Effective Health Care Program

Comparative Effectiveness Review
Number 71

Breathing Exercises and/or Retraining Techniques in the Treatment of Asthma: Comparative Effectiveness

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting Comparative Effectiveness Reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see the Web site http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input. CERs will be updated regularly.

We welcome comments about this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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Key Informants

Key Informants are the end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the Key Questions for research that will inform healthcare decisions. The EPC solicits input from Key Informants when developing questions for a systematic review or when identifying high-priority research gaps and future research needs. Key Informants are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the public review mechanism.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end users, individuals are invited to serve as Key Informants, and those who present with potential conflicts may be retained. The Task Order Officer and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Breathing Exercises and/or Retraining Techniques in the Treatment of Asthma: Comparative Effectiveness

Structured Abstract

Objectives. To examine evidence for whether breathing exercises and retraining techniques lead to improvements in asthma symptoms, reductions in asthma medication use, improved quality of life, or improved pulmonary function in asthma sufferers.

Data Sources. MEDLINE; PsycInfo; Embase; Cumulative Index to Nursing and Allied Health Literature; Physiotherapy Evidence Database; Cochrane Central Register of Controlled Trials; AltHealthWatch; Allied and Complementary Medicine; Manual, Alternative and Natural Therapy Index System; and Indian Medical Journals from 1990 through December 2011. Searches were supplemented with manual searching of reference lists and grey literature, including regulatory documents, conference abstracts, clinical trial registries, and Web sites of professional organizations.

Methods. Analytic framework, Key Questions, and review protocol were developed with input from Key Informants and technical experts. Two independent reviewers screened identified abstracts against predefined inclusion/exclusion criteria. Two investigators reviewed full-text articles and independently quality-rated those meeting inclusion criteria. Data from fair- and good-quality trials were abstracted into standardized forms and checked by another investigator. We summarized data qualitatively and, where possible, used random effects meta-analysis.

Results. We identified four types of interventions: hyperventilation reduction breathing techniques, yoga breathing techniques, inspiratory muscle training (IMT), and other nonhyperventilation reduction breathing techniques. We found the most robust body of evidence for hyperventilation reduction breathing techniques in adults, including the only large-scale trial (n=600, aged 14+). Hyperventilation reduction interventions (particularly those with 5 hours or more of patient contact) achieved medium to large improvements in asthma symptoms and reductions in reliever medication use of approximately 1.5 to 2.5 puffs per day, but did not improve pulmonary function. These trials also were more applicable to the U.S. setting than trials examining other interventions due to similarities in applicable treatment guidelines to U.S. guidelines and similar levels of development in the countries in which these studies were conducted, although applicability was still somewhat limited since none were conducted in the United States. Limited evidence suggested yoga breathing may improve pulmonary function in adults in addition to reducing asthma symptoms, but medication use was rarely reported and applicability to the United States was very low. Evidence for IMT and other breathing retraining techniques was limited to small, heterogeneous trials providing insufficient evidence to determine effectiveness. The only harms of breathing retraining techniques identified were minor annoyances associated with mouth-taping. Almost all trials were limited entirely or primarily to adults.

Conclusions. Behavioral approaches that include hyperventilation reduction techniques can improve asthma symptoms or reduce reliever medication use over 6 to 12 months in adults with poorly controlled asthma and have no known harmful effects. However, available evidence is

limited in its strength and applicability to the United States. Evidence supporting yoga breathing is weaker and applicability to the United States is very low.

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Executive Summary

Background

In 2009, an estimated 8.2 percent of Americans (9.6 percent of children and 7.7 percent of adults) had asthma, and the prevalence of asthma has increased substantially in recent years.[1,2] In 2007, asthma accounted for 456,000 hospitalizations and more than 3,447 deaths.[3]

The goal of asthma treatment is to achieve asthma control, as evidenced by normal or near normal pulmonary function, maintenance of normal activity levels, and minimal need for short-acting beta$_2$-agonist inhalers for "quick relief" of asthma symptoms ($\leq$ twice per week).[4] Persistent asthma treatment includes the use of long-term control medications (most commonly inhaled corticosteroids [ICS]) to reduce airway inflammation and quick-relief medications for acute exacerbations.

While the benefits of asthma treatment generally outweigh the potential risks, these medications can be associated with adverse effects.[5,6] Additionally, some asthma patients have concerns about asthma medications, and some patients would likely prefer to reduce their use of medication if alternative treatments were available.[7,8]

A number of nonpharmacologic methods for asthma management involve breathing retraining. Some of these, such as the Buteyko and Papworth methods, are predicated on the theory that asthma is related to hyperventilation. These treatments seek to reduce hyperventilation by encouraging shallow or slow nasal breathing, breath-holding at the end of expiration, and minimizing sighs and yawns and related breathing patterns that are characterized as "over-breathing."[9] The idea behind these treatments is that hyperventilation leads to a reduction in blood and alveolar carbon dioxide (CO_2), to which the airways respond by constricting to prevent further loss of CO_2. The evidence supporting the hyperventilation theory of the pathophysiology of asthma is mixed. People with asthma do appear to have lower end-tidal CO_2 levels (i.e., blood levels of CO_2 at the end of exhalation) than those without asthma.[10] A reduction in end-tidal CO_2 levels has been shown to increase airway resistance in people with asthma and a history of bronchial hyperresponsiveness to histamine, but not in matched controls without asthma.[11] Further, airway resistance decreases when hypercapnia (high level of CO_2 in the blood) is induced.[11] Another study, however, found that longer breath-holding time was associated with a reduction in end-tidal CO_2, which is counter to Buteyko's theory.[12]

Nonhyperventilation-targeted methods include yoga breathing techniques and other physical therapy methods. Treatment based on yoga theory generally encourages slowing and regularizing the breath by prolonging the expiratory phase, enhancing abdominal/diaphragmatic breathing, and imposing resistance on both inspiration and exhalation.[13] Other physical therapy methods may use elements consistent with these traditions to reduce the rate of breathing, or in other ways control the depth, flow, or timing of breathing. Physical therapists may also prescribe exercises that increase inspiratory and expiratory muscle strength. Devices such as breathing trainers or biofeedback may aid this training..

Twenty-seven percent of children with asthma report using complementary and alternative medicine approaches to manage their asthma, and this approach was usually a breathing technique of some kind.[14] The specific techniques used are unknown, however, and it appears the breathing exercises are not guided by a practitioner in most cases.

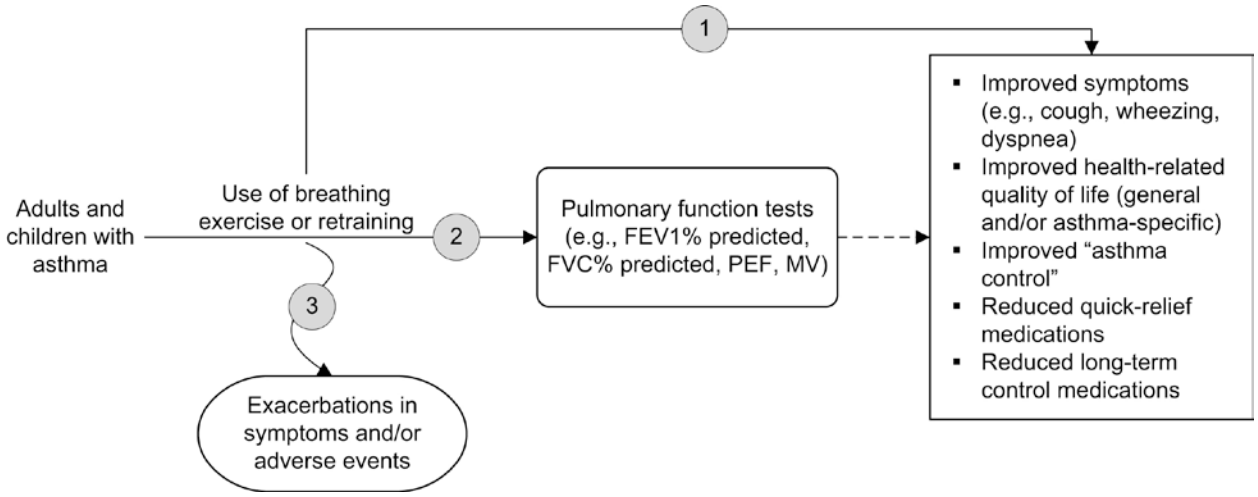
Objectives

The current review examines the effect of breathing retraining methods on asthma symptomatology, medication use, quality of life, and pulmonary function in both adults and children. We also examine adverse effects of these techniques. The analytic framework we developed to guide our review is shown in Figure A. The Key Questions for this review are as follows:

1. In adults and children 5 years of age and older with asthma, does the use of breathing exercises and/or retraining techniques[a] improve health outcomes, including symptoms (e.g., cough, wheezing, dyspnea); health-related quality of life (general and/or asthma-specific); acute asthma exacerbations; and reduced use of quick-relief medications or reduced use of long-term control medications, when compared with usual care and/or other breathing techniques alone or in combination with other intervention strategies?
    a. Does the efficacy and/or effectiveness of breathing techniques for asthma health outcomes differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?
    b. Does the efficacy and/or effectiveness of breathing techniques for asthma health outcomes differ according to variations in implementation (e.g., trainer experience) and/or nonbreathing components of the intervention (e.g., anxiety management)?
2. In adults and children 5 years of age and older with asthma, does the use of breathing exercises and/or retraining techniques improve pulmonary function or other similar intermediate outcomes when compared with usual care and/or other breathing techniques alone or in combination with other intervention strategies?
    a. Does the efficacy and/or effectiveness of breathing techniques for other asthma outcomes differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?
    b. Does the efficacy and/or effectiveness of breathing techniques for other asthma outcomes differ according to variations in implementation (e.g., trainer experience) and/or nonbreathing components of the intervention (e.g., anxiety management)?
3. What is the nature and frequency of serious adverse effects of treatment with breathing exercises and/or retraining techniques, including increased frequency of acute asthma exacerbations?
    a. Do the safety or adverse effects of treatment with breathing techniques differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?

