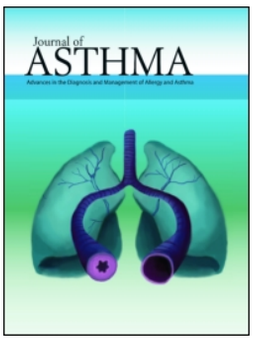
Effectiveness of cognitive behavioural therapy in reducing anxiety in adults and children with asthma



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Effectiveness of cognitive behavioural therapy in reducing anxiety in adults and children with asthma: a systematic review

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Abstract

Objective: Asthma and anxiety are known to interact, leading to exacerbations for both conditions. This systematic review summarised evidence regarding the effectiveness of cognitive-behavioural therapy (CBT) in reducing anxiety for individuals with asthma, with results presented separately for adults and children.

Data Sources: PRISMA statement and CRD guidance was followed to conduct and report the current review. Three major electronic databases (Ovid Medline, PsycINFO, and EMBASE) and manual searches were used to find relevant published and unpublished research.

Study Selections: Sixteen trials (twelve adult and four child) met inclusion criteria, and were evaluated with adapted quality criteria. Both controlled trials and repeated-measure designs were eligible. All CBT intervention formats were eligible (group, individual, computerised, self-help). Nine studies (eight adult and one child) focused upon participants with either an anxiety condition diagnosis or above threshold anxiety scores on a validated measure of anxiety at baseline.

Results: The review indicates tentative preliminary support for the use of CBT for anxiety in adults with asthma, with the evidence-base for interventions with children appearing promising, but under-developed. Studies were more likely to indicate beneficial effects where anxiety-focused (rather than illness-focused) intervention protocols were utilised, asthma-related education was provided and where the trials focused on individuals with likely clinical levels of anxiety at baseline.

Conclusion: Whilst further high quality research is needed, available evidence is supportive of anxiety-focused CBT interventions tailored to target the particular mechanisms thought to maintain this comorbidity in asthma.

Keywords

anxiety, asthma, cognitive behavioural therapy, psychological interventions, systematic review, CBT, adults, children and adolescents

Introduction

Asthma is the most common chronic health condition, affecting more than 300 million individuals worldwide [1], one fifth of which are children [2]. There are well-established links between asthma and anxiety conditions. A review of 15 studies reported an average prevalence of 34% of any anxiety disorder amongst adults with asthma, primarily panic attacks (25%) [3]. Children with asthma also experience a significantly higher risk of meeting criteria of several anxiety disorders, including separation anxiety, social anxiety, specific phobia, panic and generalised anxiety disorder [4,5].

Asthma attacks are particularly aversive, which can reinforce anticipatory anxiety or avoidance and increase health-related fear or hypervigilance regarding threatening bodily symptoms [6,7]. Cognitive behavioural models predict that such factors maintain health anxiety and panic [8]. Individuals with asthma and anxiety, in turn, tend to over-perceive symptoms of asthma and overreact during asthma episodes, resulting in increased medication and healthcare use [9-11].

Strategic planning and clinical guidelines [12-14] recommend the provision of psychological interventions for individuals with asthma experiencing complications related to anxiety. However, policy reports also highlight that the evidence regarding the usefulness of psychological interventions in this context is equivocal [e.g., 15].

Whilst some reviews have examined the effectiveness of psychological interventions in enhancing asthma-related outcomes more broadly, none have as yet focused specifically on the effectiveness of such interventions in improving anxiety in individuals with asthma. For example, a meta-analysis by Devine [16] indicated that psycho-educational interventions with

adults had benefits across a range of asthma-related outcomes, including amongst six studies that used measures of psychological wellbeing. Smith and colleagues [17] reviewed the impact of psycho-educational interventions in improving outcomes for adults and children with asthma, finding some evidence of reduced hospital admissions, but with mixed findings for other outcomes, including anxiety.

More recently, two Cochrane reviews examined the effectiveness of psychological interventions in improving asthma-related outcomes in adults and children respectively [18,19]. These reviews primarily focused on health care utilisation, with improving psychological functioning, including anxiety, as a secondary outcome. Those studies which considered anxiety outcomes were split across a range of intervention and measurement types and the authors were unable to draw firm conclusions due to the lack of good quality evidence.

Evidence supports the effectiveness of cognitive behavioural therapies (CBT) in improving anxiety in individuals without a medical comorbidity [20,21] and in reducing anxiety within other chronic respiratory conditions, such as chronic obstructive pulmonary disease [22].

However, our examination of the literature did not reveal reviews to date that examined the effectiveness of CBT for anxiety in individuals with asthma, whilst several studies indicate limited support for this model improving psychological functioning in the context of asthma [23-28]. Given the consistent observations of how these two conditions exacerbate one another and reduce the effectiveness of respective treatments and the number of avoidable complications related to their interaction [6,7,29-31], it is considered important to examine whether a well-established psychological intervention for anxiety, CBT, is effective in this context and which treatment components would most helpful.

Most studies included in the relevant Cochrane reviews [18,19] involved broadly defined psychological techniques, such as biofeedback or relaxation, to address the physiological symptoms of anxiety, without targeting other aspects of the phenomenology of anxiety or the factors that psychological research has identified to maintain it (e.g., cognitive or emotional factors or safety-seeking behaviours) [32]. Only three CBT trials that evaluated anxiety outcomes met standards for inclusion in the relevant adult Cochrane review and one in the child review [18,19]; with some positive outcomes, but not enough to evidence the effectiveness of this treatment mode for anxiety. These reviews did not include other study designs, such as non-randomised, quasi experimental studies, although given the limited number of good quality randomised controlled trials (RCTs) in this field, the inclusion of other study designs may help address whether CBT is effective with anxiety in asthma populations. In addition, a further analysis of the components of each trial may allow for an explanation regarding the limited and often contradictory outcomes in this field.

Aim

To systematically evaluate the effectiveness of cognitive-behavioural interventions in reducing anxiety in adults and/or children and adolescents with asthma.

Methods

Search strategy

The systematic search was conducted in July 2014 and updated in January 2017. Initially, the Cochrane database was searched to explore relevant systematic reviews in the field and ensure that no similar review was recently undertaken. Subsequently, the following databases were searched: Ovid Medline (1946-2014), PsycINFO (1806-2014) and Embase (1974-2014). Terms

used to search for keywords in all fields included: CBT or cognit* therap* or behav* therap* or cognitive-behav* therap* or problem-solving therap* and anx* and asthma*.

