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Non-pharmacological interventions aimed at modifying health and behavioural outcomes for adults with asthma: a critical review

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Abstract

Background: Evidence suggests that living with asthma is linked with psychological and behavioural factors including self-management and treatment adherence, and therefore there is a reasonable hypothesis that non-pharmacological treatments may improve health outcomes in people living with this condition.

Method: A systematic review of randomised controlled trials of non-pharmacological interventions for adults with asthma was designed. Databases searched included The Cochrane Airways Group Register of trials, CENTRAL and Psycinfo. The literature search was conducted until May 2014.

Results: 23 studies met the inclusion criteria and were organised into four groups: relaxation-based therapies (n = 9); mindfulness (n = 1), biofeedback techniques (n = 3); cognitive behavioural therapies (CBT) (n = 5); and multicomponent interventions (n = 5). A variety of outcome measures were used, even when trials belonged to the same grouping, which limited the ability to conduct meaningful meta-analyses.

Conclusions: Deficiencies in the current evidence-base, notably trial heterogeneity, means that application to clinical practice is limited and clear guidelines regarding the use of non-pharmacological therapies in asthma is limited. Relaxation and CBT, however, appear to have a consistent positive effect on asthma-related quality of life and some psychological outcomes, and lung function (relaxation only). Future trials should be informed by previous work to harmonise the interventions under study and outcome measures used to determine their effectiveness; only then will meaningful meta-analyses inform clinical practice.

INTRODUCTION

Asthma is a multifactorial chronic respiratory disease characterised by recurrent episodes of airways obstruction. Clinical trials have demonstrated that pharmacotherapy is capable of achieving high levels of asthma control for most patients yet poor control remains common in clinical practice [1]. Living with asthma has been linked with psychological comorbidity including anxiety, depression, panic attacks, and behavioural factors such as suboptimal self-management skills and non-adherence to treatment [2, 3]. As a result, asthma is a major cause of

absenteeism from school and work, and is likely to impact on overall quality of life [4]. In particular, in patients with severe or difficult-to-control asthma there is high prevalence of psychological co-morbidity, greater healthcare utilisation, and fatal or near fatal asthma attacks [5]. Therefore, non-pharmacological interventions aimed at facilitating adjustment to and coping with asthma, and decreasing the burden of living with asthma are likely to be important in its overall management, even if lung function does not improve.

A Cochrane review [6] of psychological interventions for adults with asthma has evaluated 14 trials of varied psychological intervention. That review was limited by poor methodological quality in the studies with small sample sizes, lack of between group analyses and heterogeneous interventions and outcome measures. No firm conclusion as to the benefit of psychological interventions could be made but directions for future research were prescribed; notably improved trial quality that adhered to CONSORT principles [7], and emphasis placed on defining study participants such as asthma severity (defined by internationally recognised guidelines) [8] and psychological co-morbidity (presence of anxiety, depression, or panic disorder). We set out to review the current literature and whether any clinical guidelines can now be derived to inform non-pharmacological asthma management. In doing so, we extend the inclusion criteria to include non-pharmacological interventions more broadly.

AIMS

The aims of the review are to:

1. Establish the types of non-pharmacological interventions used to modify health outcomes in adults with asthma and whether they are effective.
2. Identify the research studies in the field and evaluate the methodological rigour of the included studies.
3. Identify how research participants are categorised in terms of asthma severity.
4. Determine the outcomes used to assess the effectiveness of non-pharmacological interventions.

METHODS

Types of studies and interventions included

Randomised controlled trials (RCT) of non-pharmacological interventions for adults (over the age of 16 years) with asthma were included. Self-management educational and action plan interventions were excluded since they have been evaluated elsewhere [9, 10].

Quality assessment

The modified Jadad score (0 to 5, where a score of 5 indicates a high quality) [11] was applied to provide an overall assessment of trial quality. A modified version was necessary as, due to the nature of the psychological interventions, it would be difficult to conduct double-blinded trials. Therefore in steps 2 and 5 'double-blind' is changed to 'single-blind' indicating that at least data collection was blind to allocation and/or clinicians and research staff (see Box 1).

Box 1: Jadad quality assessment

- 1) Was the study described as randomised (1 = yes; 0 = no)?
- 2) Was the outcome assessment blinded (1 = yes; 0 = no)?
- 3) Was there a description of withdrawals and dropouts (1 = yes; 0 = no)?
- 4) Was the method of randomisation well described and appropriate (1 = yes; 0 = no)?
- 5) Was the method of blinding well described and appropriate (1 = yes; 0 = no)?
- 6) Deduct one point if methods for randomisation or blinding were inappropriate.

Search strategy

For studies before 2007, 12 of the 14 trials included in the original Cochrane review [6] were included. Two were excluded because they were not available in a peer review format (dissertations only) [12,13]. For the period after 2007 to October 2013 (up-dated May 2014), a second search was done using the same search procedures as the Cochrane review which included the The Cochrane Airways Group Register of trials 2007 onwards; CENTRAL Issue 5, 2014; and Psycinfo 2007 onwards and the following exemplar search terms: "asthma" and "self-management" or "psychological"

or “cognitive behavioral therapy” or “relaxation” or “biofeedback” or “hypnosis” or “mindfulness”. Reference lists of all papers were reviewed for additional studies.

