with no difference between formats—individual, group and family/parental (Chi<sup>2</sup> = 0.03, d.f. 2, P = 0.99,  $I^2 = 0\%$ ) (Analysis 1.6).

#### CBT versus active controls: completers-only analysis

# 2.6 Remission of anxiety diagnoses

Five studies examined CBT versus active controls with respect to remission of anxiety diagnoses; findings were significant (OR 2.18, 95% CI 1.31 to 3.64, Z = 2.98, P = 0.003) (Analysis 2.6).

# CBT versus treatment as usual (TAU): completers-only analysis

# 3.4 Remission of anxiety diagnoses

Only two studies examined CBT versus TAU with respect to remission of anxiety diagnoses; findings were non-significant (OR  $1.10\,95\%$  CI 0.45 to 2.68, Z = 0.2, P = 0.84) (Analysis 3.4).

# Other analyses

#### CBT for those with autism spectrum disorders (ASDs)

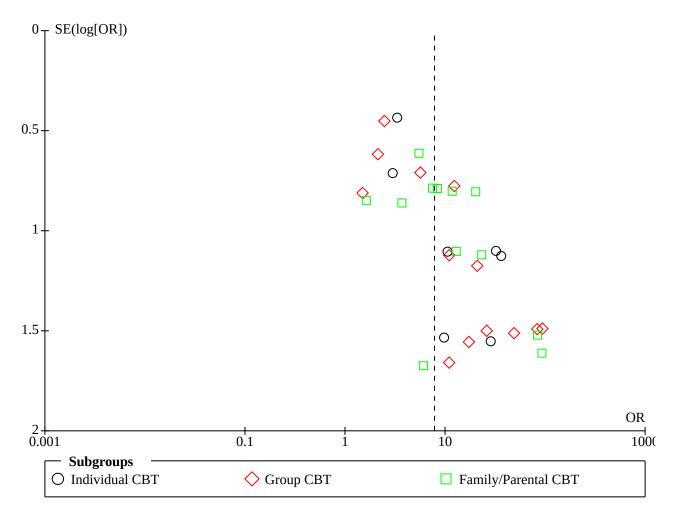
Post hoc analyses of those with high-functioning ASD revealed a significant reduction in anxiety diagnoses compared with W/L controls (Chalfant 2007; McNally Keehn 2012; Schneider 2011; Wood 2009). Odds ratio was 16.74 (95% CI 6.30 to 44.48, Z = 5.65, P < 0.0001), with a significant reduction in anxiety symptoms (Chalfant 2007; McNally Keehn 2012; White 2012; Wood 2009) (SMD -1.6, 95% CI -3.00 to -0.2, Z = 2.24, P = 0.03,  $I^2 = 95\%$ ), indicating a positive outcome of CBT for children and adolescents with ASD.

#### **Publication Rias**

With respect to remission of anxiety diagnoses, an indication of publication bias was shown by an asymmetrical funnel plot (Figure 5), confirmed by a highly significant Egger's test (bias -2.03, t = -3.95, P < 0.001). The funnel plot (with Egger's regression line, not shown) indicates smaller studies (those with larger standard errors) tending to have larger (more beneficial) ORs -a finding compatible with publication bias. Although funnel asymmetry may indicate selection biases, in particular publication bias, other explanations include citation bias, true heterogeneity, with size of effect differing according to study size, intensity of intervention and differences in underlying risk. Data irregularities, poor methodological design of small studies and inadequate analyses may also result in asymmetry. A contour-enhanced funnel plot (Peters 2008), however, showed that the studies in this review were in the region of statistical significance, indicating that the cause of the asymmetry was more likely to involve factors other than publication bias, such as variable study quality.



Figure 5. Funnel plot of comparison: 1 CBT versus wait-list, outcome: 1.1 Remission of anxiety diagnoses (ITT analysis).



# DISCUSSION

# **Summary of main results**

Since the last Cochrane review (James 2005), the number of studies available for review increased considerably from 18 to 41, with more than two times the total number of participants. This larger, more adequately powered review should increase confidence in the findings. The present systematic review indicates that cognitive behavioural therapy (CBT) is a useful treatment for anxiety disorders in children and adolescents. Using conservative intention-to-treat (ITT) criteria, the remission rate for anxiety disorders (58.9% for CBT vs 16% for controls) is similar to that reported in a meta-analysis by Cartwright-Hatton (Cartwright-H 2004). The number needed to treat (NNT) using conservative ITT data is 3.0 (95% CI 1.75 to 3.03), which means that for one additional participant to attain remission from anxiety disorder using CBT, one needs to treat thre participants. In terms of medical and psychological treatments, this is a very acceptable finding (Laupacis 1988), allowing one to recommend CBT in clinical practice. Research trials now include non-specialist therapists in community clinic settings and inner city schools (Ginsburg 2012), suggesting that the findings are generalisable.

This review has shown CBT to be superior to waiting list controls; however, the notion that CBT might be superior to active controls, including psycho-education, other supportive interventions, bibliotherapy and treatment as usual, was not confirmed, although the sensitivity analysis with completer-only participants was significant for remission of anxiety diagnoses for CBT versus active controls ( $Z=2.98,\ P=0.003$ ) (Analysis 2.6). Evidence is limited, however, by the small number of studies.

The question whether CBT is superior to medication, or indeed if there is any specificity to treatment response, remains unclear with only one study (Walkup 2008), although a study of a behavioural treatment with fluoxetine showed a similar pattern of results (Beidel 1995). Further work in this area is needed.

An important question is the durability of treatment effects. Evidence, unfortunately, is limited. Three studies examining the longitudinal reduction in anxiety diagnoses compared with follow-up W/L controls (Dadds 1999; Hayward 2000; Gil-Bernal 2009) with only 124 participants showed a non-significant treatment effect (OR 3.22, 95% CI 0.96 to 10.75, Z=1.89, P=0.06)( Analysis 1.4)These studies were of relatively short duration. Many studies report the persistence of the treatment effects of CBT over periods of 2 to



24 months, and one up to eight years (Saavedra 2010); however, these studies were not controlled follow-up studies; therefore, one cannot discount the natural remission rate.

Some uncertainty remains as to whether younger patients can use or benefit from CBT. Children need a certain level of cognitive maturity to participate in the treatment (Kendall 1990b), and in general they need to be able to use de-centring techniques such as narratives or stories. It was not clear, for instance, whether children younger than six years of age were capable of these cognitive manoeuvres. A recent study (Hirshfeld-Becker 2010) included in this review found positive effects in children younger than six years. It is likely that children respond more to the behavioural than to the demanding cognitive elements of CBT (Essau 2004). Researchers aware of the problems of using CBT with very young children have instead involved parents, directly or indeed entirely (Cartwright-Hatton 2011).

It is recognised that children and adolescents with autism spectrum disorders (ASDs) have high rates of anxiety disorders (White 2009), particularly social phobia (Settipani 2012). Several trials are exploring the use of CBT for anxiety disorders in children and adolescents with ASD (Chalfant 2007; McNally Keehn 2012; Reaven 2012; Sung 2011; Wood 2009; White 2012), but none have included those with an intellectual disability specifically. In a review, Lang (Lang 2010) noted the need for CBT to be modified for individuals with ASD by adding interventional components typically associated with applied behaviour analysis (e.g. systematic prompting and differential reinforcement). It is interesting to note that a post-hoc analysis suggests that CBT is particularly effective for children and adolescents with ASD.

This review did not confirm previous findings that severity of anxiety and comorbidity were related to outcome (Liber 2010); indeed age, severity of the initial anxiety disorder, gender, and the number of sessions did not substantially affect the outcome. It has to be noted, however, that the numbers of sessions in this review were restricted. Indeed, one study of brief CBT found a positive outcome (Gallagher 2004) with only three sessions but was not included, as per the original exclusion criteria.

Last, this review has shown that CBT is an acceptable form of therapy, as shown by comparison of the rates of those lost to follow-up between CBT and control groups.

# Overall completeness and applicability of evidence

# **Demographics and clinical characteristics**

Apart from one pilot study (Hayward 2000), all studies included participants of both sexes and covered a range of socioeconomic classes. Nine studies did not give details on ethnicity (Barrett 1996; Barrett 1998; Hayward 2000; Mendlowitz 1999; Nauta 2003; Olivares 2005; Spence 2000; Spence 2006; Schneider 2011). Although overall age ranged from 4 to 18 years, only three studies included participants younger than the age of 7 (Hirshfeld-Becker 2010; Lau 2010; Silverman 1999), which means that younger children were relatively under-represented.

It is of note that only community or outpatient participants were included in these studies, so it is not possible to extrapolate the results to patients with the most severe cases of anxiety disorder, who might have received day patient or inpatient treatment. Comorbid disorders such as depression, other anxiety

disorders, ADHD and conduct disorders were included, allowing more generalised conclusions to be drawn and comparison made with more routine clinical practice. Since the last Cochrane review, a number of studies (Chalfant 2007; McNally Keehn 2012; Reaven 2012; Sung 2011; White 2012; Wood 2009) have focused on children and adolescents with high-functioning ASD. CBT appears effective in these groups of participants. A considerable limitation, however, is the exclusion of participants with learning disabilities, who were not represented in this review.

The consistency of the rate of remission of anxiety diagnosis using CBT versus waiting list controls in this review and other reviews and meta-analyses (Compton 2004; Cartwright-H 2004; James 2005; Scott 2005; Silverman 2008; Seligman 2011; Reynolds 2012) is encouraging and suggests that this is a fairly robust finding. Evidence for CBT versus active controls or TAU is negative, but a smaller number of studies are available. Only one study (Walkup 2008) looked at the comparative efficacy of CBT versus pharmacotherapy and combination therapy (Walkup 2008); therefore it is clear that further work is needed in this area.

The number of follow-up studies with controls is very limited (n = 4), making it difficult to draw any conclusions. The findings are non-significant. A number of studies show that the effects of CBT appear to persist, but the evidence is limited without controls. Most of the studies offer CBT to W/L controls after completion of the study.

# Quality of the evidence

In considering these findings, several methodological issues need to be addressed. The review identified 41 studies (n = 41) with a reasonably large number of study participants (1806). Most of these studies (78%) were in the direction of showing benefit for CBT. For remission of anxiety diagnosis (OR 0.12, 95% CI 0.08 to 0.18), an estimate of effect size is medium, according to Cohen's criteria (Cohen 1988), with tight confidence intervals suggesting some uniformity in the findings.

Methodological shortfalls were noted in some studies, most notably inadequate details on the process of randomisation and allocation. In the previous review (James 2005), reporting of those lost to therapy was inadequate; however, more recent studies have adopted the revised CONSORT criteria for RCTs (Consolidated Standards of Reporting Trials, http://www.consort-statement.org) (Altman 2012). It is not possible in this type of research to blind the participants—an obvious potential for bias; however, the evaluations were carried out blind, although details of this processing in several cases were not made clear.

With respect to remission of anxiety diagnoses, evidence of moderate heterogeneity (Chi² = 44.58, d.f. = 31, P = 0.05, I² = 30%) was noted across all formats, with no subgroup heterogeneity (I² = 0%), indicating a similar degree of heterogeneity across formats for the delivery of CBT—individual, group and family/parental. Uniformity was noted in the variability in effect sizes, with no particular studies contributing to the heterogeneity as shown by sensitivity analyses. Meta-regression (STATA 2009) showed that only modest variability was accounted for by participant age (1.06%), sex (5.32%), level of comorbidity (6.7%) or initial level of anxiety (5.5%) or by the number of CBT sessions (0.23%).

CBT is not a uniform intervention; considerable clinical variations are possible and hence heterogeneity in the methods of delivering



CBT is noted, even within major groupings. For instance, within the family/parental CBT group, some therapists see whole families, others only parents, and family involvement may include elements of CBT or psycho-education. Variations in the CBT programmes are evident in group and individual CBT studies with regard to the extent of cognitive versus behavioural work, and when and how this is carried out. One question, particularly with regard to anxiety symptoms, is whether the heterogeneity is due, in part, to the differing anxiety diagnoses such as generalised anxiety disorder (GAD), social phobia (SOP), etc.; however, it was not possible to analyse the diagnoses separately, although some studies focused specifically on social phobia (Gil-Bernal 2009; Hayward 2000; Masia-Warner 2005).

One of the sources of heterogeneity, particularly in comparisons of anxiety symptoms, is the large number of rating scales used, some of which measure non-specific emotional symptoms rather than anxiety symptoms. Therefore, when studies are compared in the future, it would be important to use fewer, but more standardised, anxiety rating scales. A naturalistic problem is the wide range of anxiety disorders covered in this review under the term *anxiety disorders*, which may account for some of the heterogeneity. Subgroup analysis by diagnosis was not possible.

Although there was an indication of publication bias with an asymmetrical funnel plot and a highly significant Egger's test, further analysis with a contour-enhanced funnel plot (Peters 2008) with all studies in the area of significance points, instead, to study variability as the cause of the asymmetrical funnel plot.

# Potential biases in the review process

Meta-analyses are limited by the robustness of any search method. The electronic search was thorough and large in scale with broad parameters. In this review we were able to obtain all the referenced papers, and we were able to be in contact with leading researchers in the field. Non-English studies were also included.

The selection criteria may have limited the review as the length of the study was arbitrarily set at nine sessions. One study of brief CBT (Gallagher 2004) was reported to be effective, but as this study only involved three sessions, it was excluded. The analysis of studies with three arms—CBT in two formats versus waiting list controls or active controls—is problematic in that double counting of any group is wrong. We chose to split the controls sample into two equal halves between the CBT groups. However, analysis with some differing methods (lumping together) did not alter the outcome of the analyses.

# Agreements and disagreements with other studies or reviews

A previous Cochrane review (James 2005) of eighteen studies with 498 participants and 311 controls found a response rate for remission of any anxiety diagnosis using an ITT analysis of 56% for CBT versus 28.2% for controls with the number needed to treat (NNT) of 3.0 (95% CI 2.5 to 4.5). For reduction in anxiety symptoms, the standardised mean difference (SMD) was -0.58 (95% CI -0.76 to -0.40). Overall, very considerable agreement is evident between meta-analyses of CBT for the treatment of anxiety disorders in children and adolescents (Cartwright-H 2004; Compton 2004; James 2005; Silverman 2008; Seligman 2011; Reynolds 2012). Using conservative ITT criteria, the remission rate for anxiety

disorders of 58.9% for CBT versus 16 % for controls is similar to the findings of the meta-analysis reported in the previous Cochrane review (James 2005), The finding that no advantage was derived, for instance, from adding parent training to individual CBT was in line with other meta-analyses (Silverman 2008; Reynolds 2012) and a recent review (Breinholst 2012). One review in assessing 10 anxiety studies found moderate effect sizes (ESs) of 0.50 (SE 0.12) for changes in cognitive processes, with a noted smaller effect when CBT was compared with active controls (Chu 2007). Taken together, these provided a reasonably solid evidence base for the use of CBT in the treatment of childhood anxiety disorders.

A review of CBT for anxiety disorders in ASD (Lang 2010) has shown positive results of CBT, albeit with a smaller number of studies than were reviewed here (Chalfant 2007; McNally Keehn 2012; Reaven 2012; Schneider 2011; Sung 2011; Wood 2009; White 2012). Furthermore, CBT has to be modified in the ASD population because of cognitive biases, and it is not clear how CBT with a greater emphasis on behavioural rather than cognitive changes matches CBT delivered generally (Lang 2010). In a recent review (Reaven 2011), the lack of detail on parental involvement in treatment, particularly for teenagers, was noted; however, several studies in this review did include parents (Chalfant 2007; McNally Keehn 2012; Reaven 2012; Wood 2009; White 2012).

#### **AUTHORS' CONCLUSIONS**

# Implications for practice

Cognitive behavioural therapy (CBT) is an important therapy for the treatment of anxiety disorders in children and adolescents. This review alongside those in adults (Otte 2011) and older adults (Gould 2012) suggests that CBT is effective across the age range, and CBT can, therefore, be recommended more generally for the treatment of anxiety disorders. The number of studies and reviews is now reasonably large; however, studies are confined to community or outpatient samples with mild to moderate cases only. Evidence derived from this review indicates that CBT is effective in 58.9% of cases compared with a natural remission rate of 16.1% in waiting list controls, and with an NNT of 3, CBT is associated with a clinically robust effect (Laupacis 1988). Evidence of differences between the formats of individual, group and parent/family CBT is lacking.