Manual searches were also undertaken to reduce potential limitations associated with the selection of these keywords. All references in the originally identified studies and the relevant Cochrane reviews [18,19] were examined. Moreover, publications which subsequently cited the included studies, as they appear in the Google Scholar search engine, were also screened. Key journals in the field were further searched. To address publication bias, web searches and searches in citations of included papers for unpublished documents, conference presentations and dissertations were also conducted. Key authors (e.g., Lehrer, Grover) were contacted to suggest relevant work.

Inclusion and exclusion criteria

Guidance from the Centre for Reviews and Dissemination [33] and the PRISMA statement [34] was followed to conduct and report the current review. Inclusion and exclusion criteria were based on the 'PICOS' approach: population, interventions, comparators, outcomes and study design [33].

Population

Included studies had participants with a diagnosis of asthma. No limitations were set on the severity of asthma symptomatology or on the diagnostic method/criteria. All types and levels of severity of anxiety symptomatology at baseline were included. Studies involving populations with other chronic medical/respiratory/mental health conditions were eligible, if results for asthma and anxiety were presented separately. No age, gender or other limitations on the included population were stipulated.

Intervention

Included studies examined CBT interventions that involved both cognitive and behavioural components as defined by Butler and colleagues in their review of the empirical status of CBT [35]. Therefore, studies examining the effectiveness of behavioural only interventions, e.g., progressive muscle relaxation, were not included. Anxiety improvement was a primary or secondary treatment goal in all studies. All CBT intervention formats were eligible (e.g., individual and group treatment protocols, computerised or self-help interventions). No exclusions were set based on the level of therapist input, length or number of sessions. Studies providing additional input to significant others (parents or partners) were eligible.

Outcome

Studies were eligible only if severity of anxiety symptomatology was assessed at baseline and at post-treatment using a standardised measure (validated observation, interview protocol or self-report tool).

Study design and comparators

Despite the generally higher quality of empirical support provided by randomised controlled trials [36], other study designs were also included due to the restricted number of high quality RCTs in this field. Thus, non-randomised controlled trials and observational repeated-measures designs without controls were also included. Case studies were not included. No restrictions were set for the nature of control conditions e.g., treatment as usual, wait-list, placebo controls were all included.

Quality criteria

The methodological quality of the eligible studies was assessed using quality criteria adapted for

the purposes of this review (Table 1). Several authors suggest modifying available quality criteria to ensure that they address the requirements of specific review questions [37,38]. Existing criteria and guidelines were consulted to assist in developing quality criteria to meet the aims of this systematic review, including the SIGN 50 Checklist [39], the consolidated standards of reporting trials [40] and the guidance from the Centre for Reviews and Dissemination [33].

The ratings of each quality criterion were classified as either: well covered (3 points), adequately addressed (2), poorly addressed (1) or not addressed (0). As providing summed scores of quality criteria can be misleading, because the criteria are not truly equally weighted, the final rating was given as ++, + or -, based on whether the overall rating ranged above 75% (27-36), above 50% (18-26) or below 50% (0-17) of the highest possible rating. All studies were rated by the first author (EP) and a random sample of five studies was second-rated by the second author (PGM).

Results

Study inclusion

The electronic database search yielded 1721 results and manual searches indicated 83 potentially relevant articles. Once the initial electronic database search was completed, duplicates were removed and remaining papers were screened against the eligibility criteria. Figure 1 presents the search pathway and reasons for exclusion of reviewed studies. One paper was irretrievable [41], despite library requests and attempts to contact the author. Fourteen studies met inclusion criteria. One paper [7] described two separate trials, each of which independently met the eligibility criteria.

Quality assessment

All studies were rated based on the quality criteria purposefully developed for this review (Table

1). The second author independently evaluated the quality of a randomly selected third (n = 5) of included studies using a sequence generated by random.org. This yielded agreement on 50/60 ratings (83.3%). Disagreement of more than one point was found in four ratings, with these discrepancies discussed between raters, and the criteria amended as necessary to increase clarity and consistency.

General characteristics of the studies

Key characteristics of studies included in this review are provided in Tables 2 and 3. Twelve studies involving adult participants (aged 18+) are presented and analysed separately from the four studies recruiting children and adolescents. Overall, study quality was moderate, with substantial variation amongst included trials. Methodological issues deemed particularly pertinent to addressing the review questions included: study design, sample power and representativeness, suitability of the intervention and the data collection methods.

Studies with adults

Study design

Of the twelve trials involving adult participants, eight were RCTs, one was a non-randomised controlled trial and three uncontrolled repeated-measures designs (Table 2). Five of the RCTs were allocated the highest rating (++) [23,24,42-44] due to clearly outlined and appropriate randomisation methods. All reviewed studies had methodological limitations in relation to the current review question (Table 1).

Sample representativeness and power

Of the trials that reported descriptive statistics (Table 2), the mean age of participants ranged between 21.7 and 51.9 years. Sample sizes ranged between 10 and 93 participants in the

intervention condition. Attrition rates for the intervention groups were moderate overall (≤40%), but ranged between 0%-50%.

Most trials (n = 11) adopted suitable analyses to examine effect over time and differences between conditions. Seven studies had not outlined a power calculation and others had calculations based on varying assumptions of effect size. Consequently post-hoc power analyses were conducted for pre-post results of the intervention group of each trial (for reasons of consistency across studies) to inform our quality criteria on sample size / power. These were calculated using the G*power programme, estimating effect size to be medium (d = 0.5 for t-test; f = 0.25 for ANOVA) and alpha 0.05.

Most of the reviewed studies (n = 11) achieved power of less than 0.8. Campbell-Sills and colleagues [23] achieved the highest rating in terms of sample power for their analysis. Their overall sample representativeness and suitability, however, was rated as adequate, due to not examining the severity of the included medical conditions and not excluding mental health co-morbidities for the selection of appropriate participants, which is likely to dilute outcomes.