Three reviewers (HM, JY, SF) independently examined titles and abstracts of papers returned by the literature searches to identify potential studies for inclusion.

Disagreement was resolved by consensus.

RESULTS

The literature search identified 559 papers, of which 25 (12 included in the Cochrane review) (see Figure 1) met the inclusion criteria [14-38]. Two studies reported results in two different publications so these were combined and counted as one report [14, 15, 34, 35] resulting in 23 studies being included. All were randomised controlled trials conducted over a range of timescales from one week to two years. They included a variety of non-pharmacological interventions and were categorised into five groups according to previous publications [6, 39] and the theoretical underpinning of the interventions: relaxation therapy (n = 9); mindfulness (n = 1), biofeedback techniques (n = 3); cognitive behavioural therapy (CBT) (n = 5); and multi-component interventions (n = 5) (Table 1).

Quality assessments

The majority of reported studies were rated with a Jadad score of 2 (n = 14 studies) (Table 1). The highest Jadad score achieved was 4 (n = 5 studies) [16,30,32,34,38]. The main reasons for low quality scores was lack of a description of randomisation processes, withdrawals and dropouts.

Summary of the interventions and results

i) *Relaxation Techniques*

Types of interventions

The term relaxation suggests a sense of ease and not being tense and thus it might be assumed that teaching relaxation would follow some protocol or accepted standard technique. However this is not always the case in the studies included in this review. Various techniques are used by individuals to improve their state of relaxation (Table 2). Some of the methods are performed alone; some require the

help of another person (often a trained professional); some involve movement and some focus on stillness.

Study participants

Two studies [16,20] did not state how the a diagnosis of asthma was confirmed. Three studies specified asthma severity including, moderate-severe [22,23], mild-moderate [21]. One study assessed patients' psychological well-being prior to enrolment and recruited those described as having 'psychological disorders or psychosocial factors requiring treatment', but did not clarify how that was assessed [22]. The most recent four studies provided a power calculation [15, 16-18] and each study reached or exceeded randomisation targets.

Outcome measures

A variety of outcome measures was used; only lung function parameters were reported across all ten studies, although with different measures (Table 3). Four studies measured health-related quality of life (HRQL) using different questionnaires including the Asthma Quality of Life Questionnaire (AQLQ) [18], St George's Respiratory Questionnaire (SGRQ) [17] and the generic SF-36 [16].

Treatment effects

Studies reported a mix of between and within group analyses. Significant between group analyses that favoured relaxation included FEV₁ [15, 16, 18] and medication use [18]. In addition, relaxation consistently improved some psychological outcomes including 'anger expression' [16], anxiety [17] and depression [17], and quality of life [16, 17].

ii) Mindfulness techniques

Mindfulness training involves learning to recognise and discriminate between components of experience, including thoughts, feelings, and sensations, and developing a non-reactive awareness of these [40]. One study evaluated mindfulness-based stress reduction (MBSR) compared to an educational control programme [38]. Patients with intermittent or well controlled asthma were excluded, with more than 80% of participants prescribed inhaled corticosteroids or oral prednisolone. Outcomes included asthma-quality of life, stress and morning peak expiratory flow rate at 10 weeks, 6 and 12 months. MBSR produced lasting (12-month follow-up) and clinically significant improvements in asthma-quality of life and stress but no improvement in lung function was observed.

iii) Biofeedback techniques

Types of interventions

Biofeedback studies included in this review involve selecting variables that are postulated to influence asthma symptoms, and providing feedback to the patient on these variables, with the aim of improving the asthma symptoms. The biofeedback studies used various devices to target primarily physical rather than psychological variables. The variables and feedback devices were: exhaled carbon dioxide levels (pCO₂) using a capnograph [24], respiratory sinus arrhythmia (RSA) presumably by ECG feedback and muscle tension using electromyography (EMG) [26], and heart rate variability (HRV) using a 'physiograph' [25]. The treatment sessions were brief: one hour [23], 30 minutes [26], or 20 minutes [25]. The durations of sessions and treatments were one hour for four weeks [24], 30 minutes for six weeks, un-stated biofeedback session duration for 10 weeks [25].

Study participants

There were two pilots studies with 12 [24] and 17 [26] patients enrolled in each, and a larger study including 94 patients [25]. Asthma severity was described as mild to moderate [24], mild [25], or not described [26]. None of the three studies looked for psychological symptoms to target with biofeedback as an aim of treatment. One study used psychiatric illness needing medication as an exclusion criteria [26]. No power calculations were included and information regarding the method of randomisation was lacking from the three studies.