[a]For example: the Buteyko breathing technique; inspiratory muscle training; breathing physical therapy, including paced and pursed lip breathing exercises; the Papworth method; biofeedback- and technology-assisted breathing retraining; and yoga breathing exercises.

Figure A. Analytic framework



FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MV: minute volume; PEF: peak expiratory flow

Methods

The Oregon Evidence-based Practice Center drafted a topic refinement document with proposed Key Questions after consulting with key informants. The public was invited to comment on the Key Questions during a 4-week period. After reviewing the public commentary, the Agency for Healthcare Research and Quality approved the final Key Questions and the review commenced.

We engaged a technical expert panel (TEP) that included five individuals who specialized in asthma management from the fields of Family Medicine, Community Health and Nursing, Psychology, Physical Therapy, and Pediatrics to provide input during the project. The TEP was established to ensure the scientific rigor, reliability, and methodological soundness of the research. The TEP provided comments on the methods protocol and provided input on substantive issues such as typical use of asthma medication, clinical value of outcomes, and clinical importance of effect sizes.

A research librarian performed comprehensive literature searches in MEDLINEPsycInfo; Embase; Cumulative Index to Nursing and Allied Health Literature (CINAHL); Physiotherapy Evidence Database (PEDro); Cochrane Central Register of Controlled Trials (CCRCT); AltHealthWatch; Allied and Complementary Medicine (AMED); Manual, Alternative and Natural Therapy Index System (MANTIS); and Indian Medical Journals (IndMED) from 1990 through December 2011. We supplemented these searches with manual searches of reference lists contained in all included articles, in relevant review articles, and on Web sites advocating the use of breathing techniques. The research librarian also performed the grey literature searches.

We included English-language trials of breathing retraining techniques that included participants aged 5 years or older, reported at 4 week post-baseline or later asthma symptoms, asthma medication use, quality of life, functioning, or pulmonary function. Included trials used a control group or comparison with another breathing training technique. For the question of harms, we would also have included large observational studies as well as trials if any were

identified. We had no restriction on geographic location and did not include trials that used relaxation techniques as a comparator.

Two independent reviewers assigned ratings of "good," "fair," or "poor" quality to each trial. Discrepancies were resolved by discussion or consultation with the larger review team. Trials given a final rating of "poor" quality were excluded. We used the following major elements to assign quality ratings:

- The presence of adequate randomization methods (use of computer-generated random number tables or other process considered truly random)
- Allocation concealment
- Similarity of groups at baseline
- The specification of eligibility criteria
- Reliable and valid measurement of baseline asthma status (optimal assessment included use of pulmonary function testing to confirm reversible component)
- Retention (retention of 90% or more overall was considered good; 60 to 89% was adequate, and less than 60% was considered a fatal flaw; differential attrition of 10 to 19 percentage points was considered potentially problematic and 20 percentage points or more was considered a fatal flaw)
- Time until followup (6 months or more was preferable, fewer than 6 weeks was potentially problematic)
- Equal, reliable, and valid measurements
- Blinding of outcome assessors
- Appropriate analyses (e.g., analyzing all participants in the treatment group to which they were initially assigned, use of conservative data substitution [preferably multiple imputation, imputation-based random effects regression or similar models, or use of baseline values] when retention was below 90 percent, adjustment for potential confounders, no use of statistical tests that were inappropriate for the type of data analyzed)

Generally, a good-quality study met all major criteria, although it was possible to get a "good" rating if an item was not reported (so could not be assessed) if the rest of the methods were judged to be "good." A fair-quality study did not meet all criteria, but was judged to have no flaw so serious that it invalidated its results. A poor-quality study contained a serious flaw in design, analysis, or execution, such as differential attrition as described above, or some other flaw judged to be so serious as to cast doubt on the validity of the results, such as large baseline group differences that were not or could not be adjusted for in an analysis, no information about followup and assumption of 100 percent followup was not tenable, or where insufficient information was provided to determine the risk of bias.

We abstracted data from all included studies with a quality rating of "fair" or "good" into a standard evidence table. One reviewer abstracted data, and a second reviewer checked these data. Authors were contacted to clarify methods and results, if needed. Discrepancies were resolved by discussion or consultation with other team members. Major elements abstracted included study location; study design; recruitment setting and approach; inclusion/exclusion criteria; demographic and health characteristics of the sample, including baseline asthma; description of the intervention and control arms; any cointervention components (e.g., advice about diet, relaxation training); compliance with treatment; sample retention; asthma outcomes, including symptoms, quality of life, medication use, and pulmonary function tests; and adverse events. To assess applicability, we used data abstracted on the population studied, the intervention and

comparator, the outcomes measured, settings, and timing of assessments to identify specific issues that may limit the applicability of individual studies or the body of evidence to U.S. health care settings, as recommended in the Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[15]

We summarized all included studies in narrative form as well as in summary tables that present the important features of the study populations, design, intervention, outcomes, and results. We divided comparisons into five groups based on the primary intervention focus and control group: (1) interventions focused on hyperventilation reduction breathing training versus control, (2) hyperventilation reduction versus nonhyperventilation reduction breathing training approaches, (3) yoga breathing methods versus control, (4) inspiratory muscle training (IMT) versus control, and (5) breathing approaches that did not focus on hyperventilation reduction versus control. We discuss outcomes separately for each of the five groups. We calculated a standardized effect size (Hedges g) to facilitate comparison of effect sizes across studies reporting different outcomes. Effect sizes larger than 0.80 were considered large effects.[16] We also used previously reported thresholds for clinically significant change in health status for commonly used questionnaires.[17] A change of 0.05 has been suggested for the Juniper Asthma Quality of Life Questionnaires.[18,19] For the St. George's Respiratory Questionnaire (SGRQ), the threshold for clinical significance is estimated to be four units, and patients whose treatment was judged to have been "very effective" showed an average change of 8.1 units.[17]

Random effects meta-analyses were conducted where there were at least three trials within a group. Meta-analyses were always conducted within groups because of the high degree of clinical and methodological heterogeneity across groups. We used Stata 11.2® for all effect size calculations and meta-analyses (Stata Corp., College Station, TX).