It is likely that emphasis will be placed on psychological treatments for childhood anxiety disorders, particularly in view of safety concerns over the use of selective serotonin re-uptake inhibitors (SSRIs) in children and adolescents. However, with regard to medication, the evidence is limited: CBT appears to be as effective as SSRI antidepressants, and the combination therapy appears to be more effective than either treatment alone. Evidence of comparative efficacy is limited to one study, albeit a large multicentre study (Walkup 2008); therefore it is clear that further work is essential to guide practice.

# Implications for research

This review has identified a reasonable number of methodologically sound trials of CBT versus waiting list controls, and overall the findings are consistent with those of other reviews and meta-analyses; therefore, there does not appear to be an argument for additional similar studies. Rather, researchers need to dissect what the active components of CBT are and to explore the mechanisms of how they work, so that shortened, targeted



treatments can be developed. Further studies are required in the younger age range with an emphasis on the types of behavioural and cognitive interventions that work in younger patients. Studies should be stratified by age to allow adequate investigation of the age/developmental appropriateness of the CBT model used. In particular, studies need to employ measures of cognitive changes, rather than simple symptom changes, which are sensitive to developmental and age changes, especially in younger children and older adolescents (Grave 2004; Sauter 2009).

We would recommend, as has a recent review (Reynolds 2012), that any future studies should follow CONSORT reporting standards, be adequately powered, and assess follow-up. Future research may need to focus on modular approaches to CBT, whereby elements of evidence-based CBT are applied in routine clinic practice; evidence so far suggests that these approaches may be effective (Weisz 2012).

CBT appears equally effective in various formats—family, individual and group—which poses the question whether group CBT is possibly more cost-effective. For instance, group CBT can be delivered in schools (Dadds 1999; Ginsburg 2002; Olivares 2005; Ginsburg 2012; Galla 2012). Health economic studies are needed to answer this question. It would also be useful to see whether any particular anxiety disorder or clinical variable is associated with a better outcome with certain therapy formats. It would also be useful to see whether CBT can be delivered in a more shortened form, as the number of sessions does not seem to be a major factor in the outcome of the studies seen here. The question also arises whether the therapist is essential for all sessions, or can CBT be delivered by other means? For instance, a number of studies are already looking at delivery of CBT via the Internet.

Although rates of comorbidity among anxiety disorders are high (Kendall 2001), there is perhaps a need to focus on more specific anxiety disorders, rather than grouping together disorders such as overanxious disorder, social anxiety disorder and generalised

anxiety disorder. This has been achieved for adult studies of CBT. It remains unclear how CBT compares with other treatments, and given that overall 40% of participants in research studies of CBT do not improve, the need for alternative and/or combined treatments becomes clear. A Cochrane review (Ipser 2009) has shown that SSRIs are effective in treating paediatric anxiety disorders, suggesting that additional comparator studies with drug treatments and combined treatments, involving cost analyses, are urgently needed. A question remains about the applicability of CBT to wider populations, especially those with learning disabilities, for whom a modified form of CBT may be necessary. A major gap is the lack of studies looking at predictors of clinical response to CBT, which undoubtedly would be of use clinically. An example is the examination of the therapist-child alliance, which has been shown to positively affect outcome (Chiu 2009).

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#### **Disclaimer**:

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health.



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#### CHARACTERISTICS OF STUDIES

**Characteristics of included studies** [ordered by study ID]

# Barrett 1996

Study characteristics	
Methods	RCT, WL control; blind assessment. Completer analysis. Sample size (initial/completed): individual CBT 28/28, individual + family 25/25, W/L controls 26/23.
Participants	N = 79; age range 7-14 years; mean age = 9.3 years; 57% male; ethnicity not specified; community sample—overanxious disorder (OAD) (n = 30), separation anxiety disorder (SAD) (n = 30), social phobia (SOP) (n = 19).  Exclusion criteria: principal diagnosis of simple phobia or other (non-anxiety) diagnoses; intellectual or physical disabilities; anti-anxiety or depression medication; parents involved in acute marital break down.
Interventions	Clinic-based individual CBT 12 $\star$ 60-80 minutes; clinic-based CBT + family intervention 12 $\star$ 60-80 minutes; waiting list controls (12 weeks, then offered treatment).
Outcomes	ADIS-C. ADIS-P. RCMAS. FSSC-R. CBCL.
Notes	Follow-up 12 months.
Risk of bias	

<sup>\*</sup> Indicates the major publication for the study



### Barrett 1996 (Continued)

Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	No details given on randomisation procedure.	
Allocation concealment (selection bias)	Unclear risk	No information available.	
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.	
Blinding of outcome assessment (detection bias)	Low risk	At post-treatment and follow-up, clinicians who were unaware of the child's treatment condition conducted diagnostic interviews and rated improvement in the child.	
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study states the fate of all participants, and dropout data are identified.	
Selective reporting (reporting bias)	Low risk	Data reported.	

# Barrett 1998

Barrett 1998			
Study characteristics			
Methods	RCT, W/L control and alternative treatment; blind assessment.  Completer analysis.  Sample size (initial/completed): group CBT 23/19; group + family CBT 17/15; W/L controls 20/16.		
Participants	N = 60; age range 7-14 years; 53% male; ethnicity not specified; community sample — overanxious disorder OAD (n = 30), separation anxiety disorder (SAD) (n = 26), social phobia (SOP) (n = 4). Exclusion criteria: intellectual or physical disabilities; current antianxiety or depression medication; parents involved in acute marital breakdown.		
Interventions	Clinic-based group CBT 12 * 2 hours; clinic-based group CBT + family intervention 12 * 2 hours: waiting list controls (12 weeks, then offered treatment).		
Outcomes	ADIS. FSSC-R. CBCL.		
Notes	Follow-up 12 months.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	No details given upon randomisation procedure.	
Allocation concealment (selection bias)	Unclear risk	No information available.	



Barrett 1998 (Continued)			
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.	
Blinding of outcome assessment (detection bias)	Low risk	Clinicians conducting assessment were blind to participants' allocation.	
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study identifies dropouts.	
Selective reporting (reporting bias)	Low risk	Data reported.	

# **Barrington 2005**

Study characteristics	3
Methods	RCT of CBT: group versus treatment as usual (TAU).
	Sample size (initial/completed): CBT 28/23; TAU 26/23.
Participants	N = 54 children; CBT mean age (SD) 9.8 years (2.29); TAU 10.2 years (1.75); range 7-14 years. Gender: 64.8% females; ethnicity not disclosed; panic disorder 3.7%, separation anxiety disorder 27.7%, generalised anxiety disorder (GAD) 22.2%, social phobia.16.6%, obsessive-compulsive disorder 12.9%. Comorbidity 40% — anxiety disorders. Setting: community clinics.
Interventions	CBT: Treatment consisted of 12 weekly sessions; TAU consisted of a variety of treatment approaches provided in Australian CAMHS, including family therapy, play therapy, supportive psychotherapy, psychodynamic psychotherapy and non-CBT eclectic approaches. CBT interventions were based on a set of guidelines for the treatment of anxious children and their parents, summarised from recent publications including Kendall, Kane, Howard and Siqueland (1992), Kendall (1994), Barrett et al. (1996), Spence, Donovan and Brechman-Toussaint (2000) and Cobham (1998).
Outcomes	The Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds and Richmond, 1997).
	The Spence Children's Anxiety Scale (SCAS) (Spence 1998).
	The SCAS parent version (SCAS-P).
	The Behaviour Assessment System for Children (BASC): parent and teacher rating scales (Reynolds and Kamphaus, 1992).
	Depression Anxiety Stress Scales (DASS): a 21-item self-report questionnaire developed in Australia that measures depression, anxiety and tension/stress in adults (Lovibond and Lovibond, 1995).

# Notes

Bias Authors' judgement Support for judgement		Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details given on randomisation procedure.
Allocation concealment (selection bias)	Low risk	No information available.



Barrington 2005 (Continued)				
Blinding (performance bias and detection bias) All outcomes	Low risk	Research clinician conducting all assessments was blind to participants' treatment group and their therapist. The clinician was also blind to participants' initial anxiety diagnosis.		
Blinding of outcome assessment (detection bias)	Low risk	Research clinician conducting all assessments was blind.		
Incomplete outcome data (attrition bias) All outcomes	Low risk	8 withdrew after fewer than four therapy sessions, leaving a total of 54. Authors gave further information upon request.		
Selective reporting (reporting bias)	Low risk	Data reported.		

# **Chalfant 2007**

Study characteristics			
Methods	RCT of CBT: WL control; blind assessment. Completer analysis.		
	Sample size (initial/completed): CBT child and parent 28/24; W/L controls 19/19.		
Participants	N = 47 children aged 8–13 years (35 boys, 12 girls) with a mean age of 10.8 years (SD 1.35). Recruitment from community clinics and newspaper adverts; 13 (27.7%) of participants had a documented diagnosis of high-functioning autistic disorder (ASD), and 34 (72.3%) had a diagnosis of Asperger's disorder. Participants had separation anxiety disorder (SAD) $n = 8$ ; generalised anxiety disorder (GAD) $n = 14$ ; social phobia $n = 20$ ; specific phobia $n = 3$ ; panic disorder $n = 2$ .		
Interventions	CBT: 12-session CBT or W/L condition. Participants in the CBT condition were seen by therapists for weekly sessions of 2 hours' duration. Adaptations to the Cool Kids programme were made to account for the visual and concrete learning styles of higher-functioning autistic children. The programme was extended over a longer period (6 months), and use of visual aids and structured worksheets was increased. The largest components of the programme were devoted to relaxation (three treatment sessions and two booster sessions) and exposure.		
Outcomes	ADIS-C/P.		
	RCMAS.		
	SCAS.		
	Children's Automatic Thoughts Scale (CATS).		
	Strengths and Difficulties Questionnaire (SDQ).		

# Notes

Bias Authors' judgement Support for judgement		Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details on the process of randomisation.
Allocation concealment (selection bias)	Unclear risk	No information available.



Chalfant 2007 (Continued)			
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.	
Blinding of outcome assessment (detection bias)	Unclear risk	CBT data collected by therapists.	
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts noted; however, data on outcome measures do not include numbers of participants.	
Selective reporting (reporting bias)	Low risk	Data reported.	

# Cobham 2012

RCT of family CBT (FT) versus bibliotherapy (BT) versus W/L controls.		
hnicity: Ninety-two naining children were		
nponents or pro- second involving the		
mp		

# Risk of bias

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Used modified random assignment. Random sequence generation not mentioned.
Allocation concealment (selection bias)	Unclear risk	No information given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information given.
Blinding of outcome assessment (detection bias)	Low risk	Independent clinicians who were blind to the treatment group carried out follow-up assessments.



$C \cap D$	ham	7017	(Continued)

Incomplete outcome data (attrition bias)
All outcomes

Low risk

Consort flow diagram provided; no families dropped out once they were aware of the allocation group. Two families dropped out during allocation. The study states the fate of all participants and dropout data were noted.

Selective reporting (reporting bias)

Low risk

# **Dadds 1997**

Study characteristics	3
Methods	RCT, control, school: blind assessment. Completer analysis. Sample size (initial/completed): CBT 64/59; controls 67/64.
Participants	N = 100; age range 7-14 years; mean age = 9.5 (SD 1.6) years; 26.4% male; ethnicity not specified; schools — any DSM IV anxiety diagnosis (subclinical sample reported but not included in this analysis). Exclusion criteria: disruptive behaviour problems, developmental problems or disabilities, English not spoken at home, clinical anxiety higher than 5 on an 8-point rating scale.
Interventions	School-based group CBT: 10 * 1-2 hour parent sessions * 3.
Outcomes	ADIS-P. RCMAS. FSSC-R. CBCL.

#### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Cluster-randomisation allocation based on 8 schools. No details on the process of randomisation.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Unclear risk	Clinicians conducting the assessments were blind to participants' intervention allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Authors provide information on participants who withdrew from the study.
Selective reporting (reporting bias)	Low risk	



### **Dadds 1999**

Study characteristics	
Methods	Follow-up of Dadds 1997: 12- and 24-month follow-up data of group CBT versus monitoring.
Participants	12 months: 9 had withdrawn from intervention group (16% of completers) and 11 (17% of completers) had withdrawn from monitoring; 24 months: A further 3 had withdrawn from monitoring (22% of completers).
Interventions	See Dadds 1997.
Outcomes	ADIS-P.
	CGI.
	Parents rated 6 dimensions of change (overall functioning, overall anxiety, avoidance, family disruption, parents' ability, child's ability).
Notes	

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Allocation based on school. No details on the process of randomisation.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Unclear risk	Clinicians who conducted the assessments were blind to participants' intervention assignment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Authors provide information on participants who withdrew from the study.
Selective reporting (reporting bias)	Low risk	All data reported.

# Flannery-Schroeder 2000

Study characteristics	
Methods	RCT, WL control and alternative treatment; blind assessment, ITT completer analysis.  Sample size (initial/completed): individual CBT 18/13; group CBT 13/12; W/L controls 14/12.
Participants	N = 45; age range 8-14 years; 43% male; ethnicity 89% white; community sample—generalised anxiety disorder (GAD) (n = 21), separation anxiety disorder (SAD) (n = 11), social phobia (SOP) (n = 5). Exclusion criteria: disabling physical condition; psychotic symptoms; current use of antianxiety or antidepressant medication.



Flanner	y-Schroed	ler 2000	(Continued)
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Interventions	Clinic-based group CBT 18 * 90 minutes, some parental advice given; clinic-based individual CBT in-
	tervention 18 * 50-60 minutes, some parental advice given; waiting list controls (9 weeks, then offered
	treatment).

Outcomes ADIS- IV-C. AIDS-IV-P. RCMAS.

Notes Follow-up 12 months.

CBCL.

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned in blocks of four, generation of random sequence not mentioned.
Allocation concealment (selection bias)	Low risk	Intervention groups were concealed from teachers.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Unclear risk	No information available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study identifies dropouts.
Selective reporting (reporting bias)	Low risk	All data reported.

### **Galla 2012**

Study characteristics	
Methods	Modular CBT delivered in school. Sample size (initial/completed): individual treatment (22/21), W/L controls (18/18).
Participants	N = 40, age range 5–12 years (M = 8.51, SD = 1.74). Ethnicity male 55%. Anxiety diagnoses: social phobia (SP; n = 21; 52.5%); separation anxiety disorder (SAD; n = 21; 52.5%); generalized anxiety disorder (GAD; n = 15; 37.5%) . Fourteen children (35%) met criteria for more than one anxiety disorder.
Interventions	The modular <i>Building Confidence</i> programme contains several child modules, caregiver modules, one teacher module, and one school nurse module. Session order is not predetermined but is chosen to reflect the needs of the child. Children can participate in as few as 1 and as many as 16 60-minute sessions, depending on symptom remission. Caregivers are encouraged but not required to participate in treatment.
Outcomes	ADIS-P.
	GCI.



#### Galla 2012 (Continued)

Multidimensional Anxiety Scale for Children (MASC-C).

Notes

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised using a table of random numbers.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	Independent evaluators who were blind to the treatment condition conducted the diagnostic interviews.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2.5% dropped out before follow-up, and 16 dropped out before the 1-year follow-up.
Selective reporting (reporting bias)	Low risk	All data reported.

# Gil-Bernal 2009

Stud	, cl	ara	cto	ristics	
<b>Stuu</b> y	ľ	ıuı u	CLEI	ISLICS	

Methods	tial/completed): group treatment (6/6); group treatment plus parents (6/6); W/L controls (5/5).
Participants	N = 17; age: 13 girls mean age 9.7 years (SD 1.87) and 4 boys 10.7 years (SD 1.5). Ethnicity: Mexican.

Interventions CBT to group and to group with parental advice: 9 sessions, 90 minutes. Diagnosis: social phobia.

Outcomes SCAS (Spence's Scale of Anxiety for children).

CBCL (Acherbach's list of behaviours) \*complemented by parents.

IDFS (Instrumento de fobia social = social phobia instrument).

Notes Follow-up 3 and 6 months.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described.
Allocation concealment (selection bias)	Unclear risk	Not described.