Recruitment methods and eligibility criteria varied substantially between the reviewed studies. Two studies used convenience samples of inpatients admitted in a single department at the time of the study [25], or volunteer college students who were telephone screened for asthma [26], without applying any other specific criteria that would allow generalising conclusions based on their outcomes. The remaining studies were based on representative respiratory populations recruited by multiple specialist services, chronic disease registers, or primary care services, who had a physician-confirmed asthma diagnosis. Of the twelve adult trials, eight focused upon participants with evidence indicative of clinical levels of anxiety at baseline, using validated

methods, e.g., scoring above the clinical threshold for HADS or the Anxiety Disorders Interview Schedule for DSM-IV [7a,7b,23,24,42-45]. These were rated higher on quality criteria relating to recruitment and inclusion criteria.

Data collection

Hockemeyer and Smyth [26] used a robust measure for anxiety, but it was rated poorly as the administration instructions asked participants to rate their anxiety over the treatment period, rather than the post-treatment period. All other studies used at least one well-validated and reliable anxiety measure and administered it appropriately; for example, the HADS [46] and/or the anxiety subscale of the ASC [47]. Ten studies reported follow-up outcomes.

Treatment integrity

Six interventions were delivered in a group and four in an individual format (Table 2), offering from 3 to 14 therapist sessions. Two studies offered a minimum number of either one [23] or no therapist sessions [26].

Intervention integrity referred to both therapist experience and protocol adherence. Considerable variation existed between the background training and clinical experience of therapists, which was only reported in eight of the trials. This ranged from clinical or health psychologists and CBT therapists [42,44,48] to doctoral nurses [24], psychologists and psychology researchers [25,27] or counsellors [45]. Where therapist experience was not extensive, but suitable training was provided on the treatment protocol, intervention integrity was rated as high [i.e., 43]. Examination of adherence to treatment protocol was sufficiently addressed only by Parry and colleagues [42], Feldman and colleagues [43] and Ross and colleagues [24].

Eight of the interventions were designed to reduce anxiety as their primary aim [7a,7b,23-25,42-

44]. Three of the included trials provided minimal or no asthma-related education [23,26,45]. Two studies were rated lower regarding the suitability of the protocol for improving anxiety outcomes, as they mainly focused on improving asthma knowledge or management and addressing asthma health perceptions [27,45]. Of the 12 trials, only six were highly rated regarding the dose of CBT provided and the suitability of the protocol [7a,7b,24,42-44].

Key findings from adult studies

Three trials were excluded from consideration [7a,7b,45], as their methodological ability to address the review question was rated as relatively low and it would, thus, be less reliable to draw conclusions based on their outcomes. A further four studies were with asthmatic patients that were not recruited on the basis of also having clinical levels of anxiety [25-27,48].

The remaining five studies were with participants with clinical levels of anxiety and had stronger overall methodology in relation to addressing the review question. Of these, three found a positive effect of CBT on reducing anxiety relative to usual care or wait-list [24,42,44], with two reporting statistically significant outcomes [24,42]. Yorke and colleagues [44] recruited participants with severe asthma symptomatology, which may explain their lack of statistically significant outcomes.

Feldman and colleagues [43] found statistically significant reductions in anxiety scores over time in their CBT group, though their control music and relaxation therapy group also had significant reductions in anxiety over time, such that group x time interactions were not statistically significant in their modest sample. Their control intervention has previously been reported to have positive effects in the context of asthma [49] and thus the absence of an interaction may partially reflect genuine benefits of the control intervention. Campbell-Sills and colleagues [23]

found no significant differences between treatment as usual and computer-assisted CBT. The lack of effect in Campbell-Sills and colleagues [23] may be due to the lack of asthma-related input in their intervention (as this was part of a larger scale study examining several medical co-morbidities) or the lower intensity of their computerised CBT intervention, which may have been insufficient to enable improvements in anxiety complicated by asthma.

All the studies that reported beneficial effects of CBT in reducing anxiety incorporated asthma-related education alongside or within the CBT intervention, suggesting that asthma-related education may be important in enabling reductions in anxiety complicated by asthma.

Studies with children and young people

Study design

Only four trials involving children or adolescent participants met criteria for inclusion in this systematic review, of which one was an RCT [28], one was a non-randomised controlled trial [50], and two utilised repeated-measures designs [51,52]. The latter two were rated as significantly more limited, whereas the RCT and controlled trial, were rated as providing similarly strong evidence in relation to the review question (Table 1).

Sample representativeness and power

The age of participants ranged between 7 to 14.2 years, with sample sizes for the intervention condition of between 17 and 48 participants (Table 3). Aside from Marriage and Henderson [52], all other studies had relatively low attrition rates (0%-20%) for the treatment group and adopted suitable analyses in relation to addressing the review question. Colland [28] and Papneja and Manassis [50] were rated high for achieving a power of at least 0.8 for pre-post analyses, based on estimating medium effect size and using an alpha of 0.05.

Of the four studies with children and young people, only Papneja and Manassis [50] focused on those with evidence of clinical levels of anxiety at baseline, with participants in their study meeting criteria for at least one DSM-IV anxiety disorder. Despite their overall high rating, sample representativeness in Colland [28] was only adequately addressed as their recruitment criteria were based on coping skills rather than anxiety symptomatology. Long and colleagues [51] utilised a representative respiratory sample, but did not assess clinical need for anxiety intervention at the recruitment stage. Marriage and Henderson [52] recruited asthmatic participants, who were assessed to have health-related anxiety by a doctor, although their anxiety levels were below clinical levels at baseline. Representativeness in this study was also limited by recruitment from a single respiratory clinic.

Data collection

All reviewed studies with children and young people used well-validated primary anxiety measures. Two studies assessed the outcomes of the intervention up to six and 12 months later (Table 3).

Treatment integrity

Two trials examined CBT in group formats and one in individual format (see Table 3). One study provided the intervention in both formats, but reported their combined results, due to their outcomes not being significantly different between conditions [50]. Half of the trials involved some level of participation of significant others in treatment [28,50]. The number of offered sessions ranged between six and 12. All interventions were facilitated by therapists of varied training and experience, from psychologists, psychiatrists and psychotherapists [28,50] to graduate therapists, MSc clinicians or research assistants [51], and a respiratory nurse [52]. Only

one study recorded sessions and rated them independently to ensure adherence to treatment protocol [50].

Three studies [50-52] were designed to reduce anxiety as one of their primary aims. Two of the trials were rated lower on the treatment suitability for improving anxiety outcomes, as their protocol content focused mainly on improving asthma knowledge and illness perceptions [28,51]. Papneja & Manassis [50] was the only trial not providing asthma-related education.