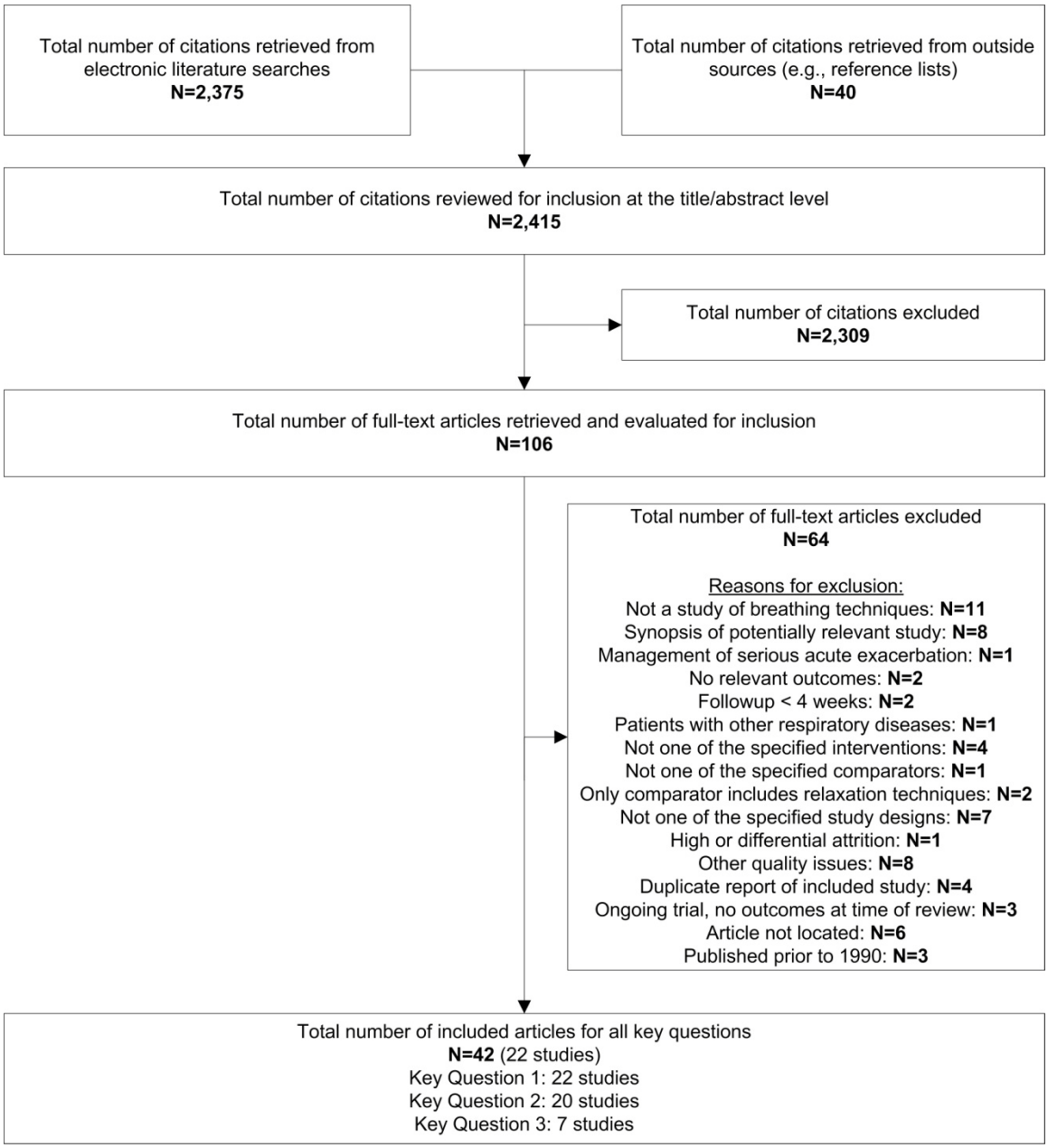
We graded the strength of evidence for primary outcomes using the standard process of the Evidence-based Practice Centers,[20] assigning grades in four domains: (1) risk of bias (low, medium, high), (2) consistency (consistent [no inconsistency present], inconsistent, unknown or not applicable), (3) directness (direct, indirect), and (4) precision (precise, imprecise). Risk of bias is the degree to which the included studies for a given outcome or comparison have a high likelihood of adequate protection against bias. Consistency refers to the degree to which reported effect sizes from included studies appear to have the same direction and magnitude of effect. We could not judge consistency when only one study was included. "Directness" relates to whether the evidence links the interventions directly to health outcomes. "Precision" refers to the degree of certainty surrounding an effect estimate with respect to a given outcome. We assigned an overall strength of evidence grade based on the total number of studies reporting an outcome and the ratings for the four domains for each key outcome. For each comparison, we used four basic grades (as described in the AHRQ Methods Guide): high, moderate, low, and insufficient.[20] We rated the evidence as insufficient when no studies were available for an outcome or comparison of interest, or the evidence was limited to small trials that were methodologically flawed and/or highly heterogeneous.

A full draft report was reviewed by experts and posted for public commentary from November 9, 2011, to December 5, 2011. We received comments, from either invited reviewers or through the public comment website, were compiled and addressed. A disposition of comments will be posted on the Effective Healthcare Program Web site 3 months after the release of the evidence report.

Results

The literature search yielded 2,415 citations. After reviewing abstracts, 106 articles were retained for possible inclusions and full text of the articles was examined (Figure B). After the screening of the full-text articles, 22 studies were judged to have met the inclusion criteria (published in 42 articles).[21-42] All included studies were randomized controlled trials (RCTs) except one, which was a randomized crossover trial.[22] We excluded the remaining 64 full-text articles. The primary reasons for exclusion were that a study was not on breathing techniques, a study did not provide primary data, a study did not use one of the specified study designs, and a study was rated as poor quality.

Figure B. Literature flow diagram



Researchers conducted all trials with individuals with symptomatic, mostly stable asthma. In some trials, researchers limited their population to individuals with a certain level of beta$_2$-agonist use, suggesting their asthma was not well controlled. Most trials confirmed reversibility of respiratory symptoms through pulmonary function testing. Trials primarily included adults; only one trial of IMT targeted children (ages 8 to 12 years)[36] and only four other trials included people younger than 16 years of age.[21,24,27,29]

Allocation was described as concealed in only 32 percent of the trials. Researchers almost always based their data about asthma symptoms, medication use, and quality of life on self-report, and only 41 percent of the trials reported that outcomes assessment were conducted blindly. Lack of blinding may be especially problematic for pulmonary function testing, which is effort-dependent and involves assessors coaching participants to get an optimal performance. Lack of blinding may also be problematic for self-reported outcomes, where social desirability could introduce bias. Most trials were small, with 68 percent including only 30 or fewer participants per treatment arm. Only one trial included more than 100 participants per treatment arm.[27] Trials were also inconsistent in the degree to which they ensured the sample was limited to people with asthma: 42 percent did not report the use of pulmonary function testing to confirm asthma diagnosis, and 39 percent did not describe excluding participants with other respiratory disorders or people at high risk for other respiratory disorders (e.g., smokers).

Outcome reporting was also variable. Researchers used a wide variety of specific measures within each of the general categories of outcomes (asthma symptoms, medication use, quality of life, and lung function testing), and in some trials, they failed to report important outcomes such as asthma symptomatology and reliever medication use, leaving open the possibility of selective reporting of outcomes.

Key Question 1

Hyperventilation Reduction Breathing Techniques Versus Control Group

Key Points:

- We found moderate evidence that hyperventilation reduction breathing technique interventions with 5 or more hours of direct instruction may reduce asthma symptoms and reliever medication use in adults, although evidence was limited to a fairly small number of trials, most of which were at moderate risk of bias due to factors such as small sample sizes, high or differential attrition, and lack of appropriate blinding.
- Evidence is low or insufficient that hyperventilation reduction training affects controlled medication use, quality of life, or functioning in adults and children.

Eight trials (n=1,088) tested a hyperventilation reduction technique versus a control and provided moderate evidence that hyperventilation reduction approaches may improve asthma symptoms and reduce reliever medication use, but do not affect pulmonary function (Table A).[22,23,25-28,30,42] Four trials were fairly intensive and involved at least 5 hours of comprehensive instruction and/or guided practice with the breathing technique.[23,25-27] The group included the only large-scale trial in the review,[27] which reported reductions in asthma symptoms and reliever medication use at a 6-month followup, but was hampered by lower retention in the control groups (82% and 73%) than the Buteyko group (90%). Three trials involved less intensive interventions (video-only or one to two hours of direct instruction), but still attempted somewhat comprehensive breathing retraining approaches.[28,30,42] One additional study examined only a

single aspect of the Buteyko breathing technique, mouth-taping at night, in a randomized crossover trial.[22]

Aside from the mouth-taping trial, interventions all encouraged nasal breathing and taught to identify and eliminate "overbreathing" or "dysfunctional" breathing using such means as shallow breathing, intermittent end-tidal breath-holding, or slow diaphragmatic breathing. All but one[42] explicitly reported encouraging daily home practice. Two trials included nonbreathing components covering stress management,[23,26] dietary restrictions,[23] and instruction to avoid oversleeping.[23]

All four of the most intensive and comprehensive interventions reported improvements in asthma symptoms at 6 to 12 months of followup.[23,25-27] The lower intensity trials generally did not find improvements in asthma symptoms after 1 to 6 months.[22,28,30,42] The largest trial showed the largest effect, with standardized mean difference (SMD) of -2.58 (95% CI, -2.86 to -2.29). Symptom ratings on a scale of 0 (no symptoms) to 3 (severe symptoms) dropped from an average of 2.2 at baseline for all groups to 0.7 in the Buteyko group, while the control groups slightly increased to 2.4 to 2.5.[27] Two other trials, both with fairly intensive interventions, reported standardized effect sizes greater than 1.2, which would generally be considered large.[25,26] In the trial by Holloway and colleagues, for example, the Papworth intervention group participants showed 18- to 21-point improvements on the 100-point SGRQ symptom subscale, compared with two-point improvements in the control group at 6 and 12 month followup.[26] This change is even greater than the change on the SGRQ seen in patients whose treatment was judged to be "very effective" in other research.[17]