Outcome measures

The primary outcomes were end tidal CO₂ and FEV₁ [24] respiratory impedance [26]. Regarding the lung function tests, all the experiments reported peak expiratory flow (PEF) and some measure of respiratory impedance, termed R_i [24, 26] or Z_{rs} [25]. Patient reported outcomes were detailed in all studies but with different measurement scales (Table 3). Medication use was recorded in two studies [25, 26].

Treatment effects

Each study had a target outcome for biofeedback. Meuret [24] showed there was a (hypothetically desirable) significant increase in PCO₂ in the treatment group, while levels were stable (undesirable) in the wait list control, but there was no change in FEV₁. Lehrer [26] showed a decrease in respiratory impedance in the respiratory sinus arrhythmia group, but not other groups. Regarding changed medication use, Meuret [24] found no between-group difference, with medication remaining low and stable in both groups. Lehrer [26] found no between-group differences in medication consumption. Lehrer [25] may have demonstrated both the placebo effect and a clinical effect between groups. There was a decrease in medication use in the placebo group compared to wait list control. However there was a larger decrease in medication use in the heart rate variability group compared to the wait list control.

iv) Cognitive Behavioural Therapy (CBT)

Types of interventions

CBT incorporates elements of both behavioural therapy and cognitive therapy approaches. It facilitates the identification of irrational, anxiety-provoking thoughts, and challenges these negative automatic thoughts and dysfunctional underlying beliefs through collaborative 'hypothesis-testing', using behavioural tasks of diary-keeping and validity-testing of beliefs between sessions, and skills training within sessions [41].

Five studies using CBT are included in this review [27-31]. CBT components of the interventions varied between studies depending on the research question, and the primary outcome of the studies. One study [29] hypothesised that their intervention would reduce panic disorder in women with asthma so their intervention focused on CBT and asthma education to reduce panic attacks and another [27] focused on improving the self-management of asthma specific fear for their group of patients. The other studies delivered interventions designed to reduce generalised anxiety and/or promote asthma self-management [28, 30, 31]. The delivery of the interventions varied with respect to duration of sessions (from 60 to 90 minutes) and the number of sessions delivered varying from 3 to 12. The practitioner delivering the

interventions ranged from nurses, physiotherapists and psychologists. All studies involved face-to-face individual CBT sessions.

Study participants

All participants had a confirmed diagnosis of asthma but only two of the five studies reported asthma severity levels [27, 30]. One study screened patients for panic disorder [29] and another required participants to score positively for clinical anxiety using the HADS and asthma specific fear [27]. For all studies the numbers of participants was small with only one study reporting a power calculation, however, the time taken to recruit participants and numbers of patients dropping out meant the powered sample was not reached [27].

Outcome measures

Outcome measures also differed depending on the focus of the study (Table 3). HRQL was measured by the AQLQ in three studies [28-30] and the Asthma Symptom Control in all studies [28, 30, 31]. Anxiety was measured by different outcome measures in each of the studies

Treatment effects

All studies reported significant improvements for participants receiving CBT compared to control groups, but for different outcomes, limiting the pooling of data in a meaningful way. An improved HRQL for the CBT group compared to controls was reported in three studies [28-30] and improvement in asthma symptoms was reported in three studies [28, 30, 31] with outcomes measured using a variety of tools. One study reported increased adherence, knowledge, attitude towards asthma and self-efficacy in the CBT group [30].

v) Multi-component interventions

Types of interventions

Four studies published since the Yorke et al. review [6] consisted of a complex intervention with various components and have been grouped together under 'multi-component interventions' [32, 33, 34, 36]. In addition, the study by Hockemeyer [37] was included in this group since it had three main components.

Insert Table 3

Study participants

Patients with a mix of asthma severity were included in the five studies; mild to severe [36] and difficult asthma [32] - persistent symptoms despite treatment at BTS/SIGN step 4/5 [42]. Two studies did not state asthma severity: only one confirmed asthma diagnosis in telephone screening with the patient [37] and the other one did not describe any method of confirmation of asthma [33].

Outcome measures

No single outcome was measured across all five studies (Table 3). The most frequent was HRQL which was assessed in four studies; three used the AQLQ [32, 33, 35] and one the SF-12 [36]. All other outcome assessments were included in no more than two studies, for example self-confidence [34], self-efficacy [36] and different aspects psychological distress which was measured using a variety of scales [33, 37].

Treatment effects

Treatment effects for multi-component interventions were mixed. Clark et al [35] and Sun et al [33] reported significant improvements at two years for the entire patient reported outcome measures and use of rescue medications; however, no significant difference was reported for the main outcome of day and night-time symptoms. In contrast, Kuijer et al [36] and Hockemeyer [37] reported no significant difference between the intervention and control groups for any of the patient reported outcome measures used in their studies (for example, self-efficacy, proactive coping, and perceived stress).