Gil-Bernal 2009 (Continued)		
Blinding (performance bias and detection bias) All outcomes	Low risk	Not described.
Blinding of outcome assessment (detection bias)	Low risk	Assessors blind (*the CBCL is complemented by parents).
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No loss of participants reported.
Selective reporting (reporting bias)	Low risk	Data reported.

# **Ginsburg 2002**

Study characteristics	5
Methods	RCT, alternative control, therapist and group peer support, blind assessment, completer analysis. Initial/completed: group CBT 6/4; active controls 6/5.
Participants	N = 12; age range 14-17, mean 14.6 years; Ethnicity: African American. Inclusion criteria: DSM IV anxiety diagnosis; score > 24 on ADIS-C and > 4 on ADIS-CIR. Exclusion: obsessive-compulsive disorder and post-traumatic stress disorder; receiving other psychiatric treatment; suicidal intent or needing immediate/alternative treatment.
Interventions	School-based group CBT: 10* sessions 45 minutes.
Outcomes	ADIS- C. SCARED. SAS-A.

Notes

Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table used.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Low risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	"After treatment, the teenagers completed the same self-report question- naires and were re-administered the ADIS-IV by an interviewer who was un- aware of the participants' treatment condition".
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data about dropout are not present.



Ginsburg 2002 (Continued)

Selective reporting (reporting bias)

Low risk

Data reported.

# **Ginsburg 2012**

Study characteristics	
Methods	RCT of CBT delivered by novice therapists in an inner city school. TAU control; blind assessment. Completer analysis.  Sample size (initial/completed): CBT child and parent 17/15, TAU controls 19/15.
Participants	N = 32; CBT 17, TAU 15; mean age CBT 11.12 years SD 2.75; TAU 9.33 years SD 2.06; range 7-17 years; gender: CBT 70.6% female, W/L 53.3% female; ethnicity: CBT 87.5%, W/L 86.7%. African American; recruitment from inner city schools; GAD — CBT 35.3%, W/L 53.3%; SAD — CBT 29.4%, W/L 20.0%; separation disorder — CBT 23.5%, W/L 26.7%; specific phobia — CBT 5.9%, W/L 0%. Comorbidity 65% — GAD 25%; SP 22%; SAD 13%. Medication stable throughout. One control on psychotropic medication.
Interventions	Modular CBT with 11 school-based therapists. CBT was adapted to a modular format based on anxiety CBT manuals (Kendall 1990; Kendall 1994; Silverman et al. 1999a, b). Parent modules (e.g. psycho-education, rewards, exposure) were also included. A total of eight modules were designed to be delivered over 12 weeks. Usual care (TAU) — This condition focused on providing children therapeutic interventions that did not include CBT strategies (e.g. art, play, supportive therapy).
Outcomes	ADIS-IV-CP.
	SCARED (Birmaher et al. 1997, 1999).
	Clinical Global Impression Scale–Improvement (CGI-I).
	CGAS.
	Children's Automatic Thoughts Scale (CATS; Schniering and Rapee 2002).
	SDQ.
	Brief Symptom Inventory (BSI; Derogatis and Melisaratos 1983).
	Parenting Stress Index — Short Form (PSI/SF; Abidin 1995).
	Urban Hassles Index (UHI; Miller et al. 2002; Miller and Townsend 2005).
	Adherence and Therapist Competence (TATC) (Ginsburg 2012).
	Perception of Therapeutic Relationship Scale (PTR; Kendall et al. 1997).

### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'Randomisation was conducted using the Website randomization.com, and separate randomisation plans were created for each clinician'.
Allocation concealment (selection bias)	Low risk	No information available.
Blinding (performance bias and detection bias)	Unclear risk	No information available.



G	ns	burg	2012	(Continued)
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All outcomes
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Blinding of outcome assessment (detection bias)	Low risk	Senior clinician reviewing the scoring where blind to the treatment groups.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram, the study states the fate of all participants and dropouts were noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# **Hayward 2000**

Study characteristics	
Methods	RCT, no treatment control (W/L); blind assessment. Completer analysis. Sample size (initial/completed): group CBT 12/11; controls 23/22.
Participants	N = 35; mean age 15.8 years; age range: unspecified; 100% female; ethnicity unspecified; community sample — social anxiety disorder SOP (n = 35).  Exclusion criteria: current major depression, current or previous panic, agoraphobia, substance abuse, psychotic disorder or using psychotropic medication.
Interventions	Clinic-based group CBT 16 * 1.5 hours. No treatment control.
Outcomes	ADIS. SPAI-C.
Notes	Follow-up 12 months.

Bias	Authors' judgement	Support for judgement	
tion (selection bias) domly assigned to the CBGT-C cond		"Twelve subjects were recruited for each randomisation, with 6 subjects randomly assigned to the CBGT-C condition and 6 to an untreated condition. After 2 treatment groups were completed, a third set of 11 subjects were included in the untreated condition".	
Allocation concealment (selection bias)	Unclear risk	No information available.	
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.	
Blinding of outcome assessment (detection bias)	Low risk	"At the post-treatment and 1-year follow-up assessments, interviewers were kept blind to information regarding treatment status".	
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study states the fate of all participants, and dropouts were noted.	



Hayward 2000 (Continued)

Selective reporting (reporting bias)

Low risk

Data reported.

### **Herbert 2009**

Study characteristics	
Methods	RCT, active treatment control; blind assessment, ITT and completer analysis.  Sample size (initial/completed): group CBT 23/16; individual CBT 24/17; psycho-education/supportive therapy (PST) 26/19.
Participants	N = 73; mean age 15 years; age range 12-17 years; 56% female; ethnicity 47% Caucasian, 44% African American, 9% Latino or Asian; community sample—all SAD, generalized subtype. 59% at least one comorbid disorder.  Exclusion criteria: mental retardation, pervasive developmental disorder, organic mental disorder, bipolar disorder, psychotic disorder, borderline personality disorder, schizotypal personality disorder, suicide risk, substance abuse or dependence within 1 year, previous trials of behaviour or cognitive behavioural therapy.
Interventions	G-CBT: 12 * 2-hour sessions per week (4-6 participants per group).
	I-CBT: 12 * 1 hour per week.
	PST: 12 * 2-hour sessions per week (4-6 participants per group).
Outcomes	ADIS-C. SPAI-C.
	SAS-C.
	Reaction to Treatment Questionnaire.
	Behavioural assessment.
	CGI.
Notes	Follow-up 6 months.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block design, randomly assigned to one of three treatment groups.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Unclear risk	"Trained interviewers who conducted the outcome assessments were blind to group assignment".
Incomplete outcome data (attrition bias)	Low risk	Flow diagram, with all participants and dropouts noted.



Herbert 2009	(Continued)
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All outcomes

Selective reporting (reporting bias)

Low risk

Data reported.

#### Hirshfeld-Becker 2010

Study	characterist	ics
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Methods RCT, WL control; blind outcome assessment.

Completer analysis.

Sample size (initial/completed): parent-child CBT 30/27; W/L controls 29/27.

**Participants** 

N = 59; age range 4-7 years; mean age 5.37 years; 54% male; ethnicity 78% European-American; recruitment: community sample—outpatient child psychiatry clinic at general hospital and advertising. Study conducted at research clinic at general hospital.

DSM IV anxiety disorder (GAD), separation anxiety, (SAD) (some participants had comorbid specific phobia and agoraphobia). Solely specific phobia and or agoraphobia to be excluded. Parents were assessed for anxiety disorders. Exclusion criteria: (1) active psychosis, suicidality, or substance abuse in the parent, (2) mental retardation in the child, (3) current psychiatric treatment or past CBT, and also if 2 senior clinicians judged child to be (4) too uncooperative or distractible to take part in trial or (5) too severely symptomatic to wait 6 months to receive treatment, based on suicidal ideation, serious impairment in eating or sleeping habits, severe social isolation, severe impairment in school function or attendance or severe OCD.

Interventions

Clinic-based parent/child CBT up to 20 sessions over 6 months.

Waiting list controls (6 months, then offered treatment).

Outcomes

K-SADS.

DSM-IV symptom checklist.

Behavioural inhibition (laboratory observation by observer blind to child's condition and treatment status).

Status

CGI.

Notes

Follow-up post-treatment (6 months), then CBT group at 1 year.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The allocation sequences were generated in advance of the 2 cells (presence or absence of parental anxiety disorders) by the study coordinator".
Allocation concealment (selection bias)	Low risk	"Concealed in a computer file from all other staff".
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	Blind clinician rater.



Hirshfeld-Becker 2010 (Continued)			
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram, the fate of all participants and dropouts noted.	
Selective reporting (reporting bias)	Low risk	Data reported.	

# **Hudson 2009**

Study characteristics	
Methods	RCT, active control; blind assessment, ITT and completer analysis. Sample size (initial/completed): group CBT 58/51; group support and attention 49/46.
Participants	N = 106; mean age 10.2 years; age range 7-16 years; 38% female; ethnicity Australian (n = 63), Asian/ Asian Australian (n = 10), European/ European Australian (n = 16), other (n = 6). Social anxiety disorder (SOP) (n = 24); separation anxiety disorder (SAD) (n = 15) generalised anxiety disorder (GAD) (n = 51); panic disorder (n = 1). Exclusion criteria: mental retardation, psychoses, concurrent psychiatric treatment, major depression.
Interventions	Clinic-based group CBT: 10 * 2 hours (5-7 per group): group support and attention 10 * 2 hours.
Outcomes	ADIS-IV- C.
	ADIS-IV- P.
	Strengths and Difficulties Questionnaire (SDQ-Child).
	SCAS.
Notes	Follow-up 6 months.
	Participants with primary diagnoses of specific phobia (n = 21) were removed. The data were reanalysed by the authors using the same analyses as in the original paper, simply based on a different sample size.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The first author used a schedule from a random number generator to assign each group".
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	"Structured interviews were conducted by diagnosticians who were masked to condition".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram, the fate of all participants and dropouts noted.



Hudson 2009 (Continued)

Selective reporting (reporting bias)

Low risk

Data reported.

### Kendall 1994

Study characteristics	
Methods	RCT, W/L control, completer analysis. Sample size (initial/completed): individual CBT 30/27; W/L controls 30/20.
Participants	N = 47; age range 9-13 years; 60% male; ethnicity 76% white; community sample — overanxious disorder (OAD) (n = 30), separation anxiety disorder (SAD) (n = 8), avoidant disorder (AVD) (n = 9). Exclusion criteria: IQ below 80; disabling physical condition, psychotic symptoms, current use of antianxiety or antidepressant medication.
Interventions	Clinic-based individual CBT: 17 * 50 minutes,: W/L control (8 weeks, then offered treatment).
Outcomes	ADIS-P.
	RCMAS.
	FSSC-R.
	CBCL.

#### Notes

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	Observers were blind to the treatment condition.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# Kendall 1997

# Study characteristics



Kendall 1997 (Continued)		
Methods	RCT, W/L control, completer analysis. Sample size (initial/completed): individual CBT 75/60; W/L controls 43/34.	
Participants	N = 94; age range 9-13 years; 62% male; ethnicity 85% white; community sample—overanxious disorder OAD (n = 55), separation anxiety disorder (SAD) (n = 22), avoidant disorder (AVD) (n = 17). Exclusion criteria: psychotic symptoms, antianxiety medication.	
Interventions	Clinic-based group ind ment).	ividual CBT: mean 18 * 60 minutes: W/L control (8 weeks, then offered treat-
Outcomes	ADIS-P. RCMAS. STAIC.	
Notes	Follow-up 12 months.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Unclear risk	No information available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants and dropout data accounted for and assessed.
Selective reporting (reporting bias)	Low risk	Data reported.

# Kendall 2008

Study characteristics	s
Methods	RCT; blind assessment not clear, completer analysis.
	ICBT (individual CBT) vs FCBT (family-based CBT) vs family-based education support/attention treatment (FESA).
	Sample sizes (initial/completed): ICBT = 55/50, FCBT = 56/51, FESA = 50/40.
Participants	N = 161; age range 7-14 years; mean age 10.27 years; 56% male; ethnicity 85% Caucasian; community sample—generalised anxiety disorder (GAD) (n = 88), separation anxiety disorder (SAD) (n = 47), social phobia (SOP) (n = 63).



Kendall 2008 (Continued)	Exclusion criteria: psychotic symptoms, mental retardation, a disabling medical condition, the child's participation in concurrent treatment, the child taking antidepressant or antianxiety medications. At least one parent was required to be English speaking.
Interventions	All treatments included 16 weekly 60-minute sessions.
	ICBT had 2 * 8-part sessions.
	FCBT had 2 * 8-part sessions.
Outcomes	ADIS-C.
	ADIS-P.
	CBCL.
	MASC.
Notes	1-Year follow-up.

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The coordinator used a predetermined schedule (random number — generated) to randomly assign eligible participants".
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	"Strategies were used to help ensure that post-treatment and follow-up diagnosticians (independent evaluators) would be blind to treatment condition".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram, the fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Low risk	Data reported.

### **Lau 2010**

Study characteristics	
Methods	RCT, W/L control; blind assessment not clear, ITT and completer analysis. Sample size (initial/completed): group CBT 24/23; W/L controls 21/18.
Participants	N = 45; mean age 8.7 years (SD 14 months); age range 6-11 years; 53% males; ethnicity 100% Chinese origin.
	38% were diagnosed with generalized anxiety disorder, 24% with separation anxiety disorder, and 51% with social phobia. Eight children (18%) did not meet DSM-IV-TR criteria but had subclinical symptoms



Lau 2010 (Continued)	of anxiety disorders that the normal range.	at interfered with daily functioning. Exclusion criteria: simple phobias, IQ outside	
Interventions	Adapted version of Flannery-Schroeder and Kendall's (1996) Coping Cat CBT group treatment programme.		
	Clinic-based group CB	Γ: 9 * 120 minutes: W/L control (13 weeks, then offered treatment).	
Outcomes	K-SADS.		
	SCAS.		
	PANAS.		
	The Negative Affectivity Self-Statement Questionnaire (NASSQ).		
	Coping Questionnaire (CQ-C) for children.		
Notes	Completer analysis was conducted but was not included in the review because of pooled data.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Not mentioned.	
Allocation concealment (selection bias)	Unclear risk	No information available.	
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.	
Blinding of outcome assessment (detection bias)	Low risk	Clinical psychologists blind to treatment condition conducted clinical interviews and reports.	
Incomplete outcome data (attrition bias)	Low risk	Flow diagram, the fate of all participants and dropouts noted.	
All outcomes			

### Masia-Warner 2005

Study characteristics	
Methods	RCT of CBT (Skills for Social and Academic Success (SASS)) child group and W/L control: sample size (initial/completed) CBT (21/18); W/L control (21/17).
Participants	N = 35 children, mean age 14.8, SD 0.81 years; range 13–17 years. Gender: 74.4% females. Ethnicity: Caucasian 82.9%, African American 8.6%, Latin-American 2.9%, Asian-American 2.9%, other 2.9% All participants had social phobia. Any comorbid anxiety disorder 46.8%. Setting schools.
Interventions	CBT consists of 12 weekly group school sessions (approximately 40 minutes each), two brief individual meetings (15 minutes), and two group booster sessions. Additionally, four weekend social events (90



#### Masia-Warner 2005 (Continued)

minutes) that include prosocial peers, called "peer assistants," provide real-world exposure and opportunities for skills generalization. Parents attend two group meetings (45 minutes) at school, during which they receive psycho-education regarding social anxiety and learn techniques to address their child's anxiety. Teachers participated in two psycho-educational meetings (30 minutes) and conducted classroom exposures supervised by group leaders.

#### Outcomes

ADIS-PC.

CGI-I.

SPAI-C.

Liebowitz Social Anxiety Scale for Children and Adolescents (LSAS-CA; Masia-Warner, Klein, and Liebowitz, 2003).

Social Phobic Disorders Severity and Change Form (SPDSCF; Liebowitz et al. 1992).

Social Anxiety Scale for Adolescents (SAS-A; La Greca, 1998).

Social Anxiety Scale for Parents (SAS-AP; La Greca, 1998).

Loneliness Scale (LS; Asher and Wheeler, 1985).

CDI.

CGAS.

Follow-up 9 months; CBT n = 16, W/L control n = 15.