Similarly, three[23,27,28] of the six trials[22,23,27,28,30,42] reporting reliever medication use showed reductions, including both of the higher intensity trials that reported this outcome.[23,27] Reductions were generally of about 1.5 to 2.5 puffs per day. Quality of life results were reported in six trials.[22,23,28,30,42 26] Two of them showed greater improvements with hyperventilation reduction breathing retraining than control groups[28,30] and two showed mixed results (i.e., results differed at different time points or scales within the same study).[26,42] Hyperventilation reduction approaches did not improve pulmonary function in the five trials that reported this outcome (pooled standardized estimate=0.18, 95% CI, 0.00 to 0.37, k=5, I^2=18.4%).[23,25-27,30]

We rated all trials as fair quality. Three of the four lower intensity trials had only 1 month of followup for some or all outcomes,[22,28,30] and only two of the RCTs randomized more than 50 participants per group.[27,30] Two suffered from fairly high attrition,[23,30] and four had greater attrition in the intervention group by at least 10 percentage points at one or more followups.[23,26,30,42] Allocation concealment was reported in only three trials,[25,27,30] and outcomes assessment was clearly blinded in only four trials.[22,23,25,27]

The applicability of these trials to U.S. practice was acceptable. While all trials were conducted in health care settings outside the United States, they were conducted in English-speaking, developed countries that used care guidelines consistent with U.S. treatment guidelines.

Hyperventilation Reduction Breathing Techniques Versus Other Breathing Techniques

Key Points:

- Hyperventilation reduction breathing techniques may be more likely to reduce reliever medication use in adults than other breathing techniques, but strength of evidence is low.
- Hyperventilation reduction training is no more likely to improve symptoms, controller medication use, or quality of life than other breathing techniques in adults, but strength of evidence is low.

Only medication outcomes showed group differences in the four RCTs (n=285) comparing the use of breathing techniques targeting hyperventilation reduction with other breathing techniques, and all favored hyperventilation reduction techniques (Table A).[21,23,24,29] The strength of the evidence was judged to be low. One trial showed very large reductions in reliever medication use among high medication users: participants in the hyperventilation group went from using approximately 9 to 10 puffs of beta$_2$-agonist per day to approximately one puff every other day, compared with less than one puff per day reduction in the abdominal breathing group.[21] No group differences were reported for asthma symptoms or quality of life. One trial showed reductions in asthma symptoms and medication use in both the hyperventilation reduction and the nonhyperventilation reduction breathing retraining.[29] This was the bestquality trial included in the review, and the only minor flaws were retention of less than 90 percent and small sample size.

Yoga Breathing Versus Control

Key Points:

- Yoga may improve asthma symptoms and quality of life in adults, but the strength of evidence for yoga is low due to concerns about the methodological quality of the trials.
- Evidence is insufficient to determine whether yoga can reduce asthma medication use in adults and children.

The five trials (n=360) that compared a yoga group with a control group generally showed improvements in asthma symptoms (Table A), but had a low strength of evidence due to methodological limitations of the included trials.[31-35] Four of the five trials reported reductions in asthma symptoms, although data could not be pooled due to lack of necessary data in several cases.[31,32,34,35] The largest effect size appeared to be found in one of the lower quality trials based in Indiacomparing yoga breathing exercises with meditation.[34] This trial reported a 64 percent reduction in symptoms in the intervention group at 12 weeks, compared with a 6 percent reduction in symptoms in the meditation group.

Another trial with a very intensive intervention reported a very large effect size at 2- and 4-week followup, but the effect was attenuated (yet still statistically significant) after 8 weeks.[35] In this trial and the U.S.-based trial of a comprehensive naturopathic intervention,[32] both the control and intervention groups showed improvements in a Juniper symptom subscale well beyond the level of clinical significance (i.e., improvement of 0.5 points).[17] Greater improvements were apparent, however, in those participating in the yoga interventions than those in the control groups.

Medication use was rarely reported, and evidence was considered insufficient to determine effectiveness. Quality of life was only reported in three of the trials, but did show improvement

in two of them (standardized pooled estimate for all three trials=0.66, 95% CI, 0.21 to 1.10, I^2=59.3%).[32,34,35] Strength of evidence was low. All trials were rated fair quality. Three of the trials were extremely intensive and were conducted in India. These trials had minimal applicability for the U.S. health care system because of differences in standard of care, narrow inclusion criteria, and cultural acceptance of yoga. Two of the India-based trials were among the group with fairly substantial methodological issues.[31,34] Two trials included substantial additional components beyond yoga breathing techniques, making isolation of the breathing component impossible.[32,35] The trial with the greatest applicability to the U.S. health care system showed no group differences on any measure.[33]

Inspiratory Muscle Training Versus Control

Key Points:

- Evidence is insufficient to draw conclusions about the effect of IMT on asthma symptoms, medication use, or quality of life in adults and children.

There was insufficient evidence to draw conclusions about the effect of IMT on asthma in five small trials (n=169) (Table A).[36-40] Three of the trials were conducted by a single investigator.[38-40] All trials involved 25 or fewer participants per group and varied substantially in populations, intensity, and approach. All but one[38] had substantial quality issues. These trials also had low applicability to the U.S. health care system.

Nonhyperventilation Reduction Breathing Techniques Versus Control

Key Points:

- Evidence is insufficient to draw conclusions about the effect of other nonhyperventilation reduction breathing techniques on asthma symptoms, medication use, or quality of life in adults and children.

Two trials (n=153) compared a nonhyperventilation reduction breathing technique with a control group and showed no group differences in asthma symptoms, medication use, or pulmonary function (Table A). One trial examined the use of biofeedback targeting heart rate variability (HRV), as well as training in pursed-lip abdominal breathing with prolonged exhalation.[41] This trial had three control groups: biofeedback targeting only HRV, placebo biofeedback involving placebo "subliminal suggestions designed to help asthma," and a waiting list. The other trial compared the use of a device to modify breathing to achieve an inspiration-to-expiration cycle of 1:2, with a sham device that did not modify breathing.[23] Both trials were rated as "fair" quality, and strength of evidence was insufficient.

Key Question 1a

Key Points:

- Evidence is insufficient to determine whether patient characteristics influence treatment effect in adults and children.

The trials included for this Key Question were heterogeneous on too many factors to be able to look across studies to assess the impact of population characteristics on effect size. However, three trials did report subgroup analyses examining differential effects of treatment by different characteristics.[22,30,41] Subgroup analyses were not described as being planned a priori, but were clinically logical subgroups the interventions may be expected to benefit differentially. The

United Kingdom trial comparing Papworth-style intervention with asthma education found that results were consistent between those who scored in the "disordered breathing" range on the Nijmegen questionnaire and those who did not.[30] Similarly, the trial of nighttime mouth-taping did not find larger effect among the subgroup of people who were rated as being "mouth breathers" at baseline.[22] Finally, the trial using biofeedback for breathing retraining found that there were no differences in response between those older than age 40 and though younger than 40.[41]

Key Question 1b

Key Points:

- Evidence is insufficient to determine whether the provider's certification and/or training influences effect size in hyperventilation reduction trials in adults and children.
- Exploratory analyses suggest that comprehensive approaches, especially those including additional, nonbreathing components may be more likely to show a benefit than approaches that isolate a single aspect of breathing in adults.
- Exploratory analyses suggest that intensity-matched control groups and control groups that involved either an alternate breathing approach or a technique to reduce autonomic arousal may reduce the likelihood of finding group differences in adults.

We could identify few components that had a clear impact on effect size. Among hyperventilation reduction trials, those involving certified or specially trained Buteyko practitioners[21,23,24,27] were more likely to show reductions in medication use that those that did not, however practitioner training did not appear to affect asthma symptoms results. All trials that reported improvements in quality of life did *not* use specially trained Buteyko practitioners.[26,28,30,42]

Looking across all trials, interventions that included components beyond breathing retraining[23,26,32,35] were likely to show a benefit more than interventions that isolated one aspect of breathing retraining (e.g., prolonged exhalation,[23,41] mouth-taping,[22] strengthening inspiratory muscles[38-40]). In addition, trials that matched intensity between treatment groups appeared less likely to reduce reliever medication use, although this effect was not seen for other outcomes. Finally, trials that compared breathing retraining with either another breathing technique or an intervention likely to induce relaxation or a reduced state of autonomic arousal were less likely to show group differences on asthma symptoms and quality of life when compared with control groups that did not include either of these components. These analyses were purely exploratory and did not account for effect size, so should be considered only as hypothesis generating and not as conclusive.

Key Question 2

Hyperventilation Reduction Breathing Techniques Versus Control Group

Key Points:

- There is moderate evidence that hyperventilation reduction breathing techniques do not improve lung function in adults.