Discussion

In their review of psychological interventions for adults with asthma Yorke et al [6] concluded that “the ability to make firm conclusions as to the effectiveness of psychological interventions was limited by poor study quality, insufficient reporting of data and varied outcome measures”. Since that review, a further ten studies have been reported to determine the effectiveness of psychological and, more broadly, non-pharmacological interventions for the management of adult asthma. We broadened the definition of interventions included in this review as the inclusion of some trials by Yorke et al (6) question the notion of ‘psychological’ intervention – for

example biofeedback does not necessarily include a psychological component and many of these studies did not include any psychological measures as outcomes. Additional studies included in this review were four multicomponent interventions, three relaxation techniques, two CBT, one mindfulness, and one biofeedback. Study quality was evidently improved for some but not all of these recent studies. Between group analyses were reported for each study, however, the reporting of asthma severity and psychological comorbidity, in studies evaluating a psychologically-based intervention, remains poor and a variety of outcome measures were applied which continues to limit the ability to pool data for meta-analysis.

We found a range of non-pharmacological interventions and categorised these into five groups: relaxation techniques, mindfulness, biofeedback techniques, CBT and multicomponent. These categories are not mutually exclusive, rather we categorised the interventions in such a way that best represented the underpinning theory and potential application of the intervention into practice. Relaxation therapies were reported most often ($n = 9$), although a range of relaxation techniques were applied including PMR, guided imagery and hypnosis. Overall, relaxation techniques tended to have a positive impact on lung function, HRQOL and a range of psychological outcomes. Given the variety of approaches used it is difficult to discern if one style of relaxation therapy has an advantage over another. Nonetheless, relaxation therapy is a promising intervention that could be easily incorporated into individual care plans for people with mild to moderate asthma. Only one study was included in this review that used a mindfulness based approach and positive, lasting and clinically significant improvements in asthma-related quality of life and stress were found in patients with persistent asthma symptoms. This has important implications for clinical practice since those with moderate to severe asthma are at a higher risk of experiencing poorer health outcomes [5]. Future research should focus on evaluating the benefits of relaxation and mindfulness based interventions for this at risk population.

Cognitive behavioural therapy has a strong evidence base for the management of mental health disorders [41]. In this review, five studies evaluated CBT and all consisted of individual face-to-face therapy sessions. The benefit of CBT was difficult to discern due to the variety of outcome measures and different study follow-up times used. Outcomes that did demonstrate a positive effect in more than one study

included HRQOL [28-30] and mood scores (measured using the HADS) [27, 28], although recruitment and study attrition presented limitations. Therefore, whilst it is reasonable to assert that CBT has a positive effect on asthma-related quality and psychological outcomes, future research should include evaluation of different modes of delivery such as telephone and online which may improve initial up-take and course completion.

Multicomponent interventions were not included as a separate category of intervention in the Yorke et al. review [6]. It became evident during the study selection phase for the current review that recent studies have applied complex interventions that were informed by more than one theoretical basis. That resulted in the testing of a 'package' of interventions. Interventions included components such as counselling, relaxation, education, breathing exercises, problem solving, CBT and written emotional disclosure. As such, it is not possible to identify the key ingredient for this sub-category. The benefit of multicomponent interventions was difficult to conclude due to the variety of interventions, outcome measures, as well as data collection methods and follow-up time-points across the studies. Outcomes that showed a significantly positive effect in two or more studies included use of 'as needed' medications [32, 35] and HRQL [33, 35]. The developmental processes involved in designing these complex interventions as per MRC Framework [43] were not apparent in any of the included papers. This limited the ability to scrutinise the underpinning theory and development of such interventions which may also represent significant economic costs (no economic evaluation data were available). At this time the evidence base does not support the implementation of multicomponent interventions for the management of asthma.

In common with other non-pharmacological interventions for asthma the studies of biofeedback could be improved by samples size calculations to ensure they are large enough to demonstrate effects. A special problem for biofeedback studies is that there was often a change in a measured physiological variable, but whether a change in this particular variable is clinically significant is a different issue. In all the studies researchers gave the subjects biofeedback on an experimental parameter (i.e. pCO₂, RSV, muscle tension, HRV). Unsurprisingly, when given feedback into these parameters, the experiments did not show any convincing improvements in

peak expiratory flow or medication use. Therefore, the clinical application and benefit of biofeedback is questionable and cannot be supported at this stage.

The British Thoracic Society Guidelines for control of asthma lists five treatment steps [42]. These advocate pharmacological agents, based on high quality, large-scale rigorous studies which is in contrast to the trials of non-pharmacological interventions.

An inherent difficulty with trials of non-pharmacological interventions is the application of a suitable control. In the current review the majority of trials used 'usual care' (with or without a waiting list element) as the control. Rarely was the content of 'usual care' described. Despite the existence of evidence-based international guidelines for the management of asthma in adults [8, 42, 44] application of these to individual patients in practice varies, and is often sub-optimal [45, 46]. This makes it difficult to discern from the papers included in our review how trial participants were actually clinically treated during the course of the study.