Key findings from studies with children and young people

All four trials reported significant post-intervention reductions in anxiety outcomes following the CBT intervention. Two studies were excluded from consideration as their overall methodological quality was rated as low (i.e., -) [51,52].

Of the two methodologically stronger studies, Colland [28] found that CBT and asthma training led to greater improvements in anxiety compared to a single information session for families or to no treatment, despite not having selected participants for clinical levels of anxiety. The only relative benefits maintained after 6 months were in state anxiety amongst children with relatively high levels of baseline anxiety.

In the study by Papneja and Manassis [50], the control group were matched children with anxiety but without asthma. They reported statistically significant improvements in general anxiety in both groups, but the intervention was slightly less effective amongst children with asthma. In the latter group physiological anxiety increased post-treatment. Their study did not provide details of asthma-related education alongside or within the CBT intervention, which appeared to have been an important consideration in the adult literature.

Discussion

This systematic review aimed to explore the effectiveness of CBT interventions for anxiety in individuals with co-morbid asthma and anxiety. The reviewed studies provide preliminary evidence to support the use of CBT for anxiety in the context of asthma for adults, albeit with weak effects in relation to active controls. More tentative support for the use of CBT for anxiety with children/young people (7-14 years) with asthma was found, due to the lack of high quality evidence in the limited number of studies available.

Half of the reviewed studies used a generic CBT approach, with some merely focusing on modifying illness perceptions and asthma knowledge as a way to reduce anxiety in the context of asthma. However, cross-national findings indicate that individuals not only experience anxiety around their condition, but present with higher risk at developing any anxiety disorder, including generalised anxiety disorder or social phobia [53]. The eight studies that were rated higher for applying a stronger CBT protocols for anxiety, all reported benefits in reducing anxiety in individuals with asthma.

More recently, this field has shifted towards adapting specific anxiety-based CBT models and exploring cognitions or behaviours, which may maintain the high comorbidity between asthma and anxiety to enhance them [54-57]. The need to tailor CBT interventions to specific asthma-related circumstances seems supported by evidence in the current review. Interventions which included asthma-related education alongside or within an empirically-validated CBT intervention seemed more likely to demonstrate significant beneficial effects of the intervention on anxiety.

Limitations of reviewed articles and future research

Five of the included studies did not have control groups, with the remaining studies usually having only non-active groups (e.g., waitlist or standard asthma care). Thus, whilst available

evidence indicates effectiveness of suitable CBT protocols, when compared with other psychological therapies evidence become less definitive [43]. Future studies may consider comparing such CBT interventions with other psychological therapies.

Considerable heterogeneity existed between outcome measures and follow-up data, limiting potential for comparisons between studies. Comparisons were also limited by the wide differences in the dose of CBT and the diversity of CBT protocols employed, some of which primarily focused on modification of asthma behaviours or knowledge, rather than directly on specific anxiety beliefs. Future trials may benefit from adapting evidenced anxiety-focused CBT interventions, tailoring them to the particular cognitions and circumstances experienced by those with co-morbid asthma and anxiety. This may address the weak effect sizes when compared to controls and improve outcomes.

Future studies would benefit from giving greater consideration to protocol adherence and the training of therapists, as these were often not well addressed in the reviewed studies, despite having consistently been found to impact on psychotherapy research findings [56,58]. Recruitment procedures were insufficiently described for a notable proportion of the included studies creating difficulties in assessing the suitability of the sample or the intervention. Of the sixteen reviewed studies, only eight adult and one of the child studies screened for clinical levels of anxiety as part of their eligibility criteria. It is likely that the other studies included individuals with lower levels of anxiety, which would inevitably dilute the effect sizes of the intervention. Studies which recruited more clinically representative co-morbid anxious samples with asthma were more likely to find beneficial effects of CBT.

Implications for clinical practice and policy

The complications of the interplay between asthma and anxiety have been extensively discussed in the literature, including overperception of asthma symptoms and overreaction during episodes [10,54], increased healthcare use, independently of pulmonary function [6,9], and substantial costs for healthcare providers [59]. Strategic planning reports and national guidelines call for appropriate interventions to manage this co-morbidity [12,13], whilst highlighting that evidence is equivocal [15]. The current systematic review endeavoured to delineate the outcomes of diverse and inconclusive research in this field, focusing on CBT interventions as the most evidence-based treatment for anxiety in other populations [20,21]. The review provides preliminary support for the use of anxiety-focused CBT interventions, particularly those incorporating psychoeducation and/or interventions specific to asthma.

Strengths and limitations of current review

The current review benefits from the use of quality criteria purposefully adapted to address the review question. In common with most reviews, the quality criteria are not truly equally weighted and, thus, summed scores across criteria should be considered tentatively, with comparisons between studies on individual criteria being more robust. Efforts were taken to separately consider key quality criteria and to check that studies summed scores were representative of their overall quality. Although the review process included efforts to identify unpublished materials, including contacting key authors, internet searches and searches of citations of included papers for unpublished documents, conference presentations or dissertations, no unpublished studies that met inclusion criteria were identified. The diversity in treatment protocols, sampling and outcome measures led to wide heterogeneity amongst trials that, together with reported limitations, prevented a meta-analysis.

Conclusion

Inconsistent outcomes of CBT trials in the context of asthma may be due to the diversity of treatment protocols and the inclusion of participants in some trials who lack evidence of clinical levels of anxiety. Evidence from the methodologically stronger trials provides preliminary support for the effectiveness of CBT interventions in reducing anxiety amongst adults with asthma, with more tentative support for children/young people with asthma. Further high quality research is needed, and studies may benefit from the use of anxiety-focused CBT interventions, which are tailored to address the particular cognitions, circumstances and difficulties experienced by individuals with asthma.

Conflict of Interest

Both authors declare that they have no known conflicts of interest.