Hyperventilation reduction techniques did not affect pulmonary function and strength of evidence was judged to be moderate (Table A). All seven trials reported one or more pulmonary function outcomes, primarily forced expiratory volume in 1 second (FEV_1), forced vital capacity

(FVC), and peak expiratory flow (PEF).[22,23,25-28,30] Group differences were only found in one trial and only in the comparison with one of the two control groups.[27] Absolute changes in the FEV_1 values in the intervention groups were small (e.g., improvements of 20 milliliters or less in FEV_1 or less than 2% improvement in the percent predicted of FEV_1). Three trials measured end-tidal CO_2, [25,26,30] which is a specific target of interventions to reduce hyperventilation, but only one found group differences at 4, 12, and 26 weeks.[25] Breathing rate was reduced in two of these trials, which suggests that participants did modify their breathing in the way they were instructed, but that modification did not always alter the CO_2 levels as hypothesized by the Buteyko method proponents.[25,26]

Hyperventilation Reduction Breathing Techniques Versus Other Breathing Techniques

Key Points:

- Hyperventilation reduction breathing techniques do not differ from other breathing techniques in terms of effect on pulmonary function in adults, but the evidence to support this is low.

All four trials in this group reported on change in FEV_1 (Table A).[21,23,24,29] No trial found group differences, and there was little change within any of the groups in any trials. Strength of evidence was judged to be low. Only one trial reported PEF, and this trial found no group differences.[21] Other measures of pulmonary function similarly showed no group differences, including end-tidal CO_2,[21,29] provocative dose of methacholine causing a 20 percent reduction in FEV_1,[23] and FVC.[29]

Yoga Breathing Versus Control

Key Points:

- Yoga breathing techniques may improve pulmonary function in adults, but the evidence to support this is low.

The strength of evidence on yoga improving pulmonary function was low. Neither of the U.S.-based trials improved pulmonary function outcomes,[32,33] despite the positive effects on other outcomes for the comprehensive naturopathic treatment program (Table A).[32] Intensive yoga training in India, however, resulted in substantial improvements in pulmonary function,[31,34,35] although the largest effect sizes were seen in the trials with the greatest methodological limitations.[31,34] The trial with the largest effect (and the greatest quality concerns) showed improvement in percent predicted FEV_1 of 12 percentage points, compared with only two percentage points in the control group.[34] The best quality trial of the three Indian trials reported improvements of 7.7 percentage points in the intervention group on percent predicted FEV_1,compared with a 2.6 percentage point reduction in the control group at 8-week followup.[35]

Inspiratory Muscle Training Versus Control

Key Points:

- Evidence is insufficient to determine whether IMT improves pulmonary function in adults and children.

Three of the four trials reporting pulmonary function found greater improvement in FEV_1 or PEF in participants who underwent IMT than those who did not (Table A).[36-38] These data, however, are best considered exploratory pilot trials and evidence insufficient, given their heterogeneity in methods and populations, small size, and quality issues.

Other Nonhyperventilation Reduction Techniques Versus Control

Key Points:

- Evidence is insufficient to determine whether other nonhyperventilation reduction techniques improve pulmonary function in adults and children.

Spirometry results did not change over time in either the trial of prolonged exhalation using a training device[23] or in any of the treatment groups in the biofeedback trial (Table A).[41]

Key Question 2a

Key Points:

- Evidence is insufficient to determine whether patient characteristics influence the effect of treatment on pulmonary function in adults or children.

The bestquality trial of yoga conducted in India showing large benefits of treatment reported that participants with exercise-sensitive asthma showed a greater improvement on FEV_1 than those whose asthma was not sensitive to exercise.[35] No other trials reported subgroup analyses for any pulmonary function outcomes, and there was no evidence that this subgroup analysis was planned a priori or that it was a clinically important subgroup expected to differentially benefit from this intervention.

Key Question 2b

Key Points:

- Evidence is insufficient to determine whether certification and/or training of the provider influences effect size in hyperventilation reduction trials.
- Exploratory analyses suggest that control groups that involved either an alternate breathing approach or a technique to reduce autonomic arousal may reduce the likelihood of finding group differences in adults.

Included trials provided little information about which intervention characteristics influence treatment effect on pulmonary function. Benefits were more likely to be seen if the control group did not involve breathing training of any kind or relaxation techniques (42% positive vs. 14% positive with breathing/relaxation comparison group). These data are preliminary, however, and are only valid for hypothesis generation and do not account for effect size.

Key Question 3

Key Points:

- Hyperventilation reduction breathing techniques do not appear to be associated with any harms in adults, other than minor annoyances associated with mouth-taping at night, but the evidence to support this is low.
- Yoga breathing techniques do not appear to be associated with any harms in adults, but the evidence to support this is low.
- There was no evidence on harms associated with IMT or other nonhyperventilation reduction approaches in adults or children.

Breathing retraining techniques appear unlikely to cause harm. Seven trials reported on adverse events, including five trials that examined a hyperventilation reduction approach compared with either a control or another breathing retraining approach.[22,24,26,28,29,32,33] The trial of mouth-taping reported some minor adverse events such as causing sore lips, causing a feeling of suffocation, or disturbing sleep. All other trials reported either no adverse events or no adverse events judged to be related to the breathing retraining.

Key Question 3a

Key Points:

- There was no evidence regarding whether patient characteristics influenced the likelihood of experience harm from any treatment included in the review in adults or children.

No trials examined harms of treatment within subgroups or compared subgroups on likelihood of harms.

Table A. Strength of evidence

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: asthma symptoms (global symptom severity or control, specific symptoms, exacerbations)	Hyperventilation reduction breathing technique vs. control	8	Medium	Consistent	Direct	Imprecise	Moderate	Effects in 7 comprehensive interventions ranged from no effect to large effect, 5 of 7 reported benefit; 1 narrowly focused trial showed no benefit for mouth-taping
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	4	Medium	Consistent	Direct	Imprecise	Low	No trial found a benefit of one approach over another; both groups improved in 2 trials, neither group improved in 2 trials
	Yoga breathing technique vs. control	5	Medium-High	Consistent	Direct	Imprecise	Low	4 of 5 trials report benefit, 3 with substantial quality concerns
	IMT vs. control	2	Medium-High	Consistent	Direct	Imprecise	Insufficient	2 small trials with different populations and methods, both show benefit, 1 with high risk of bias
	Non-hyperventilation reduction breathing technique vs. control	2	Medium	Consistent	Direct	Imprecise	Insufficient	No benefit in trials using biofeedback or breathing device, mixed results in 1 trial of physical therapy

Table A. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: medication use (reliever)	Hyperventilation reduction breathing technique vs. control	6	Medium	Consistent	Direct	Imprecise	Moderate	3 trials found reduction in reliever medication and the 3 lowest intensity trials did not.
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	3	Medium	Consistent	Direct	Imprecise	Low	Greater reduction in use with hyperventilation reduction breathing training in 2 of 3 cases, both groups improved in 1 trial
	Yoga breathing technique vs. control	2	Medium	Inconsistent	Direct	Imprecise	Insufficient	2 trials with substantial differences in intensity, location, and population, and reported contradictory results
	IMT vs. control	4	High	Inconsistent	Direct	Imprecise	Insufficient	4 small trials, 3 by 1 author, 3 with high risk of bias, no. 2 shows probable benefit
	Nonhyperventilation reduction breathing technique vs. control	1	Medium	N/A	Direct	Imprecise	Insufficient	No benefit of treatment

Table A. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: medication use (controller)	Hyperventilation reduction breathing technique vs. control	5	Medium	Inconsistent	Direct	Imprecise	Low	1 of 4 found large benefit, but raw data NR, remaining 3 found no group differences
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	4	Medium	Inconsistent	Direct	Imprecise	Low	No differences in effectiveness in 3 of 4 trials
	Yoga breathing technique vs. control	1	High	N/A	Direct	Imprecise	Insufficient	1 trial with high risk of bias showed benefit of yoga, type of medication not listed, just that it was used "to control dyspnoea"
	IMT vs. control	0	N/A	N/A	N/A	N/A	Insufficient	0 trials
	Nonhyperventilation reduction breathing technique vs. control	2	Medium	Consistent	Direct	Imprecise	Insufficient	No benefit of treatment in either trial
Key Question 1: quality of life	Hyperventilation reduction breathing technique vs. control	6	Medium	Inconsistent	Direct	Imprecise	Low	Benefit found in 2 of 6, results mixed in another 2 trials
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	4	Medium	Inconsistent	Direct	Imprecise	Low	No differences in effectiveness in all cases; both groups met threshold for clinical improvement in 2 trials, but change only statistically significant in 1 of these trials
	Yoga breathing technique vs. control	3	Medium-High	Consistent	Direct	Imprecise	Low	3 trials, large effect seen in trial with shortest followup. Pooled effect showed benefit.
	IMT vs. control	0	N/A	N/A	N/A	N/A	Insufficient	0 trials
	Nonhyperventilation reduction breathing technique vs. control	2	Medium	Inconsistent	Direct	Imprecise	Insufficient	2 trials with mixed results