#### Notes

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details given on process.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	Assessment carried out by independent evaluator blind to treatment condition.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study states the fate of all participants and dropouts are noted.
Selective reporting (reporting bias)	Unclear risk	No information available.

# Masia-Warner 2007

#### **Study characteristics**



Masia-Warner 2007	(Continued)
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Methods	RCT of CBT (Skills for Social and Academic Success (SASS)) child group and versus active control-educational-supportive treatment. Sample size (initial/completed): CBT (19/17); active control 17/15.	
Participants	N = 36 children, mean age 15.1, SD 0.6 years, range 14–16 years. Gender 83% females. Ethnicity: Caucasian 72.2%, African American 5.6%, Hispanic 16.7%, other 5.6%. Participants had generalized anxiety disorder (25.0%), obsessive-compulsive disorder (5.6%), separation anxiety disorder (2.8%), anxiety disorder NOS (2.8%), any comorbid anxiety disorder (33.3%). Setting schools.	
Interventions	CBT consists of 12 group sessions (40 minutes); one session focuses on psycho-education, one on realistic thinking, four on social skills (starting conversations, inviting others, etc.) and five on exposures. The final group addresses relapse prevention. Two individual sessions and four weekend social events (e.g. bowling, laser tag) with prosocial school peers ('peer assistants') are also included. Parents and teachers attend two group sessions for psycho-education.	
Outcomes	ADIS-PC. CGI-I.	
	SPAI-C.	
	Social Anxiety Scale for Adolescents (SAS-A; La Greca, 1998).	
	Social Anxiety Scale for Parents (SAS-AP; La Greca, 1998).	
	BDI.	
	CGAS.	
	Treatment credibility ratings (Silverman et al. 1999).	
	Follow-up 6 months: CBT n = 15, active control n = 15.	

# Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Treatment randomisations were conducted within school, so that each school had active and control conditions.
Allocation concealment (selection bias)	Low risk	Participants did not know students in the alternate condition, so contamination across treatments was not possible.
Blinding (performance bias and detection bias) All outcomes	Low risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	Blind assessment carried out by an independent evaluator blind to treatment condition.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Details of dropouts given, the fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Unclear risk	Data reported.



#### Masia-Warner 2011

Study characteristics			
Methods	RCT of paediatric participants who experienced gastrointestinal symptoms. WL control; blind assessment; completer analysis.  Sample size (initial/completed): CBT child and parent (20/20), W/L controls (20/19).		
Participants	N = 40- 20; mean age 12.4 years, SD 2.6, range 8-16 years; 65% female; ethnicity: 72% white, 15% Hispanic, 10% other, 2.5% African American; recruitment from medical centres; 14 (35%) with separation anxiety disorder, 11 (27.5%) with social anxiety disorder, 10 (25%) with generalized anxiety disorder, 4 (10%) with specific phobia, and 1 (2.5%) with anxiety disorder, not otherwise specified. Children's principal anxiety disorders were moderately severe, with a mean of 5.7 (SD 1.0, range 4 to 7) on a 0 to 8 clinical rating scale. Most of the youths (n = 31, 77.5%) had comorbid psychiatric diagnoses. Other anxiety disorders were most prevalent (n = 30, 75%). Medication stable throughout. One control on psychotropic medication.		
Interventions	CBT: TAPS is a 10-week systematic intervention that jointly addresses anxiety and physical symptoms by applying relaxation, cognitive restructuring and exposure exercises to target fears related to physical pain and anxiety-inducing situations. It consists of 12 individual sessions (approximately 45–60 minutes each), with 3 parent meetings following the individual sessions (45 minutes each) conducted over 10 weeks.		
Outcomes	ADIS-IV-CP.		
	Clinical Global Impression Scale-Improvement (CGI-I).		
	The Children's Somatization Inventory (CSI).		
	Child and parent pain ratings: Overall physical symptom severity was measured using self and parent reports of pain on an 8-point Likert scale (from 0 no pain to 8 extreme pain).		

# Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerised number allocation; used a table of random numbers with predetermined assignment to ensure equal group numbers.
Allocation concealment (selection bias)	Low risk	"In addition, families were instructed not to disclose whether or not they had received intervention".
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	Blind independent evaluators who were blind to treatment group conducted the assessments.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data collected from all participants. The fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Low risk	Data reported.



### McNally Keehn 2012

Study characteristics	
Methods	RCT of CBT—child plus parent versus W/L control. Sample size (initial/completed): CBT (12/12); W/L control 10/10.
Participants	N = 22 children, mean age 11.26, SD 1.53, range 8-14 years. Gender 95.45% male. Ethnicity: Caucasian 54.5%; others 13.6%; Hispanic 13.6%; not reported 18.2%. All participants autistic spectrum disorder (ASD) and full scale IQ ≥ 70 and anxiety disorder—social phobia 68.2%, generalized anxiety disorder 81.8%, obsessive-compulsive disorder 9.1%, separation anxiety disorder 36.4%, and specific phobia 68.2%. Comorbidity ADHD 72.7%, ODD 41%, MDD 4.5%. Medication included SSRIs in CBT with some changes. Setting university clinics.
Interventions	CBT — Children in the CBT condition received a 16-week manualised cognitive behavioural intervention in accordance with the Coping Cat programme (Kendall and Hedtke 2006a, b).
Outcomes	ADIS-P.
	SCAS.
	SCAS-P.

Notes Follow-up 2 months.

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised to either the 16-week CBT intervention or the 16-week WL using a stratified randomisation procedure.
Allocation concealment (selection bias)	Low risk	No information available.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information available.
Blinding of outcome assessment (detection bias)	Low risk	Evaluators were blind to intervention assignment at all phases of assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram, no dropouts occurred during the study, the study states the fate of all participants and dropouts were noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# Melfsen 2011

Study characteristics	
Methods	RCT of CBT — child plus parent versus W/L control. Sample size (initial/completed): CBT (21/15); W/L control (23/21).



Melfsen 2011 (Continued)				
Participants		L; mean age 10.60 SD 1.64; 10.76 SD 1.90; range 8-14 years. Gender 47.7% fesian 100%. All participants had social phobia. Comorbidity 40.9%. Setting univer-		
Interventions	CBT — Treatment cons	isted of 20 weekly 50-minute individual sessions and 4 parent sessions.		
Outcomes	The German version of the Anxiety Disorders Interview Schedule (ADIS) for Children (DIPS-K).			
	Children's Global Asses	ssment Scale (K-GAS).		
	The German version of	the Social Phobia and Anxiety Inventory for Children (German version: SPAIK).		
	The German version of	the Coping Questionnaire—Child (German version: CQ-C).		
	The German scale, Socially Anxious Cognitions Scale for Children (SAKK).			
	Children's Depression Inventory (DIKJ) — a German self-report measure of depressive symptoms.			
Notes	Follow-up 2 months.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned to intervention or control by a webbased computerised randomisation plan generator (http://www.randomization.com).		
	Low risk	based computerised randomisation plan generator (http://www.randomiza-		
tion (selection bias)  Allocation concealment		based computerised randomisation plan generator (http://www.randomiza-		
Allocation concealment (selection bias)  Blinding (performance bias and detection bias)	Low risk	based computerised randomisation plan generator (http://www.randomization.com).		
Allocation concealment (selection bias)  Blinding (performance bias and detection bias)  All outcomes  Blinding of outcome as-	Low risk Unclear risk	based computerised randomisation plan generator (http://www.randomization.com).  No information available.  Outcome assessments were viewed by an expert who was blind to the treat-		

# **Mendlowitz 1999**

Study characteristics	
Methods	RCT, W/L control; blind assessment not clear, completer analysis.  Sample size (initial/completed): group child CBT 23/23; group child + parent 21/21; W/L controls 40/40.
Participants	N = 68; age range 9-13 years; mean age 9.3 years; 43% male; ethnicity unspecified; community sample—children with anxiety disorders using DICA-R-P. Exclusion criteria: psychotic disorder, medical disorder that interfered with participation, lacked proficiency in English.



Mendlowitz 1999 (Continued)		
Interventions		ld CBT 12 * 90 minutes; group parents CBT 12 *unspecified number of minutes; BT 12 *unspecified number of minutes; W/L control (2 to 6 months, then offered
Outcomes	RCMAS. CCSC. GIS.	
Notes	Follow-up 12 months.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned.
Allocation concealment (selection bias)	Unclear risk	_
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias)	Unclear risk	_
Incomplete outcome data (attrition bias) All outcomes	Low risk	All completed treatment.
Selective reporting (reporting bias)	Low risk	Data reported.

### Muris 2002

Study characteristics	
Methods	RCT of CBT — group versus emotional disclosure (ED — psychological placebo), and control.
	Sample size (initial/completed): CBT (10/10), ED (10/10), control (10/10).
Participants	N = 30 children, mean age 10.25, SD 0.8; range 9-12 years. Gender 66.6% female. Ethnicity: CBT and ED Caucasian 90%; Indonesian Dutch 10%. Separation anxiety disorder 50%, GAD 35%, 15% social phobia. Comorbidity 40% anxiety disorders. Setting schools.
Interventions	CBT — Treatment consisted of 12 30-minute sessions, twice per week, following the Coping Koala CBT programme (Barrett et al. 1996). ED consisted of emotional writing (Reynolds 2000).
Outcomes	DISC (Version 2.3).
	RCADS is an adaptation of the Spence Children's Anxiety Scale (SCAS; Spence, 1997, 1998).
	STAIC.
	Treatment evaluation questionnaire.



### Muris 2002 (Continued)

Notes

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Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details given.
Allocation concealment (selection bias)	Low risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	Treatment outcome measures were obtained by a child psychologist, who was not involved in the treatment sessions.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No flow chart, no participants dropped out of the study once allocated to treatment condition.
Selective reporting (reporting bias)	Low risk	Data reported.

# Nauta 2003

Study characteristics	3
Methods	RCT, WL control; unclear blind assessment; ITT analysis.  Sample size (initial/completed): individual CBT 29/26, individual + 7 sessions parental CBT 30/30, W/L controls 20/20.
Participants	N = 79; age range 7-18 years; mean age 11.0 years; 49% male; ethnicity not specified; community sample—generalised anxiety disorder GAD (n = 15), separation anxiety disorder SAD (n = 26), social anxiety disorder SOP (n = 31); panic anxiety disorder PAD (n = 7).  Exclusion criteria: principal diagnosis of simple phobia or other (non-anxiety) diagnoses; intellectual or physical disabilities; antianxiety or depression medication; parents involved in acute marital breakdown.
Interventions	Clinic-based individual CBT 12 sessions (unspecified number of minutes).
	Clinic-based 12 individual CBT + 7 sessions parental CBT family intervention (unspecified numbers of minutes).
	Waiting list controls (duration not specified, then offered treatment).
Outcomes	ADIS-C. ADIS-P. FSSC-R. CBCL. SCAS-C.
	SCAS-P.



### Nauta 2003 (Continued)

Notes Follow-up 3 months.

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned.
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Unclear risk	No details given
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study states the fate of all participants and dropouts are noted.
Selective reporting (reporting bias)	Low risk	Data reported.

### Olivares 2005

Study characteristics	
Methods	RCT, WL; blind assessment; completer analysis. Sample size (initial/completed): GCBT (17/16), waiting list (17/17).
Participants	N = 34; age range 14-17 years; mean years 15.03; 60% female; ethnicity not specified. Community sample SOP (n = 34). Exclusion criteria not specified.
Interventions	School-based group CBT: 12 * 90 minutes. Waiting list: 24 weeks, then treatment offered.
	CBT (IAFS programme) to group with individual sessions. Diagnosis — social phobia.
Outcomes	ADIS-C.
	EI (Escala de Inadaptación). SASI (Escala de Autoestima).
	Anxiety and social avoidance: SPAI (social phobia and anxiety inventory), EDAS (Evaluación diagnóstica de la ansiedad social), SAS-A (Social anxiety scale for adolescents), SIAS (Social Interactions Anxiety Scale), SADS (Anxiety and Social Avoidance Scale), SPS (Social Phobia Scale), PRCS (Personal Report of Confidence as Speaker).
	<u>Cognitive component of social phobia</u> : SSPS (Self-Assessment during Public Speaking Situations), FNES (Fear to Negative Evaluation subscale of SAS-A).
	Other parameters: RAS (Assertiveness scale), EHSPA (Escala de habilidades socials para adolescentes).



### Olivares 2005 (Continued)

Notes

Follow-up 6 months and 12 months for the treatment group, only 6 months for the waiting list controls (after this period, they were offered treatment).

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence described.
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Unclear risk	Assessors blind during the process.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The loss of one participant in the treatment group reported in the table.
Selective reporting (reporting bias)	Low risk	Data reported.

#### Reaven 2012

Study characteristics	
Methods	RCT of CBT—child plus parent versus TAU control. Sample size (initial/completed): CBT (24/21); TAU control 26/26.
Participants	N = 50 children, mean age 10.48, SD 1.66, range 7–14 years. Gender 96% male. Ethnicity: Caucasian 84%, African American 6%, Asian/Pacific Islander 2%, multi-racial 8%. All participants had a diagnosis of autism, or Asperger's syndrome, or pervasive developmental disorder not otherwise specified (PDD-NOS) and verbal IQ ≥ 70 and clinically significant symptoms of anxiety, defined as a score above the clinical significance cutoff on separation (SEP), social (SOC) and/or generalized anxiety (GAD) subscales of the Screen for Child Anxiety and Related Emotional Disorders— parent version (SCARED; Birmaher et al. 1999). Medication (92%) stable. Setting university clinics.
Interventions	CBT—Facing Your Fears (FYF):The intervention consisted of 12 multi-family group sessions, 1.5 hours in duration. The FYF intervention was developed specifically for children with ASD and incorporated the important components of prior empirically supported programmes (e.g. Coping Cat; Kendall and Hedtke, 2006).
Outcomes	ADIS-PC.
	Clinician Severity Ratings-CSR. CGIS-I.
Notes	
Risk of bias	



### Reaven 2012 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computer-generated assignment system used.
Allocation concealment (selection bias)	Low risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	Independent evaluators blind to treatment condition used to conduct assessments.
Incomplete outcome data (attrition bias) All outcomes	Low risk	CONSORT flow diagram, the fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# Sánchez-García 2009

Study characteristics	
Methods	RCT of CBT (IAFS) — Intervention With Adolescents With Social Phobia. Three-arm trial — IAFS, IAFS without cognitive re-structuring and W/L control; blind assessment. Completer analysis — only 7 dropouts but not specified from which group.  Sample size (initial/completed): CBT (IAFS) 28/28; IAFS without restructuring 29/29; W/L controls 25/25.
Participants	N = 82 children; mean age 11.91 years, SD 1.33, range 10–14 (60 girls, 22 boys). Ethnicity Spanish.  All participants had specific social phobias.
Interventions	CBT: 12-session CBT or the WL condition. Participants in the CBT condition were seen by therapists for group therapy for 90 minutes for 12 weeks.
Outcomes	ADIS-IV-C. SPAI-C.
	SASC-R (Social Anxiety Scale for Children Revised).
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Ño details given.
Allocation concealment (selection bias)	Unclear risk	No details given.



Sánchez-García 2009 (Continue	ed)	
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	Blind independent assessment of outcome video measure.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participants dropped out of the study.
Selective reporting (reporting bias)	Low risk	Data reported.

# Schneider 2011

Study characteristics		
Methods	RCT of CBT — child plus parent versus W/L control. Sample size (initial/completed): CBT (21/18); W/L control (22/21).	
Participants	N = 43 children. Mean age of the children was 6.29 years (SD 1.01) in the treatment group and 6.18 years (SD 0.73) in the waiting list group; range 5-7 years. Gender: male 4.3%. Ethnicity: not reported. All participants: autism spectrum disorder (ASD). All participants had separation anxiety disorder (SAD), comorbidity 44.18%. Setting university clinics.	
Interventions	gramme, was divided i SAD-specific psycho-ec minute sessions with t veloped to educate the	ession disorder-specific (separation anxiety disorder) SAD treatment pro- into individual and family sessions. The first 4 weeks of treatment consisted of ducation in 4 weekly 50-minute sessions with the child alone and 4 weekly 50- he parents alone. Age-appropriate materials with pictorial illustrations were de- e children. The second 8 weeks of treatment consisted of weekly 50-minute fam- into two parts: one with parents and child together, and a second with parents
Outcomes	The Kinder-DIPS Schneider Scale.	
	Separation Anxiety Inv	ventory for Children (SAI).
	RCMAS-P.	
Notes	Follow-up 2 months.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was conducted by a statistician using a computerised permuted block design, with assignments concealed until the time of group assignment.
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.