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Table 1. Quality ratings of methodological ability to address review question

		Sample representativeness		Allocation bias		Data collection		Treatment integrity				Attrition		Overall rating *
Authors	**Study design[1]**	**Recruitment & inclusion criteria[2]**	**Sample size / power[3]**	**Allocation process[4]**	**Groups similar at baseline[5]**	**Robust measures [6]**	**Follow-up measures[7]**	**Suitable protocol[8]**	**Treatment integrity/ adherence[9]**	**Appropriate analysis/reporting[10]**	**Attrition rates low & comparable[11]**	**Method to address missing data[12]**		
Adults														
Feldman et al., 2016	well covered	well covered	poorly addressed	well covered	wellcovered	wellcovered	poorly addressed	wellcovered	wellcovered	wellcovered	wellcovered	well covered	++	32/36
Parry et al., 2012	well covered	well covered	poorly addressed	well covered	well covered	well covered	adequately addressed	well covered	well covered	well covered	adequately addressed	well covered	++	32/36
Campbell-Sills et al., 2013	well covered	adequately addressed	well covered	well covered	poorly addressed	well covered	well covered	poorly addressed	adequately addressed	poorly addressed	well covered	well covered	++	28/36
Yorke et al., 2016	well covered	adequately addressed	poorly addressed	well covered	well covered	well covered	poorly addressed	well covered	adequately addressed	adequately addressed	adequately addressed	well covered	++	28/36
Ross et al., 2005	well covered	well covered	poorly addressed	adequately addressed	adequately addressed	adequately addressed	adequately addressed	well covered	well covered	well covered	adequately addressed	poorly addressed	++	27/36
Sommaruga et al., 1995	well covered	poorly addressed	poorly addressed	adequately addressed	adequately addressed	adequately addressed	well covered	adequately addressed	not addressed	adequately addressed	well covered	well covered	+	24/36
Put et al., 2003	well covered	adequately addressed	poorly addressed	adequately addressed	adequately addressed	well covered	poorly addressed	poorly addressed	not addressed	well covered	well covered	adequately addressed	+	23/36
Hockemeyer & Smyth, 2002	well covered	poorly addressed	adequately addressed	adequately addressed	well covered	not addressed	not addressed	poorly addressed	not addressed	poorly addressed	well covered	adequately addressed	+	18/36
Maes & Schloser, 1988	adequately addressed	poorly addressed	poorly addressed	poorly addressed	adequately addressed	well covered	not addressed	adequately addressed	not addressed	well covered	not addressed	well covered	+	18/36
Lehrer et al., 2008b	poorly addressed	well covered	poorly addressed	not addressed	not addressed	well covered	poorly addressed	well covered	not addressed	well covered	poorly addressed	not addressed	-	16/36
Lehrer et al., 2008a	poorly addressed	well covered	poorly addressed	not addressed	not addressed	well covered	poorly addressed	well covered	not addressed	adequately addressed	poorly addressed	not addressed	-	15/36
Spurgeon et al., 2005	poorly addressed	poorly addressed	adequately addressed	not addressed	not addressed	well covered	adequately addressed	poorly addressed	not addressed	well covered	not addressed	poorly addressed	-	14/36
Children & Young People														
Papneja &	adequately	well	well	poorly	well	well	not	well	well	well covered	well	adequately	++	

Manassis, 2006	addressed	covered	covered	addressed	covered	covered	addressed	covered	covered		covered	addressed	29/36
Colland, 1993	well covered	adequately addressed	well covered	adequately addressed	well covered	well covered	well covered	poorly addressed	not addressed	adequately addressed	well covered	well covered	++ 28/36
Long et al., 2011	poorly addressed	poorly addressed	poorly addressed	not addressed	not addressed	well covered	not addressed	adequately addressed	adequately addressed	well covered	well covered	poorly addressed	- 17/36
Marriage & Henderson, 2012	poorly addressed	adequately addressed	poorly addressed	not addressed	not addressed	well covered	adequately addressed	well covered	not addressed	not addressed	poorly addressed	poorly addressed	- 14/36

[1] Study design provides sufficient evidence that the anxiety outcomes are due to the intervention; [2] Recruitment method and inclusion criteria are appropriate to ensure a representative and suitable sample; [3] Sample size (power) is sufficient for analysis relating to pre and post anxiety outcomes; [4] Allocation process is appropriate to address allocation bias; [5] Groups are comparable at baseline on key variables (i.e., asthma or anxiety severity, age, gender); [6] Measures of anxiety are robust, appropriately administered and well-validated; [7] Follow-up measures are administered to evaluate if effects are maintained long-term; [8] Treatment protocol provides a valid CBT intervention with suitable levels of therapist input; [9] Intervention is appropriately conducted by experienced therapists and adherence to protocol is suitably assessed; [10] Analysis is appropriate for the study aims, measures or design and outcomes are appropriately reported; [11] Attrition rates are low or comparable to control group; [12] Method to address missing data is suitable.

* Summed totals for quality criteria should be interpreted cautiously as quality criteria are not all of equivalent importance in relation to methodological ability to address the review question. Comparisons between studies on individual quality criteria are more robust.