Few studies reported the mechanism of confirming an asthma diagnosis, although more recent studies appear to have used international guidelines to confirm and categorise the severity of the asthma. When severity of asthma was described most studies reported mild or moderate to severe levels rather than focusing on patients with severe or difficult to control asthma. Severe asthma affects approximately 5-10% of all patients living with the condition, yet accounts for 50% of the total costs associated with asthma [47]. In severe asthma, psychiatric comorbidity is related to impaired health-related quality of life, decreased motivation to self-manage, worse adherence to treatment (estimated non-adherence 30-40%), greater healthcare utilization, and fatal or near fatal asthma attacks [2, 5]. However, no studies included in this review targeted patients with severe asthma or those with difficult to treat asthma and a description of participant's psychological profile was rarely acknowledged.

Two studies screened patients to determine co-existing panic disorder [29] and high anxiety [27] to target patient inclusion in trials of CBT. However, only Ross et al [29] reported a positive effect of CBT for number of panic attacks and anxiety experience

measured with the Sheehan Patient-Rated Anxiety Scale and Anxiety Sensitivity Index. Given the interplay between panic/anxiety and asthma episodes targeting people with both conditions appears logical. Likewise, the prevalence of depression is also high in people with asthma, in particular severe asthma [48]. No study included in this review screened patients for depression or targeted patients with depression in their inclusion criteria.

A significant limitation of the body of evidence for non-pharmacological interventions for asthma is the variety of outcome measures used, even when studies are within the same intervention category. This hinders the ability to pool results for meta-analysis.

In primary care Peak Expiratory Flow Rate (PEFR) and asthma symptoms are used to assess asthma control by both the patient and clinicians. Normograms are used to plot expected PEFR for age, height, and sex. However the research on psychological interventions does not consistently use the chief clinical measure of asthma as an outcome measure (10 out of 22 studies used PEFR). Assessment of asthma symptoms was included in 13 studies, although only 8 of these used a validated asthma symptom questionnaire, the Asthma Control Checklist [49] and the Asthma Control Questionnaire [50]. A further five studies developed daily diaries limiting the ability to assess this outcome across studies in a reliable way. As a result, these studies tend to lend themselves more to an academic readership, rather than facilitating clinicians' application of the findings to improve the well-being of patients with asthma.

Conclusion

This review demonstrates that studies have been conducted of non-pharmacological interventions for adults with asthma, however they are limited in their interpretation by poor methodological quality, limited descriptions of the population under study (including asthma severity and psychological comorbidity), varied interventions (even when they belong to the same grouping) and diverse outcomes. To date, the most promising non-pharmacological interventions for the management of asthma include relaxation techniques that could be implemented with relatively ease. CBT is also

promising but issues regarding uptake and course completion require further attention.

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Table 1: Summary of included studies