Schneider 2011 (Continued)		
Blinding of outcome assessment (detection bias)	Low risk	Interviews were conducted by trained clinical psychologists or advanced masters students, blinded to group status at all evaluations.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram, the study states the fate of all participants and dropouts are noted.
Selective reporting (reporting bias)	Low risk	Data reported.

### Shortt 2001

Study characteristics	s
Methods	RCT, WL control; blind assessment; completer analysis. Sample size (initial/completed): group CBT 54/48, W/L controls 17/16.
Participants	N = 71; age range 7-14 years; mean age 7.85 years; 41% male; ethnicity 92% Australian; community sample — GAD (n = 42), SAD (n = 19), SOP (n = 10). Exclusion criteria: intellectual or severe physical impairment; currently receiving other treatment.
Interventions	Clinic-based group CBT children 10 (plus 2 booster sessions) * 50-60 minutes; parents 6 hours: waiting list controls (10 weeks, then offered treatment).
Outcomes	DISCAP. RCMAS. CBCL.
Notes	Follow-up 12 months.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned.
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	"At post-treatment and follow-up, diagnostic interviews were conducted by psychologists naive to the child's treatment condition or diagnostic status".
Incomplete outcome data (attrition bias) All outcomes	Low risk	The fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Low risk	Data reported.



### Silverman 1999

Study characteristics	•
Methods	RCT, WL control; blind assessment; completer analysis. Sample size (initial/completed): group + parent CBT 37/25, W/L controls 19/16.
Participants	N = 56; age range 6-16 years; mean age 9.66 years; 61% male; ethnicity 45% white; community sample—overanxious disorder (OAD) (n = 29), generalised anxiety disorder (GAD) (n = 12), social phobia (SOP) (n = 15).  Exclusion criteria: pervasive developmental disorders, psychotic symptoms, current treatment.
Interventions	Clinic-based group CBT with parent component: 15-minute joint meeting; child 12 * 55 minutes; parent 12 * 55 minutes. Waiting list controls (8-10 weeks, then offered treatment).
Outcomes	ADIS-C. ADIS-P. RCMAS. FSSC-R. CBCL.
Notes	Follow-up 12 months.

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Assigned to group randomly at a ratio of 2 to 1 (treatment to control).
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	"All post-test and post-wait assessments were completed by a staff member who was unaware of condition assignment".
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study states the fate of all participants and the data on dropouts are noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# Spence 2000

Study characteristic	rs ·
Methods	RCT, WL control; blind assessment; completer analysis.  Sample size (initial/completed): group child and parent CBT 17/16, group child CBT 19/15, W/L controls 14/9.



Spence 2000 (Continued)	
Participants	Clinic based: CBT N = 50; age range 7-14 years; mean age 10.7 years; 62% male; ethnicity not specified; community sample—SOP (n = 50).  Exclusion criteria: principal diagnosis of simple phobia or other (non-anxiety) diagnoses; intellectual or physical disabilities; antidepressant medication; parents involved in acute marital breakdown.
Interventions	Clinic-based group CBT 14 * 90 minutes; clinic-based group CBT + family intervention; child 14 * 90 minutes; parent 14 * 90 minutes.  Waiting list controls—no treatment.
Outcomes	ADIS-P. RCMAS.
Notes	Follow-up 12 months.

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned.
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Unclear risk	Telephone interview conducted blind at 12-month follow-up.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study states the fate of all participants and dropout data are noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# Spence 2006

Study characteristics	
Methods	RCT, WL control; blind assessment; completer analysis.  Sample size (initial/ completed) 72/65; clinic-based CBT 22/19, Internet CBT 27/23, W/L controls 23/23.
Participants	Total sample = 72; age range 7-14 years; mean age 9.93 years; WL control 57% males; ethnicity not specified; community sample—separation anxiety disorder (SAD) (n = 15), generalised anxiety disorder (GAD) (n = 20), social phobia (SOP) (n = 30), and SP (n = 7).  Exclusion criteria: principal diagnosis of simple phobia or other (non-anxiety) diagnoses; intellectual or physical disabilities; anti-anxiety or depression medication; parents involved in acute marital breakdown.
Interventions	ADIS-P.
	SCAS-C/P.



Spence	2006	(Continued)
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RCMAS.

Children's Depression Inventory (CDI).

CBCL.

Outcomes

Clinic CBT: 10 child sessions (conducted over 10 weeks) and 6 parent sessions (over 6 weeks), plus booster treatment at 1 and 3 months post-treatment. All sessions 60 minutes.

Internet CBT; same quantity as clinic CBT group but half sessions delivered over Net. For child, 5/10 plus the 3-month booster session were delivered via Net. For parents, 3/6 sessions and 3-month booster delivered over Net. All sessions = 60 minutes to complete.

Waiting list — no treatment.

Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"A coin was tossed in advance of the study to determine the order of randomisations for each block of participants".
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	Interviews used two trained interviewers who were blind to the children's original diagnoses.
Incomplete outcome data (attrition bias) All outcomes	Low risk	CONSORT flow diagram, the fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# **Sung 2011**

Study characteristics	
Methods	RCT of CBT versus SR social recreational programme. Sample size (initial/ completed): CBT 36/33, SR 34/31.
Participants	N = 70 children with high-functioning ASD. Mean SD 9–16 years; CBT 11.33 (2.03), SR 11.09 (1.53), gender 94.3% male; ethnicity Chinese 65, Malay 3, Indian 1, Other 1.
Interventions	Group treatment: follow-up 3 and 6 months. The manualised CBT programme consisted of 16 90-minute weekly sessions delivered in small groups of 3–4 participants. Each group was conducted by 2 therapists. The CBT programme was developed by psychologists from the Child Guidance Clinic and the Autism Resource Centre (Singapore). Modifications and adaptations were made from various CBT programmes such as the Coping Cat programme, Exploring Feelings and unpublished anxiety management programmes from the CGC and the Autism Resource Centre.



Sung 2011 (Continued)

Outcomes SCAS-C.

CGI-S.

Notes

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisations with treatment assignment in each block as ABBAABBA (A = CBT and B = SR).
Allocation concealment (selection bias)	Low risk	Group allocations were concealed from child and parent.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	Clinicians were blind to group assignment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Consort flow diagram used, the study states the fate of all participants and dropouts are noted.
Selective reporting (reporting bias)	Low risk	Data reported.

# Walkup 2008

Study	chara	ctor	icticc

Study Characteristics	
Methods	RCT, placebo control; blind assessment, ITT and completer analysis. Sample size (initial/completed): CBT 139/135; placebo 76/61; sertraline 133/110; both 140/127.
Participants	N = 488; mean age 10.7 years; 50% female; ethnicity 79% white, 12% Hispanic, 9% black, 8% other, 2.5% Asian, 1.2% American Indian, 0.4% Pacific Islander; recruitment from medical centres; separation anxiety disorder, generalised anxiety disorder or social phobia (SAD), GAD or SOP. Exclusion criteria: unstable medical condition, refusing to attend school because of anxiety, had tried but had not had a response to two adequate SSRI trials or an adequate CBT trial, girls who were pregnant or were not using adequate birth control despite being sexually active, people who presented an acute risk to themselves, people using psychotropic medication or other stable doses of stimulants and those who had a psychiatric diagnosis that made participation inappropriate.
Interventions	CBT: 14 * 60-minute sessions.
	Pharmacotherapy: 8 * 50 to 60 minutes each.
	Sertraline and matching placebo were administered on a fixed flexible schedule beginning with 25 mg per day and adjusted up to 200 mg per week by week eight. Pill counts and medication diaries were used to facilitate adherence.
Outcomes	ADIS- C.
	CGI-Improvement scale.



#### Walkup 2008 (Continued)

Pediatric Anxiety Rating scale.

Children's Global Assessment scale.

#### Notes

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The randomisation sequence in a 2:2:2:1 ratio was determined by a computer-generated algorithm and maintained by the central pharmacy, with stratification according to age, sex and study centre".
Allocation concealment (selection bias)	Low risk	
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	"The interviews were administered by independent evaluators who were unaware of study-group assignments".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram used, the fate of all participants and dropouts noted.
Selective reporting (reporting bias)	Low risk	All data reported.

#### Waters 2009

	_	_		
Stu	dv c	hara	ıcter	istics

Methods	RCT comparing CBT parent + child, parent only and W/L controls. Sample size (initial/completed): CBT child (31/24). Parent only (38/25), W/L controls (11/11).

#### **Participants**

N = 80 children; mean age child only 6.89 SD 1.25 years; child + parent 6.68 SD 1.2; W/L controls 6.79 SD 1.03. Gender males/females: child only 17/14; parent + child 20/18; W/L 5/6. Ethnicity: born in Australia child 97%; parent + child 97%; W/L controls 91%. Anxiety diagnoses (child, parent + child, W/L controls) — generalised anxiety disorder (GAD) 22.58%, 10.52%, 27.27%; separation anxiety disorder (SAD) 19.35%, 26.31%, 9.09%; social anxiety disorder 12.9%, 23.68%, 27.27%; specific phobia 45.16%, 39.47%, 36.36%; more than one anxiety diagnosis 84%, 87%, 82%.

#### Interventions

CBT in a programme called ACTION. The 'Take ACTION' programme—a CBT programme for children with anxiety disorders between 4 and 18 years of age (Waters, Donaldson, and Zimmer-Gembeck, 2008; Waters, Wharton, Zimmer-Gembeck, and Craske, 2008). Treatment of children in the parent and child condition was conducted in a group format and consisted of 10 one-hour sessions conducted on a weekly basis.

The content covered in the parent sessions was identical in the parent + child and parent-only conditions. Parent sessions were also in a group format and of 1 hour duration, held weekly over 10 weeks. Parent sessions in both conditions included (1) psycho- education about child anxiety, (2) parent strategies for managing child anxiety and improving the parent-child relationship, (3) coverage of the Take ACTION steps that children complete each week along with parent strategies for assisting the



Waters 2009 (Continued)	child to learn these techniques, (4) promotion of positive parental coping, and (5) training in communication and problem-solving skills.
Outcomes	ADIS-C-IV-C/P.
	SCAS-P.
	CBCL.
	Parenting Scale (PS; Arnold, O'Leary, Wolff, and Acker, 1993).
	Parents Sense of Competency Scale (PSCS; Johnston and Mash, 1989).
	Depression, Anxiety and Stress Scale, 42-item version (DASS-42; Lovibond and Lovibond, 1995).
Notos	

# Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned.
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	Follow-up assessment conducted by blind independent clinical psychology postgraduates who were blind to children's diagnostic status and intervention group.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow diagram, the study states the fate of all participants.
Selective reporting (reporting bias)	Low risk	Data reported.

# **White 2012**

Study characteristics	S
Methods	RCT: Multimodal Anxiety and Social Skills Intervention (MASSI) programme. Sample size (initial/completed): CBT (15/13); W/L control (15/12).
Participants	N = 30, age 15; gender male 23 (77%); ethnicity Caucasian 26 (87%); Asian Pacific Islander 1 (0.03%); African American 2 (0.07%); Pacific Islander 1 (0.03%). Diagnoses — social phobia (SoP) 23 (77%); generalised anxiety disorder (GAD) 19 (63%); SP 16 (53%); separation anxiety disorder (SAD) 1 (3%); obsessive-compulsive disorder (OCD) 4 (13%); panic disorder/agoraphobia (PD/Agor) 1 (3%); post-traumatic stress disorder PTSD 1 (3%).
Interventions	Multimodal Anxiety and Social Skills Intervention (MASSI) programme. MASSI is a manual-based modular treatment programme delivered via three modalities—individual therapy (up to 13 sessions), group



White 2012 (Continued)	therapy (skills practice, 7 sessions) and parent education and coaching (after each individual therapy session).
Outcomes	ADIS-C/P; Social Responsiveness Scale (SRS; Constantino and Gruber 2005); Child and Adolescent Symptom Inventory-4 ASD Anxiety Scale (CASI-Anx; Sukhodolsky et al. 2008); Pediatric Anxiety Rating Scale (PARS; Research Units on Pediatric Psychopharmacology; Anxiety Study Group, RUPP 2002); CGI-I; Developmental Disabled Children's Global Assessment Scale (DD-CGAS; Wagner et al. 2007).
Notes	

## Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Names drawn out of a box by an unaffiliated person to assign participants to intervention groups.
Allocation concealment (selection bias)	Low risk	
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Low risk	Coders who were rating were blind to the therapists' rating of fidelity. PARS conducted and scored by trained raters who were blind to treatment assignment. Blind independent evaluators interviewed parent and adolescents for CGI-I and DD-CGAS.
Incomplete outcome data (attrition bias) All outcomes	Low risk	CONSORT flow diagram, the study shows the fate of all participants.
Selective reporting (reporting bias)	Low risk	Data reported.

## **Wood 2009**

Study characteristics	s
Methods	RCT of CBT child plus parent versus W/L control. Sample size (initial/completed): CBT 17/14; W/L control 23/22.
Participants	N = 40 children, mean age 9.20, SD 1.49, range 7–11 years. Gender 67.5% male. Ethnicity: Caucasian 47.5%, African American 2.5%, Latino 12.5%, Asian/Pacific Islander 15%. All participants had a diagnosis of autism, or Asperger's syndrome, or pervasive developmental disorder, not otherwise specified (PDD-NOS) and verbal IQ ≥ 70 and an anxiety disorder—social phobia 87.5%, generalised anxiety disorder 47.5%, obsessive-compulsive disorder 42.5%, separation anxiety disorder 60%, comorbidity ADHD 60%, MDD 7.5%; medication stable. Setting university clinics.
Interventions	CBT consists of 16 weekly sessions, each lasting 90 minutes—about 30 minutes with the child and 60 minutes with the parents/family, implementing a version of the Building Confidence CBT programme (Wood and McLeod, 2008).
Outcomes	ADIS-PC. MASC.



#### Wood 2009 (Continued)

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomised assignment using a computer randomisation programme; therapists were also randomly assigned to cases.
Allocation concealment (selection bias)	Low risk	Concealment of the randomisation sequence from investigators until interventions were assigned.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details given.
Blinding of outcome assessment (detection bias)	Unclear risk	Independent evaluators were blind to treatment condition. The diagnostic review team was blind to participants' condition.
Incomplete outcome data (attrition bias) All outcomes	Low risk	CONSORT flow diagram, the study states the fate of all participants.
Selective reporting (reporting bias)	Low risk	Data reported.

ADIS-P = Anxiety Disorder Interview Schedule for Parents; ADIS-C = Anxiety Disorder Interview Schedule for Children; CBCL = Child Behavior Checklist; FSSC-R = The Fear Survey for Children Revised; CCSC = Children's Coping Strategies Scale; CIS = Clinical Improvement Scale; CSR = Clinical Severity Scale; DISCAP = Diagnostic Interview Schedule for Children, Adolescents and Parents; RCMAS = The Revised Children's Manifest Anxiety Scale; SAS = Social Anxiety Scale for Adolescents; SCARED = Screen for Child Anxiety Related Emotional Disorders; SCAS = Spence Child Anxiety Scale, Child and Parent Versions; SPAI = Social Phobia and Anxiety Inventory for Children; STAIC = State-Trait Anxiety Inventory for Children; SWQ-PU = Social Worries Questionnaire — Pupil.

## **Characteristics of excluded studies** [ordered by study ID]

Study	Reason for exclusion
Alfano 2009	Uses SET-C, a behavioural treatment.
Baer 2005	Uses a behavioural treatment model based on SET-C.
Barrett 2001	Both groups received CBT interventions. No control condition.
Beidel 2000	Participants received 'testbusters'—an active but non-specified treatment.
Beidel 2007	Uses SET-C, a behavioural treatment.
Bernstein 2005	An intervention study for anxious children with mild to moderate symptoms only: no formal diagnosis, and the most symptomatic children (CSR of 7–8) were excluded.
Blagg 1984	Primarily a paper on behavioural rather than cognitive behavioural therapy. Primary outcome: school refusal rather than anxiety diagnosis.
Cartwright-Hatton 2011	Parenting treatment only.