Table 2. Characteristics and key findings of included studies with adults

Study	Design/ Anxiety Criteria	Intervention description	Control	Intervention Group	Control group	Anxiety measures	Intervention Group M & SD		Pre-posteffect sizes[1] (intervention group)	Followup	Key findings	Key limitations	Quality rating[2]
							PreScoreMean(SD)	Post ScoreMean (SD)					
Group A: Studies which focused on participants with anxiety diagnoses and / or above threshold anxiety scores													
Feldman et al., 2016 [43] USA	RCT	CBT for panic, asthma education &biofeedback	music and relaxation therapy	*n* = 24	*n* = 24	PDSS	2.17 (0.16)	1.64 (0.18)	*d* = 0.45	3 months	Both groups showed statistically significant improvements over time on anxiety measures. No statistically significant differences were found between the CBT and the control group on the anxiety measures	Small sample size	++
		8 individual sessions with post-doc fellow & graduates with extensive training on protocol		Mean age = 43.8	Mean age = 42.6		2.45 (0.16)	2.3				Increased attrition rates	
	DSM-IV diagnosis of PD, PDSS 8+	Weekly supervision provided & all sessions were videotaped to assess integrity		Female 91.7%	Female 95.8%	ACQ	16.66 (1.21)	-0.17	*d* = 0.93			Mostly female participants	
				moderate asthma 79.2%	moderate asthma 79.2%		15.39 (1.34)	10.39 (1.39)					
						ASI-Physical	14.27 (1.37)	12.28 (1.52)	*d* = 4.92				
							3.05 (0.18)	9.46 (1.58)					
						ASI-Social		2.58 (0.21)	*d* = 2.22				
						ASI-Cognitive			*d* = 3.32				
						BSQ			*d* = 2.45				
Parry et al., 2012 [42]	RCT	CBT for	standard care	*n* = 50	*n* = 44		ITT	ITT		6 months	A significantly greater improvement in asthma-specific anxiety was found for the CBT group as compared to controls at post-treatment, which increased at 6-months	High drop-out in CBT group	++
UK		asthma-specific fear		Mean age = 47	Mean age = 43.8	Panic-fear subscale of ASC	24.83	24.19	*d* = 0.07		No statistically significant differences between groups were found for the general anxiety levels (HADS)	22% of the CBT group were still in the clinical range for asthma-specific fear at post-treatment	
	8+ on HADS-A or 28+ on ASC-PF	5-9 individual sessions with clinical psychologist or CBT therapist		Female 61%	Female 65%		-8.92	-9.75					
		Treatment fidelity assessed through peer supervision & session recordings		severe asthma = 39%	severe asthma								
					0.38	Anxiety subscale of HADS	Completer	Completer					
							26.82	23.94	*d* = 0.32				
							-8	-9.88					
							Not reported	Not reported	*d* cannot be calculated				
Campbell-Sills et al., 2013 [23]	RCT	Stepped care with computerised CBT	standard care	*n* = 93 [3]	*n* = 114 [3]	Anxiety subscale of BSI	11.06 [3] (5.77)	5.92 [3] (4.99)	*d* = 0.96	6, 12, 18 months	Significant improvements on anxiety were found in both groups over time	Limited data available for asthma groups (part of larger scale trial)	++
US	(part of larger scale trial)	Minimum 10-12 individual sessions & minimum 1 intervention contact with an anxiety specialist		no other demographic data available	no other demographic data available						Participants with asthma had significantly greater reductions in anxiety than those without asthma, regardless of whether they were in the intervention	Mental health co-morbidities included	

											or usual care groups		
												No reported therapist training & experience	
	Patients with GAD, PD, PTSD and/or SAD												
Yorke et al., 2016 [44] UK	RCT	CBT for chronic illness, relaxation & asthma awareness with trained clinical psychologists	standard care	*n* = 23	*n* = 21	Anxiety subscale -	12.1 (3.8)	Not reported	*d* cannot be calculated	16 weeks	Greater improvement was found in anxiety for the intervention group as compared to controls at week 16, although this was not statistically significant	Small sample size	++
		8 group sessions		Mean age = 48.6	Mean age = 45	HADs						Increased attrition Manual provided, but no other assessment of treatment adherence reported	
	8+ on HADS-A or HADS-D	Manual to enhance treatment fidelity		Female 65%	Female 48%								
				severe asthma	severe asthma								
Ross et al., 2005 [24]	RCT	Asthma education & CBT for panic	wait-list delayed treatment	*n* = 15	*n* = 10	SPRAS	73.33	31.73	*d* = 1.86	6 months	Statistically greater improvements were found in panic frequency, general anxiety & anxiety sensitivity for the CBT group as compared to controls	Small sample size	++
Canada		12 group sessions with doctoral nurses		Mean age = 37	Mean age = 40		-22.42	-22.29			Only the panic frequency results were maintained at 6-months. There was no difference between groups in agoraphobic avoidance	Sampling restricted to females	
	DSM-IV diagnosis of panic disorder	Session-by-session protocol & treatment fidelity assessed by rating videotapes in relation to protocol checklists		Female 100%	Female 100%	ASI							
				self-rated asthma severity	self-rated asthma severity		35.00 (9.52)	21.27 (9.66)	*d* = 1.43				
				(1-10)	(1-10)	Agoraphobia subscale of FQ							
				Mean = 6.80	Mean = 3.89		14.07 (7.36)	9.80 (8.88)					
						Panic attack diary (N in 14 days)			*d* = 0.52				
							6.07 (8.33)	0.13 (0.35)					
									d = 1.01				
Lehrer et al., 2008 [7]	Repeated measures design	Asthma education & CBT for panic	none	*n* = 12	none	PDSS	2	0.8	*d* = 1.16	1 & 2 months	Significant decreases were found on panic & general anxiety scores at post-treatment & follow-ups	Small sample size	-
(study b)		8 group sessions		Mean age = 31							PDSS effect sizes were large at post-treatment & follow-up, but in BAI were small to medium at post-treatment & follow-up	No control condition	
USA	DSM-IV diagnosis of PD	Session-by-session protocol		Female 67%		ASI	3.1	2.6	*d* = 0.68			No reported assessment of treatment fidelity or therapist training & experience	
				moderate asthma									
				pre&post data n = 8		ACQ	2	1.8	*d* = 0.33				
						BAI	26	20	*d* = 0.48				
						BSQ	2.7	2.2	*d* = 0.60				
Lehrer et al., 2008 [7]	Repeated measures design	Asthma education & CBT for panic	none	*n* = 10	none	PDSS	1.7	0.7	*d* = 1.01	1 & 2 months	Significant decreases were found on panic & general anxiety scores at post-treatment & follow-ups	Small sample size	-