Source; Jadad score	a) N [mean age years] b) female: male c) Asthma diagnosis d) Psychological screening	Design a) sample size calculation b) true randomisation c) blinding d) follow-up	Treatment	Control	Dropouts / withdrawals	Primary outcome/s	Results Between groups only – final follow- up + favours treatment - no difference	Secondary outcomes	Results Between groups only – final follow- up + favours treatment - no difference
Relaxation n = 5									
Lahmann et al. (2009) [14], 2010 [15] Jadad: 2	a) 64 [42±12] b) 64% 36% c) Specialist physician, positive skin prick test to house dust mite d) Structured clinical interview – exclusion purposes only	RCT 4 groups a) Yes b) Yes c) Not clear who was blinded, study nurse did allocation d) 4 months	E1: 16 FR E2: 16 GI E3: 16FR/GI	Placebo C: 16	E1: 0 E2: 1 E3: 1 C: 3	1) FEV ₁ % pred 2) sR ₅₀ %pred	1) + FR (compared to control) 2) + FR and FR/GI	Not specified	
Nickel et al. 2006 [16] Jadad: 4	a) 64[E: 25±3; C: 26.9] b) 64:0 c) Not described d) Structured clinical interview – exclusion purposes only	RCT 2 groups a) Yes b) Yes c) Yes d) 8 weeks	PMR E: 32	Shame relaxation C: 32	E = 2 C = 4	1) SBP 2) FEV ₁ 3) PEF 4) HR	1) + 2) + 3) + 4) +	1) Anger Expression Inventory 2) SF-36	1) + 2) +
Holloway and West 2007 [17] Jadad: 2	a) 85[E: 39; C: 50] b) 49:36 c) GP database d) None	RCT 2 groups a) Yes b) Yes c) Not stated d) 12 months	Papworth Method E: 39	Usual care C: 46	E: 7 C: 6	1) SGRQ	1) +	1) HADS 2) Nijmegen 3) FEV ₁ 4) FVC 5) PEF	1) + 2) + 3) - 4) - 5) -
Epstein et al. 2004 [18] Jadad: 2	a) 68[E: 50.2±14; C: 49±14] b) 32:36 c) FEV ₁ and reversible airway obstruction d) Structured interview – exclusion purposes only	RCT 2 groups a) Yes b) Yes c) Not stated d) 16 weeks	GI E: 34	Usual care C: 34	E = 17 C = 16	1) FEV ₁ 2) Medication use 3) AQLQ 4) BDI 5) STAI	1) + 2) + 3) + 4) - 5) -	Not specified	
Lehrer et al. 1994 [19]	a) 106[E1: 41±10; E2: 40±11; C: 45±9]	RCT 3 groups a) Not described b) Not described	PMR E1: 36 Music E2: 13	Waitlist C: 30	E1: 12 E2: 13 C: 9	1) Metacholine Challenge Test 2) Spirometry	Within group analyses only	1) Medication use 2) ASC	Within group analyses only
Jadad: 2	b) 55:52 c) Physician – mild to moderate d) Not described	c) Not stated d) 8 sessions, not clear						3) Healthcare utilisation	
Deter and Aller 1993 [20] Jadad: 2	a) 31[43] b) 17:14 c) Treated for asthma last 2 years d) Not stated	RCT 3 groups a) Not described b) Not described c) Not stated d) 1 year	Autogenic training E1: 9 FR E: 10	C: 12	E1: 2 E2: 3 C: 4	1) Medications 2) FVC 4) GP visits 5) Hospital days/year	Within group analyses only	Not specified	
Ewer and Stewart 1986 [21] Jadad: 3	a) 35[range 18–44] b) 24:15 c) Physician diagnosed – mild to moderate d) Susceptibility to hypnosis	RCT 4 groups a) Not described b) Not described c) Yes d) 5 weeks - not clear	Hypnosis E1: 10 (low susceptibility) E2: 12 (high susceptibility)	C1: 7 (low susceptibility) C2: 10 (high susceptibility)	C: 5	1) FVC 2) FEV ₁ 3) PEF 4) Residual volume 5) Maximum expiratory flow rate at 50% VC 6) Airways resistance	Within group analyses only	1) Rescue medication 2) Symptoms: Sleep, Wheeze, Cough, Phlegm	Within group analyses only
Henry et al. 1983 [22] Jadad: 1	a) 24[39] b) 21:3 c) Physician – moderate to severe d) Described as 'psychopathological disorders or psychosocial factors requiring treatment'	RCT 2 groups a) Not stated b) Not described c) Not stated d) 8 months	Autogenic therapy E: 12	Supportive group psychotherapy C: 12	Not described	1) FVC 2) FVC%pred 3) FEV ₁ 4) FEV ₁ %pred	Within group analyses only	Not specified	
Erskine and Schonell 1979 [23] Jadad: 2	a) 12[30, range 16–48] b) Not stated c) ATS – moderate to severe d) Not stated	RCT 2 groups a) Not stated b) Yes c) Not stated d) 13 weeks	Mental & PMR E: 6	PMR C: 6	E: 1 C: 1	1) FEV ₁ 2) Daily symptoms	1) - 2) -	Not specified	
Mindfulness-based stress reduction n = 1									
Pbert et al. (2012) [38] Jadad: 4	a) 83 [52.8] b) 56:27 c) NIH/NHLBI: mild, moderate, severe asthma d) None	RCT 2 groups a) Yes b) Yes c) Outcome assessment blind d) 12 months	MBSR E: 42	Education C: 41	E: 7 C: 3	1) AQLQ 2) PEF	1) + 2) -	1) Asthma control 2) Perceived Stress 3) Medication use 4) Healthcare utilisation 5)	1) - 2) + 3) - 4) - 5) -

								work/school absenteeism	
Biofeedback n = 3									
Meuret et al. 2007 [24] Jadad: 2	a)12[E:43; C:34] b) 75%/25% c) Not described d) Not done	RCT 2 groups a) Not stated b) Not described c) Not stated d) 8 weeks	Breathing training to achieve sustained increases in pCO ₂ E:8	Waitlist C: 4	None	1) End-tidal pCO ₂	1)+	1) FEV ₁ 2) RR 3) PEFR 4) ACO 5) PANAS distress 6) R _i 7) meds change 8) SF-12	1) - 2) + 3) + 4) + 5) - 6) - 7) - 8) -
Lehrer et al. 2004 [25] Jadad: 2	a)94[37] b) 64.30 c) Physician – mild asthma d) Not described	RCT 4 groups a) Not described b) randomisation method not described c) assessors blinded d) none	E1: HRV and abdominal breathing E2: HRV	C1: placebo EEG C2: Waitlist	E1: 6 E2: 5 C1: 5 C2: 2	1) HRV	1) +	1) Controller medication 2) PEFR 3) Asthma symptoms – unknown scale	1) - 2) - 3) -
Lehrer et al. 1997 [26] Jadad: 1	a)17[37] b) 12.5 c) Physician, severely not described d) Psychiatric screening for exclusion criteria only	RCT 3 groups a) Not stated b) Not described c) Not stated d) none	E1: RSA Biofeedback E2: incentive spirometry E3: EMG	Waitlist C: 6	E: 2 C: 0	1) Airway impedance, R _i	1) +	1) Medication use 2) RIAS 3) abdominal and thoracic strain gauge 4) PEFR 5) cardiac Traub- Hering- Mayer wave 6) End tidal CO ₂	1) - 2) - 3) - 4) - 5) + 6) -
CBT n = 5									
Perry et al. 2012 [27] Jadad: 2	a)94 [E:47; C:44] b) E: 60%/40% C: 65%/35% c) Physician d) HADS Anxiety >8, ASC-F >28	RCT 2 groups a) Yes b) Yes c) Not stated d) 6 months	Individual CBT E: 50	Usual Care C: 44	E: 22 C: 13	1) ASC-Panic-fear	1) -	1) EQ-5D 2) HADS 3) ABP 4) AMHCC 5) healthcare use	1) - 2) - 3) - 4) - 5) -
Grover et al. 2007 [28]	a) 40 b) Not stated c) ATS criteria	RCT 2 groups a) Not stated b) Yes	Individual CBT E: not stated	Self- managemen t	12 total	1) ASC 2) ABP 3) HADS	1) + 2) +	Not specified	