Study	Reason for exclusion
Cornwall 1996	Simple phobia included: data on those responding not available.
Forman 2007	Included those with anxiety or depression as primary diagnosis.
Gallagher 2004	Study of a brief intervention involving only three sessions.
Joorman 2002	Allocation of cases on an alternating basis, not randomised.
King 1998	Target was school refusal rather than primary anxiety diagnosis. Primary outcome measure was school attendance (% days present) rather than an anxiety diagnosis.
Last 1998	Primary target was anxiety-based school refusal rather than anxiety diagnosis.
Leong 2009	Both groups received CBT interventions. No control condition.
Lowry-Webster 2003	Prevention study.
Menzies 1993	Simple phobia; alternative treatment control; categorical outcomes not reported; insufficient data to calculate effect size; too few sessions.
Mifsud 2005	No formal diagnosis made; only children with high levels of anxiety recruited.
Olivares 2007	No primary outcome.
Ordeig 2004	No primary outcome, relied on self-reports.
Silverman 1999b	Treatment primarily of simple phobia (84% of cases).
Sofronoff 2005	Contained participants with OCD. No formal diagnosis of anxiety disorder. Treatment by therapists trained for one day and treatment only six sessions.
Treadwell 1996	Not manualised CBT.
Warren 1984	No formal diagnosis of anxiety disorder.

## **Characteristics of ongoing studies** [ordered by study ID]

## Jansen 2012

Study name	Thinking, Doing = Daring (TDD).
Methods	CBT versus Treatment as Usual.
Participants	120, 60 in each arm.
Interventions	СВТ.
Outcomes	Primary child anxiety SACRED, CBCL, TRF (Teacher Rate Form).
Starting date	
Contact information	m.jansen@pwo.ru.nl



Jansen 2012 (Continued)

Notes

## DATA AND ANALYSES

## Comparison 1. CBT versus wait-list

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1.1 Remission of anxiety diagnoses (ITT analysis)	26	1350	Odds Ratio (IV, Random, 95% CI)	7.85 [5.31, 11.60]
1.1.1 Individual CBT	7	325	Odds Ratio (IV, Random, 95% CI)	7.92 [3.37, 18.63]
1.1.2 Group CBT	13	546	Odds Ratio (IV, Random, 95% CI)	7.86 [3.83, 16.12]
1.1.3 Family/Parental CBT	12	479	Odds Ratio (IV, Random, 95% CI)	8.65 [5.01, 14.92]
1.2 Acceptability -participants lost to follow-up	26	1321	Odds Ratio (IV, Random, 95% CI)	0.94 [0.58, 1.51]
1.3 Reduction in anxiety symptoms	30	1483	Std. Mean Difference (IV, Random, 95% CI)	-0.98 [-1.21, -0.75]
1.3.1 Individual	8	344	Std. Mean Difference (IV, Random, 95% CI)	-0.59 [-0.82, -0.36]
1.3.2 Group	15	608	Std. Mean Difference (IV, Random, 95% CI)	-1.27 [-1.74, -0.80]
1.3.3 Family/Parental	13	531	Std. Mean Difference (IV, Random, 95% CI)	-0.93 [-1.29, -0.56]
1.4 Remission of anxiety diagnoses: long term follow-up	3	124	Odds Ratio (IV, Random, 95% CI)	3.22 [0.96, 10.75]
1.5 Reduction in anxiety symptoms: long term follow-up	4	186	Std. Mean Difference (IV, Random, 95% CI)	-1.55 [-3.20, 0.10]
1.6 Sensitivity analysis: Remission of anxiety diagnoses (completers only analysis)	26	1365	Odds Ratio (IV, Random, 95% CI)	11.09 [7.47, 16.45]
1.6.1 Individual CBT	7	325	Odds Ratio (IV, Random, 95% CI)	11.09 [5.46, 22.56]
1.6.2 Group CBT	13	568	Odds Ratio (IV, Random, 95% CI)	11.36 [5.47, 23.59]
1.6.3 Family/Parental CBT	12	472	Odds Ratio (IV, Random, 95% CI)	11.35 [6.36, 20.25]



Analysis 1.1. Comparison 1: CBT versus wait-list, Outcome 1: Remission of anxiety diagnoses (ITT analysis)

	CBT		Wait-list			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Individual CBT							
Barrett 1996	16	28	4	13	4.7%	3.00 [0.74, 12.11]	
Flannery-Schroeder 2000	7	18	0	7	1.5%	9.78 [0.48 , 197.85]	
Galla 2012	15	22	1	18	2.5%	36.43 [4.01, 331.19]	
Kendall 1994	17	27	1	20	2.6%	32.30 [3.74, 279.31]	
Kendall 1997	32	60	11	43	7.4%	3.32 [1.42 , 7.80]	
McNally Keehn 2012	7	12	0	10	1.4%	28.64 [1.37 , 600.41]	
Nauta 2003	20	37	1	10	2.5%	10.59 [1.22 , 92.25]	
Subtotal (95% CI)		204		121	22.6%	7.92 [3.37 , 18.63]	
Total events:	114		18			. , .	_
Heterogeneity: Tau <sup>2</sup> = 0.42; (		= 6 (P = 0)		4%			
Test for overall effect: $Z = 4$ .		,					
1 1 2 Comme CDT							
1.1.2 Group CBT	0	22	2	10	4.007	1 50 50 24 7 203	
Barrett 1998	9	23	3	10	4.0%	1.50 [0.31 , 7.36]	<del>- -</del> -
Chalfant 2007	20	28	0	19	1.5%	94.06 [5.08 , 1741.83]	-
Dadds 1997	35	46	27	48	7.2%	2.47 [1.02 , 6.00]	<b></b>
Flannery-Schroeder 2000	7	13	0	7	1.4%	17.31 [0.82 , 365.21]	-
Gil-Bernal 2009	3	6	0	5	1.3%	11.00 [0.43 , 284.30]	<del>                                     </del>
Hayward 2000	6	12	1	22	2.3%	21.00 [2.10 , 210.14]	<del></del>
Lau 2010	16	24	0	21	1.5%	83.47 [4.49 , 1552.94]	
Masia-Warner 2005	12	21	4	21	4.7%	5.67 [1.41 , 22.76]	<del></del>
Melfsen 2011	7	21	1	23	2.5%	11.00 [1.22 , 99.26]	_ <del>-</del>
Olivares 2005	10	17	0	17	1.5%	49.00 [2.53, 948.62]	
Silverman 1999	16	37	5	19	5.5%	2.13 [0.64 , 7.16]	+
Spence 2000	23	36	0	7	1.5%	26.11 [1.38 , 493.87]	-
Spence 2006	13	20	3	23	4.2%	12.38 [2.70 , 56.73]	<del></del>
Subtotal (95% CI)		304		242	39.2%	7.86 [3.83 , 16.12]	•
Total events:	177		44				
Heterogeneity: Tau <sup>2</sup> = 0.68; C Test for overall effect: Z = 5.0		•	= 0.04); 1² =	÷ 45%			
1.1.3 Family/Parental CBT							
Barrett 1996	21	25	5	13	4.1%	8.40 [1.79, 39.44]	
Barrett 1998	7	17	3	10	3.7%	1.63 [0.31, 8.61]	
Cobham 2012	18	23	0	12	1.5%	84.09 [4.26, 1659.99]	
Gil-Bernal 2009	2	6	0	5	1.3%	6.11 [0.23, 162.73]	
Hirshfeld-Becker 2010	16	30	5	29	5.5%	5.49 [1.65, 18.23]	
Masia-Warner 2011	11	20	1	20	2.5%	23.22 [2.59, 208.61]	
Nauta 2003	23	39	1	10	2.5%	12.94 [1.49 , 112.44]	
Schneider 2011	16	21	3	22	4.0%	20.27 [4.18, 98.23]	
Shortt 2001	33	54	2	17	4.0%	11.79 [2.44, 56.85]	
Spence 2000	15	17	0	7	1.3%	93.00 [3.95 , 2189.96]	
Waters 2009	14	31	2	11	3.7%	3.71 [0.69 , 20.04]	
Wood 2009	9	17	3	23	4.1%	7.50 [1.60 , 35.07]	<u> </u>
Subtotal (95% CI)		300		179	38.3%	8.65 [5.01 , 14.92]	_
Total events:	185	<del>-</del>	25		·- · •		_
Heterogeneity: Tau <sup>2</sup> = 0.08; (		f = 11 (P		9%			
Test for overall effect: $Z = 7$ .		,	// -	-			
Total (95% CI)		808		E 40	100.0%	7 95 [5 24 - 44 60]	
, ,	476	808	87	542	100.0%	7.85 [5.31 , 11.60]	◆
Total events:							



## Analysis 1.1. (Continued)

Heterogeneity:  $1au^2 = 0.34$ ;  $Cni^2 = 44.58$ , Cii = 31 (P = 0.05);  $I^2 = 30\%$ 

Test for overall effect: Z = 10.34 (P < 0.00001)

Test for subgroup differences: Chi<sup>2</sup> = 0.06, df = 2 (P = 0.97),  $I^2$  = 0%

Analysis 1.2. Comparison 1: CBT versus wait-list, Outcome 2: Acceptability -participants lost to follow-up

	СВ	Т	Wait-	list		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Barrett 1996	5	53	4	26	7.3%	0.57 [0.14 , 2.34]	
Barrett 1998	6	40	4	20	7.3%	0.71 [0.17, 2.86]	
Chalfant 2007	4	28	0	19	2.3%	7.16 [0.36 , 141.27]	<del></del>
Dadds 1997	1	42	1	60	2.5%	1.44 [0.09, 23.67]	
Flannery-Schroeder 2000	6	31	2	12	5.4%	1.20 [0.21, 6.98]	
Galla 2012	1	22	0	18	1.9%	2.58 [0.10, 67.27]	
Gil-Bernal 2009	0	12	0	5		Not estimable	
Hayward 2000	1	12	1	23	2.4%	2.00 [0.11, 35.09]	<del></del>
Hirshfeld-Becker 2010	3	30	2	29	4.9%	1.50 [0.23, 9.70]	<del></del>
Kendall 1994	3	30	10	30	7.2%	0.22 [0.05, 0.91]	
Kendall 1997	9	75	9	43	10.5%	0.52 [0.19 , 1.42]	
Lau 2010	1	24	3	21	3.4%	0.26 [0.02 , 2.72]	
Masia-Warner 2011	0	20	1	20	1.9%	0.32 [0.01, 8.26]	
McNally Keehn 2012	0	12	0	10		Not estimable	
Melfsen 2011	6	21	2	23	5.5%	4.20 [0.74, 23.74]	<del>  -</del>
Muris 2002	0	10	0	10		Not estimable	
Nauta 2003	3	59	0	20	2.2%	2.54 [0.13, 51.32]	
Olivares 2005	1	17	0	17	1.9%	3.18 [0.12, 83.76]	
Schneider 2011	3	21	1	22	3.4%	3.50 [0.33, 36.67]	
Shortt 2001	1	54	4	17	3.6%	0.06 [0.01, 0.60]	<del></del>
Silverman 1999	12	37	3	19	7.2%	2.56 [0.62, 10.51]	<del>  -</del>
Spence 2000	5	36	5	14	7.0%	0.29 [0.07, 1.23]	
Spence 2006	2	22	0	23	2.1%	5.73 [0.26 , 126.42]	
Waters 2009	5	31	0	11	2.3%	4.77 [0.24, 93.67]	<del></del>
White 2012	2	15	3	15	4.6%	0.62 [0.09 , 4.34]	
Wood 2009	2	17	1	23	3.1%	2.93 [0.24 , 35.33]	
Total (95% CI)		771		550	100.0%	0.94 [0.58 , 1.51]	•
Total events:	82		56				Ť
Heterogeneity: $Tau^2 = 0.29$ ; C Test for overall effect: $Z = 0.2$		lf = 22 (P	= 0.15); I <sup>2</sup> =	= 23%			0.02 0.1 1 10 50 Favours CBT Favours wait-list

Test for overall effect: Z = 0.27 (P = 0.79) Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1: CBT versus wait-list, Outcome 3: Reduction in anxiety symptoms

Study or Subgroup	Mean	CBT SD	Total	Mean	Wait-list SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
1.3.1 Individual									
Barrett 1996	9.8	6.8	28	11.6	6	13	3.0%	-0.27 [-0.93, 0.39]	
Flannery-Schroeder 2000	43.8	5.71	13	53.83	16.52	12	2.6%	-0.80 [-1.62, 0.02]	
Galla 2012	47.83	17.91	22	52.5	15.29	18	3.1%	-0.27 [-0.90 , 0.35]	-
Kendall 1994	41.43	10.9	27	51.9	13.5	20	3.1%	-0.85 [-1.46, -0.25]	
Kendall 1997	43.05	11.89	60	49.67	10.16	34	3.5%	-0.58 [-1.01, -0.15]	
McNally Keehn 2012	26.75	20.79	12	36.11	16.11	10	2.6%	-0.48 [-1.33, 0.38]	
Nauta 2003	19.6	8.1	39	28.7	12	10	2.8%	-1.00 [-1.72 , -0.27]	
Spence 2000	10.31	4.68	19	13.36	8.69	7	2.5%	-0.50 [-1.38, 0.38]	
Subtotal (95% CI)			220			124	23.2%	-0.59 [-0.82 , -0.36]	<b>A</b>
Heterogeneity: $Tau^2 = 0.00$ ; C Test for overall effect: $Z = 5.0$	,	`	).76); I <sup>2</sup> = (	)%					•
1.3.2 Group									
Barrett 1998	116.2	13	19	136.2	12.1	8	2.4%	-1.52 [-2.46 , -0.59]	
Chalfant 2007	4.93	2.55	24	16.74		19	2.4%	-3.21 [-4.14 , -2.28]	<del></del>
Dadds 1997	11.52	7.32	64	11.46	7	67	3.6%	0.01 [-0.33 , 0.35]	+
Flannery-Schroeder 2000	38.4	11.24	12	53.83	16.52	12	2.6%	-1.05 [-1.92 , -0.19]	<u></u>
Gil-Bernal 2009	39.83	5.91	6	48.83	8.59	5	1.7%	-1.14 [-2.47 , 0.19]	<del></del>
Hayward 2000	2.7	1.7	11	4.8	1.7	22	2.7%	-1.21 [-1.99 , -0.42]	<u> </u>
Lau 2010	24.6	10.5	23	38.8	13.7	18	3.0%	-1.16 [-1.83 , -0.49]	
Masia-Warner 2005	3.1	1.1	18	5.8	1.6	17	2.6%	-1.93 [-2.75 , -1.11]	
Melfsen 2011	12.3	9.13	20	18.41	8.53	23	3.1%	-0.68 [-1.30 , -0.06]	-
Muris 2002	23.7	14.4	10	43.5	12.2	10	2.3%	-1.42 [-2.43, -0.42]	
Olivares 2005	64.29	28.7	17	126	18.3	17	2.4%	-2.50 [-3.43, -1.58]	
Silverman 1999	8.87	6.19	25	12.79	7.53	16	3.0%	-0.57 [-1.21, 0.07]	
Spence 2006	41	8	19	48.91	13.05	23	3.1%	-0.70 [-1.33, -0.07]	-
Sánchez-García 2009	15.45	7.77	28	30.8	5.75	25	2.9%	-2.19 [-2.89 , -1.50]	<del></del>
White 2012	14	3.44	15	15.47	5.26	15	2.9%	-0.32 [-1.04, 0.40]	
Subtotal (95% CI)			311			297	40.7%	-1.27 [-1.74, -0.80]	•
Heterogeneity: $Tau^2 = 0.70$ ; C Test for overall effect: $Z = 5.2$		,	< 0.00001)	; I <sup>2</sup> = 84%					·
1.3.3 Family/Parental									
Barrett 1996	6.6	4.6	25	11.6	6	13	2.9%	-0.96 [-1.67 , -0.25]	
Barrett 1998	110	8.2	15	136.2	12.1	16	2.4%	-2.45 [-3.41 , -1.49]	
Cobham 2012	10.91	5.78	23	16.92	3.5	10	2.7%	-1.12 [-1.92 , -0.33]	
Gil-Bernal 2009	39.8	8.87	6	48.83	8.59	5	1.8%	-0.94 [-2.23 , 0.34]	<del></del>
Hirshfeld-Becker 2010	58.9	10.1	27	60.69	8.11	27	3.3%	-0.19 [-0.73 , 0.34]	-
Masia-Warner 2011	3.3	0.3	20	5.5	3	19	3.0%	-1.02 [-1.70 , -0.35]	
Mendlowitz 1999	45	13	41	47	10	40	3.4%	-0.17 [-0.61 , 0.27]	+
Nauta 2003	22.2	16.1	37	28.7	12	10	2.9%	-0.42 [-1.12 , 0.29]	<del></del>
Schneider 2011	0.87	0.9	14	1.65	1	17	2.8%	-0.79 [-1.53 , -0.06]	<u> </u>
Shortt 2001	8.62	0.97	48	9.82	2	16	3.1%	-0.91 [-1.50 , -0.33]	
Spence 2000	10.06	5.78	17	13.36	8.69	7	2.5%	-0.48 [-1.37 , 0.42]	
Waters 2009	2.73	2.98	31	5.4	2.2	11	2.9%	-0.93 [-1.65 , -0.21]	
Wood 2009	2.36	1.15	14	4.77	0.81	22	2.5%	-2.47 [-3.37 , -1.57]	
Subtotal (95% CI)			318			213	36.1%	-0.93 [-1.29 , -0.56]	•
Heterogeneity: $Tau^2 = 0.30$ ; Consideration of the effect: $Z = 4.9$		•	< 0.0001);	$I^2 = 70\%$					•
Total (95% CI)			849			634	100.0%	-0.98 [-1.21 , -0.75]	•
Heterogeneity: $Tau^2 = 0.36$ ; C Test for overall effect: $Z = 8.2$ Test for subgroup differences	21 (P < 0.0000	01)		•	6				-4 -2 0 2 4 Favours CBT Favours wai