(study a)		14 group sessions		Mean age = 44.1							PDSS and BAI effect sizes remained large at post-treatment & follow-up	No control group	
USA	DSM-IV diagnosis of panic disorder	Session-by-session protocol		Female 60%		ASI	3	2	*d* = 0.19			High attrition (50%)	
				mild asthma								No reported assessment of treatment fidelity or therapist training & experience	
				pre&post data n = 5		ACQ	1.8	1.5	*d* = 0.65				
						BAI	25.5	12	*d* = 1.21				
						BSQ	2.5	1.9	*d* = 0.72				
Spurgeon et al., 2005 [45]	Repeated measures design	CBT focused on health perceptions & reactions	none	*n* = 29	Control group did not complete anxiety measures	Anxiety subscale - HADS	12.55	9.17	HADS-anxiety	6 months	A statistically significant improvement in anxiety was found at post-treatment & 6-month follow-up	HADS not administered to the control group	-
UK	(part of larger trial)	8 group sessions with qualified counsellors		Mean age = 51.9					*d* = 0.94			No reported assessment of treatment fidelity or attrition levels	
				Female 64%									
	Baseline HADS-A indicates >8			asthma severity not reported									
Group B: Studies which included any asthmatic participants or where it is likely that participants did not have clinical levels of anxiety at baseline													
Sommaruga et al., 1995 [25]	RCT	Asthma education & CBT	standard care	*n* = 20	*n* = 20	STAI - CBA 2.0			*d* = 0.67	12 months	The CBT group showed statistically significant improvements in anxiety & psycho-physiological symptoms at 12 months, which were higher in comparison to the control group	Convenience sampling	+
Italy		3-6 individual CBT sessions with a psychologist		Mean age = 44	Mean age = 51		43.2 (10.0)	36.7 (9.1)				Not selected on basis of elevated anxiety	
				Female 45%	Female	QPF -- CBA 2.0			*d* = 0.38			No reported assessment of treatment fidelity	
				asthma severity: inpatients	55%		48.7 (9.3)	45.1 (9.4)				Unclear therapist experience	
					asthma severity: inpatients								
Put et al., 2003 [27]	RCT	Asthma-specific CBT facilitated by a workbook	wait-list	*n* = 12	*n* = 11	Panic-fear subscale of ASC	1.9 (0.6)	1.6 (0.8)	*d* = 0.42	3 months	No statistically significant differences on the ASC panic-fear subscale between intervention and control groups	Small sample size	+
Belgium		6 individual sessions with psychology researchers		Mean age = 43	Mean age = 48							Not selected on basis of elevated anxiety No reported assessment of treatment fidelity	
				Female 42%	Female 62%							or therapist experience	
				mild - moderate asthma	mild - moderate asthma								
Hockemeyer & Smyth, 2002 [26]	RCT	Four weeks of self-help CBT with relaxation tasks & 20min exercises writing about stressful events	placebo self-help workbook	*n* = 27	*n* = 27	Perceived Stress Scale	Not reported	Not reported	*d* = 0.34	none	No statistically significant differences in PSS levels were found over time or between groups	Convenience sampling	+
USA		No therapist input		Mean age = 21.7	Mean age = 19.67							Not selected on basis of elevated anxiety PSS assessed stress levels over treatment period	
				Female 56%	Female 52%							No therapist input	
				self-rated health (0-6)	self-rated health (0-6)							No follow-up	
				Mean = 4.48	Mean = 4.63								
Maes & Schloser, 1988 [48]	Controlled trial	Asthma education & Rational Emotive Therapy	standard care	*n* = 10	*n* = 9	Dutch STAI state anxiety	54.5	52.8	*d* cannot be calculated	none	A statistically greater improvement in general anxiety was found for the CBT group as compared to controls, but not in state anxiety during an asthma attack	Small sample size	+
Netherlands		8 weekly group sessions with patients & partners, facilitated by a health psychologist & other health		no other information reported	no other information reported							Convenience sampling	

		professionals											
						Dutch STAI trait anxiety						Not selected on basis of elevated anxiety Participants not randomised in groups	
							47.8	40.5				No follow-up or assessment of fidelity	

Abbreviations: PDSS: Panic disorder severity Scale; ASI: Anxiety Sensitivity Index; ACQ: Agoraphobic Cognitions Questionnaire; BSI: Brief Symptom Inventory; BSQ: Body Sensations Questionnaire; BAI: Beck Anxiety Inventory; STAI: State Trait Anxiety Inventory; ASC: Asthma Symptom Checklist; HADS: Hospital Anxiety & Depression Scale; FQ: Fear questionnaire; SPRAS: Sheehan Patient-Rated Anxiety Scale; CBA: Cognitive Behavioural Assessment Batteries; QPF: Psycho-physiological symptoms; GAD: Generalised Anxiety Disorder; PD: Panic Disorder, PD: Panic Disorder, SAD: Social Anxiety Disorder, PTSD: Post-traumatic Stress Disorder

[1] Cohen [60] suggested interpreting effect sizes as small $d = .2$, medium $d = .5$, and large $d = .8$.

[2] These relate to ratings of methodological ability to address the current review question and do not necessarily reflect the study's ability to address its own study aims. Summed totals for quality criteria should be interpreted cautiously as quality criteria are not equally important, but those rated ++ are likely to be strongest in addressing the review question.

[3] Data available following correspondence with author.

Table 3. Characteristics and key findings of included studies with children & young people

Study	Design / Anxiety Criteria	Intervention description	Control	Intervention Group	Control group	Anxiety measures	Intervention Group M & SD		Pre-post effect sizes[a] (intervention group)	Follow up	Key findings	Key limitations	Quality rating *
							Pre Score	Post Score					
							Mean (SD)	Mean (SD)					
Group A: Studies which focused on participants with anxiety diagnoses and / or above threshold anxiety score													
Papneja & Manassis, 2006 [50]	Controlled trial	CBT for anxiety	CBT for matched group without asthma	*n* = 36	*n* = 36	RCMAS total anxiety	45.2	43.5	*d* = 0.14	none	Statistically significant reductions in anxiety for both groups at post treatment. A trend towards less improvement in total anxiety in children with asthma as compared to those without asthma was found	No follow-up measures	++

Canada	(data from larger scale trial)	12 group or individual sessions with psychiatrists or psychologists (potential parental involvement)		8-12 years	8-12 years		-12.5	-12.3			Physiological anxiety increased for the asthma group compared to the group without asthma		
		Session-by-session protocol, audio-taped sessions independently rated for adherence										Intervention group combined group and individual CBT	
	Met criteria for at least one DSM-IV anxiety disorder			Asthma severity not reported	No asthma	RCMAS physiol. anxiety							
												Treatment not adjusted for asthma	
				Gender not reported	Matched to intervention group by gender & anxiety diagnosis		8.3	8.5	d = 0.06				
							-3.5	-3.7					
Group B: Studies which included any asthmatic participants or where it is likely that participants did not have clinical levels of anxiety at baseline													
Colland, 1993 [28]	RCT	Self-management asthma training & CBT with homework assisted by parents	control group	n = 48	n_a = 34;	STAI			d cannot be calculated	1, 6, 12 months	Significant reductions in trait anxiety were found at post-treatment in the CBT group, but these did not differ significantly from controls at 6 months	No reported assessment of treatment fidelity	++