Table A. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: Functioning or mental health	Hyperventilation reduction breathing technique vs. control	4	Medium	Consistent	Direct	Imprecise	Low	2 of 2 trials found small benefit for anxiety and depression, 2 of 2 trials found mixed results for functioning
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	1	Medium	N/A	Direct	Imprecise	Insufficient	1 study showing greater benefit of Buteyko breathing training than yoga breathing training via device on some functioning subscales
	Yoga breathing technique vs. control	1	High	N/A	Direct	Imprecise	Insufficient	1 trial with substantial non-yoga components showed benefit
	IMT vs. control	2	High	Consistent	Direct	Imprecise	Insufficient	2 trials with high risk of bias showing benefit, 1 in children, 1 in adults
	Nonhyperventilation reduction breathing technique vs. control	1	Medium	N/A	Direct	Imprecise	Insufficient	1 trial with mixed results, benefit primarily seen on role limitations due to physical problems, not other subscales

Table A. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 2: pulmonary function (FEV_1)	Hyperventilation reduction breathing technique vs. control	5	Medium	Consistent	Indirect	Imprecise	Moderate	Small or no benefit found in all trials
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	4	Medium	Consistent	Indirect	Imprecise	Low	No benefit for FEV_1 in any trials
	Yoga breathing technique vs. control	5	Medium-High	Consistent	Indirect	Imprecise	Low	3 of 5 show benefit of yoga, all 3 high-intensity interventions, 2 with large effects
	IMT vs. control	3	High	Inconsistent	Indirect	Imprecise	Insufficient	2 of 3 trials showed benefit, 2 with high risk of bias
	Nonhyperventilation reduction breathing technique vs. control	2	Medium	Consistent	Indirect	Imprecise	Insufficient	2 trials with different treatment approaches showing no benefit of treatment

Table A. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 2: pulmonary function (PEF)	Hyperventilation reduction breathing technique vs. control	3	Medium	Consistent	Indirect	Imprecise	Low	No benefit found in any trial
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	1	High	N/A	Indirect	Imprecise	Insufficient	1 trial showing no benefit in either group
	Yoga breathing technique vs. control	4	Medium-High	Consistent	Indirect	Imprecise	Low	3 of 4 show benefit of yoga, all 3 high-intensity interventions, 2 with large effects
	IMT vs. control	1	High	N/A	Indirect	Imprecise	Insufficient	1 trial with large effect, high risk of bias
	Nonhyperventilation reduction breathing technique vs. control	0	N/A	N/A	Indirect	N/A	Insufficient	0 trials

Table A. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 3: harms	Hyperventilation reduction breathing technique vs. control	3	Medium	Consistent	Direct	Imprecise	Low	None found adverse effects related to the intervention, one listed minor annoyances associated with mouth-taping
	Hyperventilation reduction breathing technique vs. nonhyperventilation reduction breathing technique	2	Medium	Consistent	Direct	Imprecise	Low	No adverse effects related to interventions
	Yoga breathing technique vs. control	2	Medium	Consistent	Direct	Imprecise	Low	No adverse effects related to yoga
	IMT vs. control	0	N/A	N/A	N/A	N/A	Insufficient	N/A
	Nonhyperventilation reduction breathing technique vs. control	0	N/A	N/A	N/A	N/A	Insufficient	N/A

FEV_1: forced expiratory volume in 1 second; IMT: inspiratory muscle training; N/A: not applicable; PEF: peak expiratory flow

Discussion

Summary of Results

The body of evidence suggests that selected intensive behavioral approaches that include breathing retraining or exercises may improve asthma symptoms or reduce reliever medication use in adults with poorly controlled asthma. However, the overall body of evidence primarily consisted of small, methodologically limited trials with widely heterogeneous samples, settings, and treatment approaches, few outcomes beyond 6 months, and inconsistent outcome reporting. Also, primary outcomes (symptom reduction and reliever medication use) were self-reported, making them susceptible to social desirability bias. Hyperventilation reduction techniques provided the strongest evidence for improvement in asthma symptoms and reliever medication use, including the only large-scale trial[27] and the applicability to U.S. health care systems was the best (although still limited, since no trials were conducted in the United States). Reductions in asthma symptoms (when they occurred) were likely clinically significant: standardized effect sizes were frequently greater than 0.80, which is considered a large effect, and scale scores for symptoms and quality of life often changed in an amount associated with clinically significant differences. Reductions in reliever medication use were generally in the 1.5 to 2.5 puffs per day range, which were also likely of clinical significance. This technique, however, did not improve pulmonary function.

Intensive yoga breathing training, on the other hand, did improve pulmonary function in addition to improving symptoms in three trials of intensive yoga breathing training conducted in India.[31,34,35] Quality issues in these trials, however, limit confidence in results and applicability to U.S. health care systems was very low.

Evidence for IMT and other breathing retraining techniques were limited to small, heterogeneous trials best characterized as pilot studies that did not provide sufficient evidence to conclude that they are effective. There were five IMT trials, three of which were conducted by the same researcher, and all but one had substantial methodological limitations. The two small nonhyperventilation reduction trials used very different approaches, and neither showed the intervention to be beneficial.

Specific Versus Nonspecific Effects

Despite the relatively positive results for hyperventilation reduction, improvements could not be definitively attributed to the use of the specific techniques. Subjective assessment of asthma symptoms is responsive to placebo interventions (e.g., sham acupuncture or a placebo inhaler), and participants in hyperventilation reduction interventions were instructed to delay use of reliever medication.[43] Rather than directly improving asthma, trials might have helped participants eliminate overuse of reliever medications, which is still an important positive outcome. Some trials attempted to control for the nonspecific effects of the treatment modality by including comparison groups that involved other, plausible breathing retraining. It is difficult to say, however, whether the treatment providers were comparable in their espousal of the effectiveness of their techniques.

A subset of articles in a Cochrane review on psychological treatments for asthma suggests that relaxation methods may reduce reliever medication use, and breathing retraining techniques may similarly benefit participants by reducing levels of anxiety and/or autonomic arousal.[44]

In summary, there are a number of possible explanations for the improvements in asthma outcomes reported with the use of hyperventilation reduction techniques. Lowered autonomic arousal through relaxation or reduced anxiety may improve asthma symptoms, deliberately delayed use of reliever medication may reduce reliever medication use, lifestyle changes (diet, stress management, nutritional supplements) may affect asthma control, bias in outcome measurement may affect any of outcomes, or the use of the specific breathing techniques may genuinely improve asthma symptoms and lead to reductions in medication use. It is very difficult to isolate critical treatment elements in complex interventions and use of some elements in isolation may underestimate their importance if the components are dependent on each other or interact with each other, or if individuals vary in the degree to which specific components are necessary or sufficient to gain improvements. Thus, critical intervention components often cannot be elucidated, particularly in a relatively poor and heterogeneous body of research.

Strength of Evidence

In most cases, the strength of evidence was insufficient or low. The evidence that hyperventilation reduction breathing techniques can reduce asthma symptoms and reliever medication use was judged moderate, as was evidence that hyperventilation reduction approaches are unlikely to improve pulmonary function.

Applicability

The trials in this review generally had low applicability to U.S. health care, primarily due to the settings in which the trials took place as well as other factors. Only three trials were conducted in the United States.[32,33,41] Trials of hyperventilation reduction techniques had the best applicability, being primarily conducted in health care settings in the United Kingdom and Australia. Guidelines governing the United Kingdom's[45] and the United States'[4] providers are generally consistent, so treatment of asthma is likely similar, although standards of care may still differ slightly and availability of hyperventilation reduction practitioners may also differ. Results were primarily limited to 6 months or less, so applicability is limited to short-term outcomes. However, given the evidence supporting a beneficial effect of hyperventilation reduction training on reliever medication use, in particular, patients with poorly controlled asthma who are motivated to use complementary and alternative methods to reduce their use of medication and avoid overuse of reliever medications may be good candidates to try these techniques, if they can find a practitioner with the appropriate training. There are approximately 50 certified Buteyko practitioners in the United States, practicing in at least 21 states. Most practitioners were located in complementary and alternative medicine settings. Some trials showed a benefit of treatment related methods that were not described as "Buteyko," specifically, conducted by respiratory therapists who were not Buteyko practitioners but had special training in hyperventilation reduction methods. Even among Buteyko practitioners, however, there is disagreement as to what constitutes necessary and sufficient training, so some certified practitioners likely would not be universally recognized as having the appropriate training.