Analysis 1.4. Comparison 1: CBT versus wait-list, Outcome 4: Remission of anxiety diagnoses: long term follow-up

	СВ	T	Wait	-list		Odds Ratio	Odd	s Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Rand	om, 95% CI
Dadds 1999	32	40	24	39	53.1%	2.50 [0.91 , 6.85]		
Gil-Bernal 2009	10	12	0	5	12.1%	46.20 [1.87, 1141.18]		<del>-</del>
Hayward 2000	6	10	8	18	34.7%	1.88 [0.39, 9.01]	-	-
Total (95% CI)		62		62	100.0%	3.22 [0.96 , 10.75]		
Total events:	48		32					
Heterogeneity: Tau <sup>2</sup> = 0	0.45; Chi <sup>2</sup> = 3	3.23, df = 2	2 (P = 0.20)	$I^2 = 38\%$			0.002 0.1	1 10 500
Test for overall effect: 2	Z = 1.90 (P =	0.06)					Favours wait-list	Favours CBT

Test for overall effect: Z = 1.90 (P = 0.06) Test for subgroup differences: Not applicable

Analysis 1.5. Comparison 1: CBT versus wait-list, Outcome 5: Reduction in anxiety symptoms: long term follow-up

		CBT		1	Wait-list			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Dadds 1997	9.25	7.45	46	9.57	6.35	48	28.2%	-0.05 [-0.45 , 0.36]	
Gil-Bernal 2009	29.69	4.13	6	49.33	4.93	5	17.9%	-3.99 [-6.38 , -1.59]	
Hayward 2000	96.4	34.6	10	99.2	41.8	18	27.0%	-0.07 [-0.84, 0.70]	<b>.</b>
Sánchez-García 2009	11.91	6.03	28	27.64	4.01	25	26.9%	-2.99 [-3.79 , -2.19]	•
Total (95% CI)			90			96	100.0%	-1.55 [-3.20 , 0.10]	
Heterogeneity: Tau <sup>2</sup> = 2.4	18; Chi² = 50.9	9, df = 3 (	P < 0.0000	1); I <sup>2</sup> = 949	6				<b>\</b>
Test for overall effect: Z	= 1.84 (P = 0.0	07)							-10 -5 0 5 10
Test for subgroup differen	nces: Not appl	icable							Favours CBT Favours wait-list

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Analysis 1.6. Comparison 1: CBT versus wait-list, Outcome 6: Sensitivity analysis: Remission of anxiety diagnoses (completers only analysis)

1.6.1 Individual CBT Barrett 1996 Flannery-Schroeder 2000	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Barrett 1996 Flannery-Schroeder 2000							, ,
Barrett 1996 Flannery-Schroeder 2000							
•	16	28	6	23	6.0%	3.78 [1.14 , 12.47]	
•	7	18	0	6	1.5%	8.48 [0.41 , 173.72]	<u> </u>
Galla 2012	15	22	1	18	2.6%	36.43 [4.01, 331.19]	
Kendall 1994	17	27	1	20	2.7%	32.30 [3.74 , 279.31]	<u></u>
Kendall 1997	32	60	2	34	4.5%	18.29 [4.02 , 83.27]	
McNally Keehn 2012	7	12	0	10	1.5%	28.64 [1.37 , 600.41]	
Nauta 2003	20	37	1	10	2.7%	10.59 [1.22 , 92.25]	
Subtotal (95% CI)	20	<b>204</b>	1	121	21.3%	11.09 [5.46, 22.56]	
Total events:	114	204	11	121	21.570	11.05 [5.40 , 22.50]	_
Heterogeneity: Tau <sup>2</sup> = 0.00; C		- 6 (D - (		0/_			
Test for overall effect: $Z = 6.6$		•	).42), 1 <sup>-</sup> – 0	70			
1.6.2 Group CBT							
Barrett 1998	9	19	4	16	4.8%	2.70 [0.64 , 11.47]	<u>l</u> .
Chalfant 2007	20	28	0	19	1.6%	94.06 [5.08 , 1741.83]	T-
Dadds 1997	49	64	38	67	8.9%	2.49 [1.17, 5.30]	
Flannery-Schroeder 2000	6	12	0	6	1.5%	13.00 [0.60 , 281.46]	-
Gil-Bernal 2009	3	6	0	5	1.3%	11.00 [0.43 , 284.30]	<del>                                     </del>
Hayward 2000	6	12	1	22	2.4%	21.00 [2.10 , 210.14]	<del>                                     </del>
Lau 2010	16	24	0	21	1.6%		
Lau 2010 Masia-Warner 2005						83.47 [4.49 , 1552.94]	
Melfsen 2011	12 7	18	1	18	2.5%	34.00 [3.61 , 320.10]	
		21	1	23	2.6%	11.00 [1.22 , 99.26]	_ <del>-</del>
Olivares 2005	9	16	0	17	1.6%	44.33 [2.28 , 863.86]	
Silverman 1999	14	25	2	16	3.9%	8.91 [1.66 , 47.75]	
Spence 2000	23	36	1	14	2.7%	23.00 [2.69 , 196.40]	
Spence 2006	13	20	3	23	4.5%	12.38 [2.70 , 56.73]	
Subtotal (95% CI)		301		267	39.8%	11.36 [5.47, 23.59]	◆
Total events:	187		51				
Heterogeneity: Tau² = 0.68; C Fest for overall effect: Z = 6.5		,	= 0.05); 12 =	= 43%			
iest for overall effect. 2 0.5	2 (1 0.0000	,1)					
1.6.3 Family/Parental CBT							
Barrett 1996	21	25	5	13	4.4%	8.40 [1.79 , 39.44]	_ <del>-</del>
Barrett 1998	7	17	4	16	4.6%	2.10 [0.47, 9.30]	+-
Cobham 2012	18	23	0	10	1.5%	70.64 [3.54 , 1408.12]	
Gil-Bernal 2009	2	6	0	5	1.3%	6.11 [0.23 , 162.73]	<del></del>
Hirshfeld-Becker 2010	16	30	5	29	5.9%	5.49 [1.65 , 18.23]	_ <del>-</del>
Masia-Warner 2011	11	20	1	20	2.6%	23.22 [2.59 , 208.61]	_ <del></del>
Nauta 2003	23	39	1	10	2.7%	12.94 [1.49 , 112.44]	<del></del>
Schneider 2011	17	21	3	22	4.0%	26.92 [5.25 , 137.89]	_ <del></del>
Shortt 2001	23	48	1	16	2.8%	13.80 [1.69 , 112.91]	<del></del>
Spence 2000	15	17	1	14	2.1%	97.50 [7.90 , 1203.00]	
Waters 2009	18	24	2	11	3.6%	13.50 [2.26, 80.79]	
Wood 2009	9	14	2	22	3.5%	18.00 [2.92 , 110.96]	
Subtotal (95% CI)		284		188	38.9%	11.35 [6.36, 20.25]	
Total events:	180		25				•
Heterogeneity: Tau <sup>2</sup> = 0.14; C	hi <sup>2</sup> = 12.66, d	f = 11 (P	= 0.32); I <sup>2</sup> =	13%			
Test for overall effect: $Z = 8.2$		`	**				
Total (95% CI)		789		576	100.0%	11.09 [7.47 , 16.45]	•
Total events:	481		87				
Heterogeneity: Tau <sup>2</sup> = 0.31; C		f = 31 (P	= 0.09): I <sup>2</sup> =	= 26%		0.0	001 0.1 1 10



## Analysis 1.6. (Continued)

Heterogeneity: 1au<sup>2</sup> = 0.31; Cn1<sup>2</sup> = 41.96, at = 31 (P = 0.09); 1<sup>2</sup> = 26% Test for overall effect: Z = 11.96 (P < 0.00001) Test for subgroup differences: Chi² = 0.00, df = 2 (P = 1.00),  $I^2$  = 0%

1000 0.001 0.1 10 Favours CBT

## Comparison 2. CBT versus active controls

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2.1 Remission of anxiety diagnoses (ITT analysis)	6	426	Odds Ratio (IV, Random, 95% CI)	1.51 [0.77, 2.96]
2.2 Acceptability -participants lost to fol- low-up	5	424	Odds Ratio (IV, Random, 95% CI)	0.53 [0.31, 0.91]
2.3 Reduction in anxiety symptoms	8	411	Std. Mean Difference (IV, Random, 95% CI)	-0.50 [-1.09, 0.09]
2.4 Remission of anxiety diagnoses: long term follow-up (ITT analysis)	2	273	Odds Ratio (IV, Random, 95% CI)	2.03 [1.22, 3.36]
2.5 Reduction in anxiety symptoms: long term follow-up	4	395	Std. Mean Difference (IV, Random, 95% CI)	-0.91 [-2.06, 0.24]
2.6 Sensitivity analysis: remission of anxiety diagnoses (completers only analysis)	5	337	Odds Ratio (IV, Random, 95% CI)	2.18 [1.31, 3.64]

Analysis 2.1. Comparison 2: CBT versus active controls, Outcome 1: Remission of anxiety diagnoses (ITT analysis)

	СВ	Т	Active co	ontrols		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Cobham 2012	18	23	19	20	6.9%	0.19 [0.02 , 1.78]	
Ginsburg 2002	1	4	1	5	3.9%	1.33 [0.06, 31.12]	
Herbert 2009	4	23	4	13	11.2%	0.47 [0.10, 2.34]	
Herbert 2009	5	24	4	13	11.7%	0.59 [0.13, 2.75]	
Hudson 2009	25	58	7	46	18.8%	4.22 [1.62 , 11.00]	
Kendall 2008	36	56	12	25	18.8%	1.95 [0.75, 5.07]	-
Kendall 2008	35	55	12	25	18.8%	1.90 [0.73, 4.94]	-
Masia-Warner 2007	7	19	2	17	9.9%	4.38 [0.76 , 25.06]	-
Гotal (95% СІ)		262		164	100.0%	1.51 [0.77, 2.96]	
Total events:	131		61				_
Heterogeneity: Tau <sup>2</sup> = 0	0.38; Chi <sup>2</sup> = 1	2.67, df =	7 (P = 0.08)	); I <sup>2</sup> = 45%	ó		0.005 0.1 1 10 200
Test for overall effect:	Z = 1.21 (P =	0.23)				Favou	irs active controls Favours CBT

Test for overall effect: Z = 1.21 (P = 0.23)

Test for subgroup differences: Not applicable



Analysis 2.2. Comparison 2: CBT versus active controls, Outcome 2: Acceptability -participants lost to follow-up

	CB	T	Active c	ontrols		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Cobham 2012	0	23	0	20		Not estimable	
Herbert 2009	7	23	5	13	14.6%	0.70 [0.17, 2.92]	l
Herbert 2009	6	23	4	13	13.2%	0.79 [0.18 , 3.56]	l
Hudson 2009	7	60	6	52	22.1%	1.01 [0.32 , 3.23]	l
Kendall 2008	7	56	8	25	22.3%	0.30 [0.10, 0.96]	l
Kendall 2008	6	55	8	25	20.9%	0.26 [0.08, 0.86]	l
Masia-Warner 2007	2	19	2	17	6.9%	0.88 [0.11 , 7.06]	l
Total (95% CI)		259		165	100.0%	0.53 [0.31 , 0.91]	ı 🍝
Total events:	35		33				<b>~</b>
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> = 4	l.11, df = 5	5 (P = 0.53)	$I^2 = 0\%$			0.01 0.1 1 10 100
Test for overall effect:	Z = 2.28 (P =	0.02)					Favours CBT Favours active controls

Test for subgroup differences: Not applicable

Analysis 2.3. Comparison 2: CBT versus active controls, Outcome 3: Reduction in anxiety symptoms

		CBT		Acti	ive contro	ls		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Ginsburg 2002	28.75	28.27	6	34.75	17.25	6	10.0%	-0.24 [-1.37 , 0.90]	
Herbert 2009	34.37	19.08	23	34.34	16.28	23	13.8%	0.00 [-0.58, 0.58]	+
Hudson 2009	23.46	17.7	53	21.81	17.9	46	14.8%	0.09 [-0.30 , 0.49]	<b>.</b>
Kendall 2008	36.65	19.2	49	39.13	19.37	39	14.7%	-0.13 [-0.55, 0.29]	4
Masia-Warner 2007	13.4	1.9	17	24.6	2	15	7.2%	-5.61 [-7.23 , -3.98]	
Muris 2002	23.7	14.4	10	47.3	31.3	10	11.3%	-0.93 [-1.86, 0.01]	-
Sung 2011	26.54	15.57	28	27.62	13.57	29	14.1%	-0.07 [-0.59 , 0.45]	+
Sánchez-García 2009	15.45	7.77	28	12.75	8.03	29	14.1%	0.34 [-0.19, 0.86]	+
Total (95% CI)			214			197	100.0%	-0.50 [-1.09 , 0.09]	•
Heterogeneity: Tau <sup>2</sup> = 0.5	7; Chi <sup>2</sup> = 51.0	3, df = 7 (	P < 0.0000	1); I <sup>2</sup> = 869	6				<b>Y</b>
Test for overall effect: Z =	= 1.66 (P = 0.1	.0)							-4 -2 0 2 4
Test for subgroup differen	ices: Not appl	icable							Favours CBT Favours active controls

Analysis 2.4. Comparison 2: CBT versus active controls, Outcome 4: Remission of anxiety diagnoses: long term follow-up (ITT analysis)

	CB	Т	Active co	ontrols		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Hudson 2009	35	60	20	52	44.3%	2.24 [1.05 , 4.78]	_
Kendall 2008	30	56	11	25	28.4%	1.47 [0.57, 3.79]	<del></del>
Kendall 2008	36	55	11	25	27.3%	2.41 [0.92 , 6.33]	-
Total (95% CI)		171		102	100.0%	2.03 [1.22 , 3.36]	•
Total events:	101		42				•
Heterogeneity: Tau <sup>2</sup> = 0	0.00; $Chi^2 = 0$	.63, df = 2	2 (P = 0.73)	$I^2 = 0\%$		0.0	01   0.1   1   10   100
Test for overall effect: 2	Z = 2.74 (P =	0.006)				Favours	active controls Favours CBT