							Not reported	Not reported			Only a reduction in state anxiety amongst extremely anxious children remained significant at 6-months		
Netherlands		10 group sessions with a behaviour therapist & a group psychotherapist	a: one information session	Mean age = 10	n_b = 30	state anxiety						Not selected on basis of elevated anxiety	
			b: no therapy	Female 39%	Mean age = 10		34.5						
					Females 38.9%								
								30.4					
						STAI trait anxiety							
Long et al., 2011 [51]	Repeated measures design	Asthma education & CBT with physiological feedback & relaxation	none	n = 22	none	PSS	21.06	12.44	d = 1.65	none	Statistically significant improvements were found in PSS & anxious mood at post-treatment, but not for the state-trait anxiety measure	No follow-up measures	-
USA	(two combined trials)	6 individual sessions with graduate CBT therapists, MSc clinicians & research assistants		(trial 1 n = 14			-4.84	-5.57				Not selected on basis of elevated anxiety No control condition	
		Session-by-session protocol & supervision		trial 2 n = 8)								Limited therapist clinical experience	
				7-12 years		POMS	2.79	1.74	d = 0.60				
				Female 36%		anxiety	-1.78	-1.73					
				mild-moderate persistent asthma									

						STAI state anxiety	44.33	44.39	$d < 0.01$				
							-13.75	-14.06					
						STAI trait anxiety							
									$d = 0.40$				
							34.22	31.22					
							-7.67	-7.22					
Marriage & Henderson 2012 [52]	Repeated measures design	Asthma education & CBT with mindfulness	none	$n = 17$	none	SCAS	35.2	28.9	d cannot be calculated	3 & 6 months	A reduction of up to 30% on anxiety scores was found at post-treatment and at 6 months	Descriptive statistics only	-
UK		6 group sessions with a respiratory nurse specialist trained in behavioural techniques		Mean age = 14.2				(3 mth post)				High attrition	
	Diagnosed with 'health-related anxiety' but anxiety at non-clinical level			Female 50%								Convenience sample	
				mild-severe asthma								Baseline anxiety levels were elevated, but not in clinical range	
												No reported assessment of treatment fidelity	

Abbreviations: STAI: State Trait Anxiety Inventory; POMS: Profile of mood states; RCMAS: Revised Children's Manifest Anxiety Scale; SCAS: Spence Children's' Anxiety Scale; PSS: Perceived Stress Scale

[a] Cohen [60] suggested interpreting effect sizes as small $d = .2$, medium $d = .5$, and large $d = .8$.

* These relate to ratings of methodological ability to address the current review question and do not necessarily reflect the study's ability to address its own study aims. Summed totals for quality criteria should be interpreted cautiously as quality criteria are not equally important, but those rated ++ are likely to be strongest in addressing the review question.

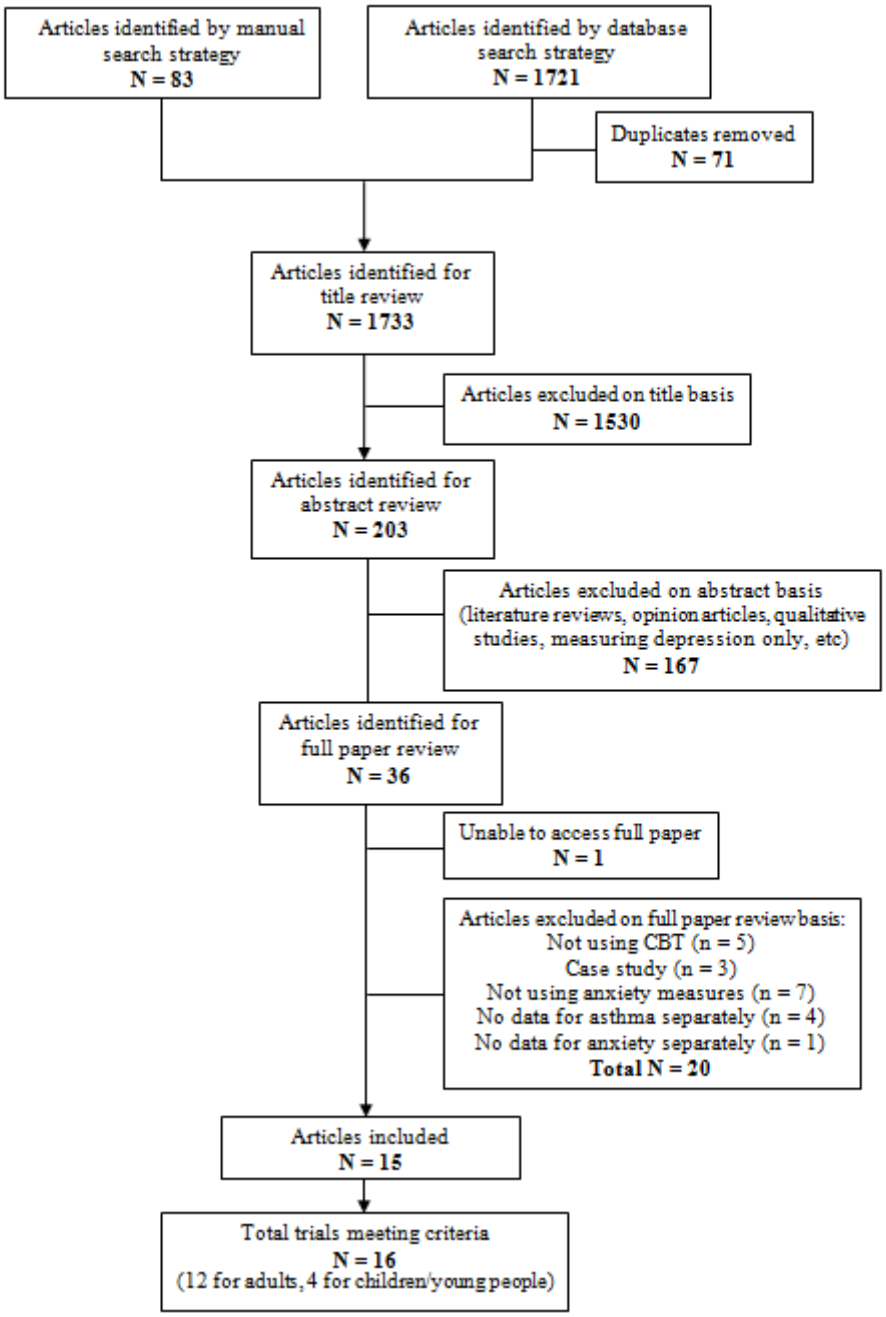

Figure 1. Flowchart of search strategy pathway and results