The yoga and IMT trials had particularly low applicability, as these trials were conducted primarily in India, Brazil, South Africa, and Israel, which are countries with substantial cultural and/or economic differences from the United States, where standards of usual asthma care may differ, and where the availability of practitioners may also differ. Some yoga and IMT trials were even further limited in their applicability to the general U.S. population by limiting samples to males[31] or females only,[39] vegetarians within a fairly narrow age range,[31] people with 6 months

of yoga experience and not using medications,[34] and children with untreated asthma.[36] In some of these trials, there was some evidence that the standard of care was likely different from the current U.S. standard of care due to nonuse of controller medications[31,34] or poor success in managing asthma.[36]

Evidence was primarily applicable to adults; only a single trial of IMT targeted children (ages 8 to 12 years),[36] and only four other trials included people younger than 16 years of age, all addressing hyperventilation reduction training.[21,24,27,29] However, it is unlikely that many teens were included in these trials since, where it was reported, the average participant age was in the forties in these studies. Subgroup analyses of teens and/or emerging adults were not reported.

Clinical Implications

One goal of National Asthma Education and Prevention Program (NAEPP)-consistent treatment is for people with asthma to require theuse ofreliever medications no more than twice per week. Participants in the hyperventilation reduction trials were on average using relievers more frequently than twice per week at baseline, generally averaging about two puffs per day or more. While there are flaws in this research, participants generally reduced reliever medication to a level consistent with NAEPP guidelines, at least in the short term. This was achieved without increases in asthma symptoms, exacerbations, or declines in lung function. For people whose asthma is not well controlled, hyperventilation reduction techniques may provide a low-risk approach to achieve better control and avoid overuse of reliever medications. Participants in the trials were admonished only to reduce the use of controller medications in consultation with their medical providers, and this is a very important safety consideration for all users of these techniques. Inflammation may increase with reduction in controlled medications without the patient realizing it, and lead to longer term exacerbations. Hyperventilation reduction techniques may be a useful asthma management tool, along with medication and other components such as environmental controls, symptom monitoring, and a plan for handling exacerbations.

The body of evidence for yoga is smaller and at higher risk of bias than the evidence for hyperventilation reduction techniques, but there is limited evidence suggesting that intensive yoga training may reduce asthma symptoms and improve lung function. Patients who would like to undertake intensive training need not be discouraged, but again should not change their use of asthma medication without consulting with their medical provider.

Limitations

There were several limitations and potential limitations to our review, both in our approach to the review and in the evidence base. In terms of our approach, potential limitations include the fact that we did not include non-English publications, that we excluded “poor-quality” publications, that we excluded trials that used relaxation training as a comparison group, that we relied on personal communication with authors for some data, and that we were unable to locate seven publications that could possibly have been eligible for inclusion in the review.

The evidence was limited in a number of ways. There were no trials rated as “good” quality and a number of trials could barely be considered “fair” quality. There was only one trial that could be considered large, and more than half of the trials included 25 or fewer participants per treatment group. Outcome reporting was very heterogeneous and inconsistent, with important outcomes missing in many trials, and outcomes assessment was not consistently blinded. In addition, there was little consistency of asthma-related terms used in these trials, and terms were sometimes used vaguely or differently, making it difficult to characterize interventions.

Strengths

The methodological limitations are counterbalanced by some strengths of our report, including extensive grey-literature searching, examination of abstracts of non-English publications, and efforts to contact authors to include all possible eligible English-language trials. These measures were undertaken to limit the effects of publication bias. Other strengths include extensive input from experts during protocol development, rigorous adherence to inclusion/exclusion rules, and conservative use of meta-analysis.

Future Research

Additional evidence would improve our understanding for all intervention types. Future trials should detail breathing retraining techniques, as described by Bruton,[46] and these trials should include asthma symptoms outcomes, reliever medication use, quality of life, and pulmonary function at minimum. In addition, controller medication use should always be described. Best practices regarding randomization, blinding, and followup are also crucial to any further research in this area. For hyperventilation reduction techniques, top priorities for future research include replication of results of the large, good-quality trial with intensity-matched comparator, trials that attempt to isolate the necessity or efficacy of specific components of treatment, and trials focused on hyperventilation reduction techniques in children. A well-designed and executed replication of a high-intensity yoga breathing approach in the United States, without additional nonyoga components would be an important next step for the use of yoga in asthma.

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Introduction

Condition Definition

Asthma is a chronic disorder of the airways characterized by the complex and variable interaction of underlying inflammation, bronchial hyper-responsiveness, and airway obstruction.[1] Asthma's principal symptoms result primarily from bronchoconstriction and a resulting reduction in airflow. These symptoms include shortness of breath, cough, wheezing, and chest pain or tightness. The associated reduction in airflow is usually reversible spontaneously or with treatment.[1] The specific clinical manifestations and severity of asthma can vary among and within susceptible individuals. Asthma further varies in its chronicity, cellular pathophysiology, triggers, and responsiveness to medication.

Prevalence and Disease Burden

In 2009, the estimated prevalence of asthma in the United States was 8.2 percent, representing 24.6 million adults and children. The prevalence was 9.6 percent among children and 7.7 percent among adults.[2]

The prevalence of asthma has increased substantially during the past 30 years. While it is difficult to compare exact prevalence figures over this period due to changes in surveillance methods, it appears that the prevalence has roughly doubled in most age, sex, and race subgroups.[3] Asthma is also more common among people of certain ethnic and racial groups, with Puerto Ricans, African Americans, American Indians, and Alaska Natives having the highest prevalence rates.[4] In addition, the prevalence of asthma is highest among people of low socioeconomic status.[4]

When poorly controlled, asthma is associated with increased health care use, decreased quality of life, and significant activity limitations.[5,6] In 2007, asthma accounted for 456,000 hospitalizations and 3,447 deaths in the United States.[2] The morbidity associated with asthma adds to the costs incurred by both patients and health care organizations. In the United States, the projected annual cost (direct and indirect) of asthma in 2010 was estimated to be over $20 billion.[3]

Etiology and Natural History of Asthma

Our knowledge of the pathogenesis of asthma has evolved over the past 25 years from a primary focus on bronchospasm to an understanding of the role of airway inflammation. We currently describe these processes along a continuum that includes severe persistent disease resulting from airway remodeling due to chronic inflammation.[1] The onset of asthma can occur at any age and the disease may or may not persist.[7] While causes of childhood asthma are not well understood, we do know that children who develop asthma are more likely to have mothers with asthma, have increased airway resistance, have allergic sensitization by 3 years of age,[8] and are atopic (especially if the atopy is accompanied by high levels of exposure to perennial allergens early in life).[9] Although the definitive etiology or etiologies of adult-onset asthma have not been identified, it is estimated to be work-related in 11 to 50 percent of cases, depending on age and sex.[10]

The clinical course of asthma is largely unpredictable and is widely variable. The progression of asthma appears to vary in different age groups, as measured by pulmonary function.[1] In

children, deficits in pulmonary function growth appear to generally occur by the age of 6 years, and primarily in those whose symptoms began before the age of 3 years. In adults, there is evidence that pulmonary function may progressively decline, but the implications of this decline for the development of fixed airflow obstruction are not understood.[1]

Diagnosis and Assessment of Asthma

Diagnosing and assessing asthma requires clinical judgment based on medical history, physical examination, and pulmonary function testing.[1] Guidelines from an expert panel recommend that before establishing a diagnosis of asthma a clinician should determine that: (a) episodic symptoms of airflow obstruction or airway hyperresponsiveness are present; (b) airflow obstruction is at least partially reversible; and (c) alternate diagnoses are excluded.[1] Because other diagnoses cannot be reliably excluded by medical history and physical examination, and because patients vary considerably in their ability to perceive of airflow obstruction, an objective assessment of pulmonary function is necessary for an asthma diagnosis. While peak expiratory flow (PEF) meters are useful for monitoring the disease, spirometry is more reliable and recommended for establishing the diagnosis.[1] Guidelines recommend assessing forced expiratory volume for 1 (FEV_1) or 6 seconds and/or forced vital capacity (FVC, the total volume of air that can be forcibly exhaled after maximal inhalation) before and after use of a short-acting bronchodilator. Maximal patient effort during spirometry testing is crucial for accurate assessment. A skilled technician who adheres to American Thoracic Society (ATS) performance guidelines is also important.[11]

Airway obstruction is considered reversible if there is an increase in FEV_1 of more than 200 milliliters and 12 percent from baseline after two to four puffs of albuterol. In patients who are not taking long-term control medications (e.g., inhaled corticosteroids [ICS]), an FEV_1 below 60 percent of predicted (based on age and sex) is categorized as "severe" asthma, 60 to 80 percent of predicted is "moderate," and above 80 percent is "mild."

Distinguishing severity of underlying disease from current control is important in characterizing asthma. Asthma severity is the intrinsic intensity of the disease. Asthma control is the degree to which symptoms and functional limitations are minimized (e.g., a person may have severe underlying disease that is well controlled). Severity is assessed before introduction of long-term controller medications such as inhaled corticosteroids. Once therapy is initiated, asthma control is monitored and treatment modifications are based on degree of control.