Test for subgroup differences: Not applicable



# Analysis 2.5. Comparison 2: CBT versus active controls, Outcome 5: Reduction in anxiety symptoms: long term follow-up

		CBT		Act	ive contro	ls		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Hudson 2009	1.52	0.27	51	2.67	0.29	44	19.3%	-4.08 [-4.80 , -3.37]	
Kendall 2008	36.9	22.04	56	39.1	19.4	25	20.2%	-0.10 [-0.57, 0.37]	<b>+</b>
Kendall 2008	32.2	18.4	55	39.1	19.4	50	20.4%	-0.36 [-0.75, 0.02]	-
Sung 2011	21.54	14.82	28	21.17	11.97	29	20.0%	0.03 [-0.49, 0.55]	<b>+</b>
Sánchez-García 2009	11.41	7.44	28	13.03	10.07	29	20.0%	-0.18 [-0.70 , 0.34]	+
Total (95% CI)			218			177	100.0%	-0.91 [-2.06 , 0.24]	
Heterogeneity: $Tau^2 = 1.65$ ; $Chi^2 = 104.27$ , $df = 4$ (P < 0.00001); $I^2 = 96\%$									
Test for overall effect: Z =	= 1.56 (P = 0.1	2)							-4 -2 0 2 4
Test for subgroup differer	ices: Not appl	icable							Favours CBT Favours active control

Analysis 2.6. Comparison 2: CBT versus active controls, Outcome 6: Sensitivity analysis: remission of anxiety diagnoses (completers only analysis)

	СВ	T	Active c	ontrols		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Ginsburg 2002	3	6	2	6	4.8%	2.00 [0.19 , 20.61]	
Herbert 2009	5	17	3	11	9.2%	1.11 [0.21, 6.01]	
Herbert 2009	4	16	3	11	8.6%	0.89 [0.16, 5.08]	
Hudson 2009	18	51	7	46	26.8%	3.04 [1.13 , 8.17]	-
Kendall 2008	32	51	9	20	23.9%	2.06 [0.72 , 5.87]	
Kendall 2008	32	50	9	20	23.6%	2.17 [0.76 , 6.23]	<del>  -</del>
Masia-Warner 2007	7	17	0	15	3.0%	22.14 [1.14 , 430.73]	
Total (95% CI)		208		129	100.0%	2.18 [1.31 , 3.64]	•
Total events:	101		33				•
Heterogeneity: Tau <sup>2</sup> = 0	0.00; Chi <sup>2</sup> = 4	.42, df = 6	6 (P = 0.62)	$I^2 = 0\%$			0.005 0.1 1 10 200
Test for overall effect:	Z = 2.98 (P =	0.003)				Favor	urs active controls Favours CBT

## Comparison 3. CBT versus treatment as usual (TAU)

Test for subgroup differences: Not applicable

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
3.1 Remission of anxiety diagnoses (ITT analysis)	2	88	Odds Ratio (IV, Random, 95% CI)	0.53 [0.23, 1.25]
3.2 Acceptability -participants lost to follow-up	2	90	Odds Ratio (IV, Random, 95% CI)	1.01 [0.31, 3.31]
3.3 Reduction of anxiety symptoms	3	98	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.77, 0.36]
3.4 Sensitivity analysis: remission of anxiety diagnoses (completers only analysis)	2	78	Odds Ratio (IV, Random, 95% CI)	1.10 [0.45, 2.68]



Analysis 3.1. Comparison 3: CBT versus treatment as usual (TAU), Outcome 1: Remission of anxiety diagnoses (ITT analysis)

	CBT	Γ	TA	U		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Barrington 2005	11	28	13	26	62.4%	0.65 [0.22 , 1.91]	
Ginsburg 2012	6	15	12	19	37.6%	0.39 [0.10 , 1.56]	-
Total (95% CI)		43		45	100.0%	0.53 [0.23 , 1.25]	
Total events:	17		25				•
Heterogeneity: Tau <sup>2</sup> = 0	0.00; Chi <sup>2</sup> = $0.0$	32, df = 1	(P = 0.57);	$I^2 = 0\%$			0.005 0.1 1 10 200
Test for overall effect: 2	Z = 1.44 (P = 0)	0.15)					Favours TAU Favours CBT

Test for overall effect: Z = 1.44 (P = 0.15) Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3: CBT versus treatment as usual (TAU), Outcome 2: Acceptability -participants lost to follow-up

	CB	T	TA	U		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Barrington 2005	5	28	3	26	58.7%	1.67 [0.36 , 7.80]	
Ginsburg 2012	2	17	4	19	41.3%	0.50 [0.08, 3.15]	
Total (95% CI)		45		45	100.0%	1.01 [0.31 , 3.31]	
Total events:	7		7				
Heterogeneity: Tau <sup>2</sup> = 0	0.00; Chi <sup>2</sup> = 0	0.96, df = 1	1 (P = 0.33)	$I^2 = 0\%$			0.01 0.1 1 10 10
Test for overall effect: $Z = 0.02$ ( $P = 0.98$ )							Favours CBT Favours TAU

Test for overall effect: Z = 0.02 (P = 0.98)
Test for subgroup differences: Not applicable

Analysis 3.3. Comparison 3: CBT versus treatment as usual (TAU), Outcome 3: Reduction of anxiety symptoms

		CBT			TAU			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Barrington 2005	10.4	7.1	23	11.4	7.4	23	41.2%	-0.14 [-0.71 , 0.44]	•
Ginsburg 2012	25.26	11.95	17	22.37	14.57	15	34.5%	0.21 [-0.48, 0.91]	•
Reaven 2012	23.7	14.4	10	47.3	31.3	10	24.4%	-0.93 [-1.86 , 0.01]	-
Total (95% CI)			50			48	100.0%	-0.21 [-0.77 , 0.36]	•
Heterogeneity: Tau <sup>2</sup> = 0	0.12; Chi <sup>2</sup> = 3.	71, df = 2	(P = 0.16)	; I <sup>2</sup> = 46%					Ĭ
Test for overall effect: $Z = 0.72$ ( $P = 0.47$ )								-4 -2 0 2 4	
Test for subgroup differences: Not applicable								Favours CBT Favours TAU	



Analysis 3.4. Comparison 3: CBT versus treatment as usual (TAU), Outcome 4: Sensitivity analysis: remission of anxiety diagnoses (completers only analysis)

	CB	CBT		TAU		Odds Ratio	Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Barrington 2005	10	23	10	23	59.1%	1.00 [0.31 , 3.21]			
Ginsburg 2012	10	17	8	15	40.9%	1.25 [0.31, 5.07]			
Total (95% CI)		40		38	100.0%	1.10 [0.45 , 2.68]			
Total events:	20		18				T		
Heterogeneity: Tau <sup>2</sup> = 0	0.005 0.1 1 10 200								
Test for overall effect: $Z = 0.20$ (P = 0.84)							Favours TAU Favours CBT		

Test for overall effect: Z = 0.20 (P = 0.84) Test for subgroup differences: Not applicable

#### **ADDITIONAL TABLES**

Table 1. Sample sizes

Tubic 1: Jumpic Sizes					
	Number	Mean	Std. Dev.	Min	Max
	of studies				
Individual CBT	7	29.14	15.75	12	60
Individual Controls	7	21.57	10.71	10	43
Group CBT	13	24.77	14.71	6	64
Group Controls	13	21.92	14.41	5	67
Family/Parental CBT	11	25	13.02	6	54
Family/Parental Controls	11	17.18	6.62	5	29

## **APPENDICES**

## **Appendix 1. OVID MEDLINE**

## Appendix 1

## **OVID MEDLINE**

- 1. COGNITIVE THERAPY/
- 2. BEHAVIOR THERAPY/
- 3. (cogniti\$ adj3 (behavio\$ or intervention\$ or psychotherap\$ or technique\$ or therap\$ or treat\$)).ti,ab.
- 4. (behavio\$ adj3 (intervention\$ or psychotherapy\$ or technique\$ or therap\$ or treat\$)).ti,ab.
- 5. or/1-4
- 6. exp ANXIETY DISORDERS/
- 7. (anxiety or anxious or panic or phobi\$).ti,ab.



- 8. or/6-7
- 9. (child\$ or adolesc\$ or juvenile\$ or minors or p?ediatri\$ or teen\* or school\$ or young or youth\$).mp.
- 10. randomized controlled trial.pt.
- 11. controlled clinical trial.pt.
- 12. randomi#ed.ab.
- 13. placebo\$.ab.
- 14. randomly.ab.
- 15. trial.ab.
- 16. groups.ab.
- 17. (clinic\$ adj3 (trial\$ or study or studies\$)).ti,ab.
- 18. (control\$ or prospectiv\$ or volunteer\$).ti,ab.
- 19. or/10-18
- 20. 5 and 8 and 9 and 19

Limited to 2004 onwards

## **OVID MEDLINE In-Process** (2009-09-10)

- 1. (cogniti\$ adj3 (behavio\$ or intervention\$ or psychotherap\$ or technique\$ or therap\$ or treat\$)).ti,ab.
- 2. (behavio\$ adj3 (intervention\$ or psychotherapy\$ or technique\$ or therap\$ or treat\$)).ti,ab.
- 3. or/1-2
- 4. (anxiety or anxious or panic or phobi\$).ti,ab.
- 5. (child\$ or adolesc\$ or juvenile\$ or minors or p?ediatri\$ or teen\* or school\$ or young or youth\$).ti,ab.
- 6. randomized controlled trial.pt.
- 7. controlled clinical trial.pt.
- 8. randomi#ed.ab.
- 9. placebo\$.ab.
- 10. randomly.ab.
- 11. trial.ab.
- 12. groups.ab.
- 13. (clinic\$ adj3 (trial\$ or study or studies\$)).ti,ab.
- 14. (control\$ or prospectiv\$ or volunteer\$).ti,ab.
- 15. or/6-14
- 20. 3 and 4 and 5 and 15



#### **FEEDBACK**

## Error in summary of findings table, May 2014

#### Summary

The summary of findings table states that 800 per 1000 children on the wait list will experience remission of anxiety compared to 369 per 1000 of the CBT group. This is based on an odds ratio of 0.13 which I assume is taken from figure 4 (although confidence intervals are not the same). I might be reading this wrong but this suggests to me that wait list is more effective than CBT, which is not the conclusion of the review. Is there perhaps a problem with the definition of event/non-event for this outcome?

I agree with the conflict of interest statement: I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

#### Reply

Thank you for your comments on our review. We have ensured that the incorrect figures have been changed and we have amended the text to read more clearly: *Remission - the absence of a diagnosis of an anxiety disorder.* Further, In order to improve clarity we have changed our analyses to read the number with diagnosis remitted, and we have revised the summary of findings tables to take account of this.

## **Contributors**

Feedback submitted by: Jennifer Evans

Response submitted by: Anthony James

## Feedback submitted, March 2016

#### **Summary**

Comment 1: Thanks for a well written and important update of a review that remains a cornerstone for people like me, advising on policy and organizing research. I find the lack of long-term studies worrying. By reading the review I also discovered the interesting paper by Pine in Nature (2009). However, I would just point out that citing that review in this particular context (See Why it is important to do this review: 'Anxiety disorders in children and adolescents represent a considerable source of morbidity and are associated with later adult psychopathology. However, despite high prevalence and substantial morbidity, anxiety disorders in childhood remain underrecognised and undertreated (Pine 2009) and as such represent an important public health issue') seemed a bit surprising. I was looking to find summarized evidence on the important topics of underrecognition and undertreatment, but found instead other interesting findings. Anyway, the most important thing was to say thanks for putting the systematic review together.

Comment 2: Number needed to treat (NNT) of 6? Delving into this important review, well executed and clearly written, I was surprised to find an NNT of 6 with such a big odds ratio. Is it not this comparison that is used for the NNT: 'Using conservative ITT criteria, the remission rate for anxiety disorders of 58.9% for CBT versus 16 % for controls is similar to...'? That should give a NNT of 2, 3 if I am not mistaken.

Comment 3: I wonder if this study went under the radar: Southam-Gerow et al. Does cognitive behavioral therapy for youth anxiety outperform usual care in community clinics? An initial effectiveness test. Journal of the American Academy of Child and Adolescent Psychiatry 2010;10:1043-1052.

I agree with the conflict of interest statement below: I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

Best regards,

Arild

#### Reply

Response to comment 1: The reference to Pine 2009 is unfortunately incorrect. It is the case that anxiety disorders are some of the most prevalent psychiatric disorders in children and adolescents and unfortunately only a proportion of cases identified in general population studies are seen and treated in mental health settings. Recent work has shown that in clinical settings anxiety disorders are potentially under recognised, and it is suggested, therefore, that standardised instruments are used to detected and measure anxiety symptoms (1). This reference has now been replaced.

Response to comment 2: Thank you for pointing out this error. We recalculated the number needed to treat (NNT) as 3.0 and have corrected this throughout the review.

Response to comment 3: The following study was identified in the search results but was unintentionally deleted during the review-writing process (2). This study, described as an initial effectiveness trial, was well conducted; however, in the authors' own view the study involved a relatively modest sample size, and CBT did not produce better clinical outcomes than usual community clinic care. Looking at the results of



the study it is unlikely the addition of the study would have materially altered the overall fairly consistent findings from the meta-analysis. An update of this systematic review and meta-analysis is anticipated by November 2017 and this study will be fully incorporated.

#### References:

- 1. Esbjorn BH, Hoeyer M, Dyrborg J, Leth I, Kendall PC. Prevalence and co-morbidity among anxiety disorders in a national cohort of psychiatrically referred children and adolescents. Journal of Anxiety Disorders. 2010;24:866-872.
- 2. Southam-Gerow Weisz JR, Chu BC, McLeod BD, Gordis EB, Connor Smith JK. Does cognitive behavioral therapy for youth anxiety outperform usual care in community clinics? An initial effectiveness test. Journal of the American Academy of Child and Adolescent Psychiatry 2010;10:1043-1052

#### **Contributors**

Feedback submitted by: Arild Bjorndal

Response submitted by: Anthony James

## WHAT'S NEW

Date	Event	Description
16 November 2020	Amended	A new Cochrane Review entitled 'Cognitive behavioural therapy for anxiety disorders in children and adolescents' was published on 16 November 2020 which supersedes this publication.
		Citation: James AC, Reardon T, Soler A, James G, Creswell C. Cognitive behavioural therapy for anxiety disorders in children and adolescents. Cochrane Database of Systematic Reviews 2020, Issue 11. Art. No.: CD013162. DOI: 10.1002/14651858.CD013162.pub2.
		Note added to the abstract to direct readers to the new publication.

## HISTORY

Protocol first published: Issue 1, 2004 Review first published: Issue 4, 2005

Date	Event	Description
9 May 2016	Amended	Number needed to treat was corrected in response to feedback received.
4 May 2016	Feedback has been incorporated	Feedback incorporated
16 December 2014	New citation required but conclusions have not changed	Some numerical data in the abstract has been changed, and a ty- pographical error corrected, in response to feedback received
15 July 2014	Feedback has been incorporated	Feedback incorporated
21 May 2013	New citation required and conclusions have changed	New data from CBT versus active controls, treatment-as-usual (TAU) and CBT versus medication and the combination of CBT versus placebo
21 May 2013	New search has been performed	New search conducted and additional references and analyses included



Date	Event	Description
17 September 2010	New search has been performed	New search conducted and additional references and analyses included.
1 November 2008	Amended	Converted to new review format.
13 July 2005	New citation required and conclusions have changed	Substantive amendment

## CONTRIBUTIONS OF AUTHORS

Anthony James, Felicity Cowdrey, Georgina James and Angela Soler reviewed the papers. Anthony James and Georgina James were responsible for statistical analysis. Anthony James, Georgina James, Angela Soler and Felicity Cowdrey were jointly responsible for interpreting the data. All authors were involved in the writing of the text.

## **DECLARATIONS OF INTEREST**

No potential conflicts of interest were reported for any of the review authors.

## SOURCES OF SUPPORT

## **Internal sources**

- Oxford Healthcare NHS Foundation Trust, UK
- Oxford University Department of Psychiatry, Warneford Hospital, Oxford, UK

## **External sources**

• No sources of support supplied

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None.

## INDEX TERMS

## **Medical Subject Headings (MeSH)**

Anxiety Disorders [\*therapy]; \*Cognitive Behavioral Therapy; Randomized Controlled Trials as Topic

## MeSH check words

Adolescent; Child; Humans