Jadad: 1	d) Not stated	c) Not stated d) 6-8 weeks		C: not stated		4) AQLQ 5) PEFR	3) + 4) + 5) -		
Ross, Davis & MacDonald 2005 [29] Jadad: 2	a) 48[E: 38; C: 41] b) 48.0 c) Physician, not described d) Not stated	RCT 2 groups a) Not stated b) Not described c) Not stated d) 6 months	Individual CBT E: 25	Waitlist C: 23	E: 10 C: 13	1) Panic attack diary 2) SPSARS 3) ASI 4) FO-ago 5) BDI 6) Asthma symptom diary 7) PEFR 8) AQLQ	1) + 2) + 3) + 4) - 5) - 6) - 7) - 8) +	Not specified	
Put et al. 2003 [30] Jadad: 4	a) 23[E: 43; C: 48] b) 12.11 c) ATS – range of seventies d) Not stated	RCT 2 groups a) Not described b) Yes c) Yes d) 6 months	Individual CBT E: 12	Usual care C: 11	Not stated	1) AQLQ 2) ASC Obstruction Dyspnoea Fatigue Hyperventilation Anxiety Irritation 3) Adherence 4) KASE-AQ 5) PEFR	1) + 2) + - + - - + 3) + 4) + 5) -	Not specified	
Sommeruga et al. 1995 [31] Jadad: 2	a) 40[48±16] b) 21.19 c) ATS, severity not described d) Not stated	RCT 2 groups a) Not stated b) Yes c) Not stated d) 1 year	Individual CBT E: 20	Usual care C: 16	C: 4	1) Asthma attacks (number) 2) ASC 3) RIO 4) Health Locus 5) STAI 6) healthcare utilisation 7) work/school absenteeism	1) + 2) - 3) - 4) - 5) - 6) - 7) -	Not specified	
Multicomponent n = 5									
Gamble, Stevenson & Heaney 2011 (Phase 2 only) [32] Jadad: 4	a) 20 [E: 50; C: 45] b) 17.3 c) BTS/SIGN step 4/5 d) ACS x3, persistent non- adherence	RCT 2 groups a) Not described b) Not stated c) Single blind d) 12 months	See Table 3 E: 9	Usual care C: 11	DO: 2	1) %ICT inhalers filled	1) +	1) Daily ICS 2) Rescue oral corticosteroids 3) Total beta agonists 4) Hospital admissions 5) FEV ₁ %pred 6) AQLQ 7) AQLQ	1)+ 2) - 3) - 4) - 5) - 6) - 7) - 8) -

Sun et al. 2010 [33] Jadad: 2	a) 374 [E: 42.9, C: 37.5] b) 168/205 c) Not described d) Only for exclusion	RCT 2 groups a) Not stated b) Yes c) Yes d) 3 months	See Table 3 E: 228	Usual care C: 146	DO: none	1) AQLQ 2) Profile of Mood States 3) Asthma Knowledge	1) + 2) + 3) +	8) HADS Not specified	
Clark et al. 2007 [34] & Clark et al. 2010 [35] (2yr f/u) Jadad: 4	a) 808 [E: 48, C: 49] b) All female c) Physician diagnosis d) Not stated	RCT 2 groups a) Yes b) Yes c) Yes - single d) 2 years	See Table 3 E: 424	Usual care C: 384	E: 113 C: 87 at 2 years follow up	1) Symptoms (day/night time)	1) -	1) absenteeism (work/school) 2) symptoms with sexual activity 3) AQLQ 4) Self-regulation 5) self-confidence 6) rescue medicine	1) + 2) + 3) + 4) + 5) + 6) +
Kuyjer et al. 2007 [36] Jadad: 2	a) 70 [E: 41.6, C: 46.3] b) 43/27 c) ATS moderate-severe or moderate-mild d) Dispositional optimism described only	RCT 2 groups a) Not stated b) Not described c) Not stated d) 6 months	See Table 3 E: 41	Usual care C: 29	E: 16 C: 2	1) SF-12 2) Cantrill's Ladder 3) Self-efficacy 3) Proactive Coping	1) - 2) - 3) -	Not specified	
Hockemeyer & Smyth 2002 [37] Jadad: 2	a) 60 [20.7] b) 29/25 c) patient confirmed only d) Not stated	RCT 3 groups a) Not stated b) Not described c) Not stated d) 1 week	See Table 3 E: 30	Placebo workbook C: 30	E: 3 C: 3	1) FEV ₁ %pred 2) FEV ₁	1) + 2) -	1) Perceived Stress Scale	1) -

E: experimental group; C: control group; RCT: randomised controlled trial; FEV₁%, forced expired volume in one second percent predicted; MBSR: Mindfulness based stress reduction; FR: functional relaxation; GI: guided imagery; PMR: progressive muscle relaxation; $\downarrow R_{aw}$: specific airway resistance; SBP: systolic blood pressure; FEV₁: forced expired volume in one second; PEF: peak expiratory flow rate; HR: heart rate; SF-36: Short Form-36; GP: General Practitioner; AQLQ: Asthma Quality of Life Questionnaire; HADS: Hospital Anxiety and Depression Scale; RIAS: Relaxation Inventory of Asthma Symptoms; BDI: Beck Depression Inventory; FVC: forced expired volume; VC: vital capacity; pCO₂: maximal partial pressure of carbon dioxide; RR: respiratory rate; ACQ: Asthma Control Questionnaire; PANAS: Positive affect and negative affect schedule; R: interrupted resistance; HRV: heart rate variability; EEG: electroencephalography; Z_{rs}: respiratory input impedance; RSA: respiratory sinus arrhythmia; CBT: cognitive behavioural therapy; ASC: Asthma symptom control; EQ-5D: EuroQol five-dimension; ABP: asthma bother profile; AMHCC: Asthma Multidimensional Health Locus of Control; KASE-AQ: Knowledge, Attitude and Self-efficacy Asthma Questionnaire; STAI: State Trait Anxiety Index; RIO: Respiratory Illness Opinion; BTS: British Thoracic Society; SIGN: Scottish Intercollegiate Guidelines Network; ICS: inhaled corticosteroids.

Table 2: Types of relaxation therapies

Study	Progressive muscle relaxation	Autogenic/self-hypnosis	Functional	Guided imagery	Breathing relaxation	Music therapy
Lahmann et al. [14]; [15]			Yes – one group	Yes – one group		
Holloway and West [17]					Yes	
Nickel et al. [16]	Yes					
Epstein et al. [18]				Yes		
Lehrer et al. [19]	Yes – one group					Yes – one group
Deter and Allert [20]		Yes – one group	Yes – one group			
Ewer and Stewart [21]		Yes				
Henry et al. [22]		Yes				
Erskine and Schonell [23]	Yes					

Table 3: Outcome assessments – outcomes used in two or more studies across each intervention category

	FEV ₁	FVC	PEFR	AQLQ	ACQ	ASC	Meds	BDI	STAI	SF-12	Asthma symptoms	Healthcare utilisation	School / work absence	HADS	KASE-AQ
Relaxation															
Lahmann et al. [14,15]	x														
Nickel et al. [16]	x		x												
Holloway & West [17]	x	x	x											x	
Epstein et al. [18]	x			x			x	x	x						
Lehrer et al. [19]						x	x					x			
Deber and Allen [20]		x					x					x			
Ewer & Stewart [21]	x	x	x				x				x				
Henry et al. [22]	x	x	x												
Erskine & Schonell [23]	x										x				
Mindfulness															
Pbert et al. [24]			x	x			x				x	x	x		
Biofeedback															
Meuret et al. [24]	x		x		x		x			x					
Lehrer et al. [25]	x	x	x				x				x				
Lehrer et al. [26]			x				x				x				
CBT															
Perry et al. [27]						x						x		x	
Grover et al. [28]			x	x		x								x	
Ross et al. [29]			x	x		x		x			x				
Pui et al. [30]			x	x		x									x
Sommaruga et al. [31]						x			x		x	x	x		
Complex															
Gamble et al. [32]	x			x	x		x					x		x	
Sun et al. [33]															x
Clark et al. [35]				x			x				x		x		
Kuijer et al. [36]										x					
Hockemeyer et al. [37]	x	x													

FEV₁: Forced expired volume in one second; FVC: Forced vital capacity; PEFR: peak expiratory flow rate; AQLQ: Asthma Quality of Life Questionnaire; ACQ: Asthma Control Questionnaire; ASC: Asthma Symptom Control; Meds: medication use; BDI: Beck Depression Inventory; STAI: State Trait Anxiety Inventory; SF-36: Short form-36; HADS: Hospital Anxiety and Depression Scale; KASE-AQ: Knowledge, Attitude and Self-efficacy Asthma Questionnaire

PRISMA 2009 Flow Diagram for Non-pharmacological interventions aimed at modifying health and behavioural outcomes for adults with asthma: a critical review

A refers to search results from 2007 Cochrane Review (6)
B refers to the current search from 2007 to May 2014