Treatment of Asthma

As our understanding of the critical role played by inflammation in the pathophysiology has increased, so has the number of therapies targeting this inflammatory process. In addition to short-acting $beta_2$-agonist (SABA) drugs for quick-relief of acute exacerbations, pharmacologic treatment of persistent asthma often entails the use of anti-inflammatory medications for long-term control — most commonly ICS, but also including drugs that target various inflammatory cell types, such as leukotriene modifiers (see Appendix A for an overview of medications recommended for use in treating asthma).[1]

The goal of treatment is to achieve asthma control, as evidenced by normal or near normal pulmonary function, maintenance of normal activity levels, and minimal need for SABA inhalers for "quick-relief" of asthma symptoms ($\leq$ twice per week).[1] Asthma treatment is often multifocal and tailored to the individual's characteristics, including disease pattern and severity, treatment response, and side effects. Current U.S. guidelines recommend four essential components for

effective asthma management: assessing and monitoring the disease, self-management education, controlling environmental and co-morbid conditions, and adequate pharmacologic therapy. Although treatment seeks to improve asthma control, treatment does not appear to affect the underlying severity of the asthma, at least in adults.[1]

Despite clinical practice guidance on self-management education and medication use, many patients with asthma appear to adhere poorly to such recommendations.[12,13] Studies have found that adults with asthma and the parents of children with asthma have concerns about regular use of medication, including fears of long-term dependence and side effects associated with inhaled and oral steroids.[14,15] While side effects for ICS are rare, these medications can be associated with a number of possible side effects, including slowed growth in children. However, effects on growth are small, appear to be seen primarily in the first months of treatment, are generally nonprogressive, and may be reversible. On the other hand, poorly controlled asthma can also delay growth in children.

At high doses and with long-term use, ICS use can be associated with adrenal suppression, osteoporosis in adults, skin thinning/easy bruising, and possibly the increased risk of developing cataracts in adults and glaucoma in adults with a family history of glaucoma.[1] In addition, according to the product information insert for QVAR® 40 micrograms (mcg) and 80 mcg, long-term effects of chronic ICS use are still not fully known, including effects on the immunologic processes in the mouth, pharynx, trachea, and lung.[16] Possible side effects of SABAs include headache, musculoskeletal pain, tachycardia, and other cardiovascular effects. In addition, there have been rare reports of serious, even fatal, asthma exacerbations associated with overuse of SABAs, particularly older versions of these medications (isoproterenol and fenoterol).[17]

A variety of complementary and/or alternative therapies have been advocated for the control of asthma given its spectrum of severity and causes as well as concerns about long-term medication use. These include breathing exercises, herbal remedies, homeopathy, acupuncture, relaxation therapies, and manual therapy (e.g., chiropractic techniques, massage). Breathing retraining exercises are among the complementary and alternative treatments most frequently used by people with asthma, and are purported to have virtually no adverse effects.[14,18,19] Breathing retraining is generally assumed to be complementary to guideline-based care, with the primary goals of improving asthma control and reducing the use of medications, particularly SABAs. Some specific breathing retraining approaches include the Buteyko breathing technique, yoga-based approaches, and other physical therapy techniques. In the United States, 27 percent of children with asthma reported some use of complementary and alternative medicine (CAM).[20] Among those, 58 percent reporting using some sort of breathing technique to help manage asthma, which was the most common type of CAM used. The study did not provide more detail regarding the specific type of breathing exercises used, and since only 8.4 percent of the children reported using practitioner-based CAM, likely most of the children using these techniques are not involved in rigorous or supervised breathing training.

Buteyko and Other Methods Based on Hyperventilation Reduction and Carbon Dioxide Regulation

The Buteyko breathing technique, developed by Konstantin Buteyko, is based on the theory that chronic hyperventilation in people with asthma leads to decreased carbon dioxide (CO_2) in the blood (hypocapnia), which constricts the airways. Buteyko developed a breathing method to increase the amount of CO_2 in the blood. This method involves controlled shallow breathing through the nose only, with breath-holding at the end of the exhalation. The length of time a

person is able to hold their breath at the end of an exhalation indicates the extent of hyperventilation, with longer periods of breath-holding indicating less hyperventilation.[21] Buteyko practitioners also train users to eliminate or minimize sighs, yawns, and gasps, which they consider "overbreathing." This method requires commitment on the part of users, since it usually takes considerable practice to master. When experiencing asthma symptoms, Buteyko users are encouraged to utilize breathing the technique for 5 to 10 minutes before using a bronchodilator to relieve symptoms. Buteyko practitioners encourage the use of porous tape to hold the lips together at night for those who tend to breathe through their mouths at night. The British Thoracic Society (BTS) guideline developers concluded that evidence supported consideration for the use of the Buteyko breathing technique to control the symptoms of asthma.[22]

Other clinicians have used approaches not specifically identified as Buteyko breathing training, but are consistent with Buteyko methods and/or integrate Buteyko methods. For example, the Papworth method involves instruction in slow (e.g., 8 breaths per minute), steady diaphragmatic breathing through the nose, with a pause at the end of each breath and elimination of sighs and other overbreathing. In addition, they work with patients to teach them to use relaxed, controlled breathing while talking and engaging in daily activities.[23,24]

The evidence supporting the hyperventilation theory of the pathophysiology of asthma is mixed. One study showed that people with asthma have lower end-tidal CO_2 levels (i.e., blood levels of CO_2 at the end of exhalation) than those without asthma.[25] Research by ven den Elshout and colleaguesappears consistent with Buteyko's theory by demonstrating that inducing a reduction in end-tidal CO_2 levels increased airway resistance in people with asthma and a history of bronchial hyperresponsiveness to histamine, but it did not change airway resistance in matched controls without asthma.[26] When hypercapnia (high level of CO_2 in the blood) was induced in the same study, airway resistance decreased in both patients with asthma and controls.[26] Another study, however, found that longer breath-holding time was associated with a reduction in end-tidal CO_2, which is counter to Buteyko's theory.[27]

Yoga-Based Approaches

The breathing techniques used in yoga, known as pranayama, are integral to virtually all yoga traditions. While these traditions vary in the specific use of breathing techniques, they generally involve slowing and regularizing the breath by prolonging the expiratory phase, enhancing abdominal/diaphragmatic breathing, and imposing resistance to both inspiration and exhalation.[28] The prolonged expiratory phase is assumed to promote mental and physical relaxation. Increased respiratory resistance, which can be achieved through manually blocking one nostril or by using the tongue and other mouth muscles to narrow breathing passages, is thought to promote efficient alveolar gas exchange and, in asthma patients, to help reduce hyperinflation of the lungs. Like hyperventilation reduction methods, yoga practitioners usually advocate the use nasal breathing rather than mouth breathing, and both approaches appear to have the effect of slowing the passage of air in and out of the lungs. It is unclear if the two approaches have similar physiologic effects.

Physical Therapy Techniques and Inspiratory Muscle Training

Slow-paced respiration provides users with an external stimulus to encourage a specific (slow) breathing rate. Slower breathing rates have been associated with lower stress response (as measured by skin resistance, finger pulse volume, and self-reported anxiety in the face of

anticipated stressors). Slow-paced respiration is typically combined with abdominal breathing to reduce panic attacks, and thus may be of help to the extent that asthma is triggered by stress or anxiety.[29] Biofeedback has been used to indirectly target airway resistance by increasing heart rate variability (HRV), and has also been used to directly target airway resistance via the relaxation of the muscles used for breathing.[29] Biofeedback uses electronic monitoring devices to show a participant some kind of physiologic level (such as HRV or muscle tension) in order to teach him or her to control bodily functions that normally happen automatically. Training to increase HRV involves feedback to increase the amplitude of the heart rate oscillations with breathing.[30] Participants may be instructed in cognitive strategies and/or slow abdominal/diaphragmatic breathing as a means for increasing HRV,[31] though the specific mechanism of action is unknown.[30]

Another set of physical therapy techniques may be used to strengthen inspiratory and/or expiratory muscles to help reduce perception of dyspnea, aid in overcoming airway resistance, and avoiding hyperinflation due to insufficient expiratory strength.

Scope and Purpose

The original public nomination made by a Buteyko practitioner and physical therapist requested a review focused specifically on the effectiveness of the Buteyko method for reducing bronchodilator and inhaled steroid use and improving the health status of adults and children with asthma. After input from experts and consulting the literature, we expanded the topic to also address the breathing retraining approaches described above. Thus, the objective of this review is to synthesize the data on the effectiveness and comparative effectiveness of a variety of breathing retraining techniques in the management of asthma in adults and children 5 years of age or older.

Key Questions

Three systematically reviewed Key Questions are addressed in this report. These questions address the impact of breathing exercises on health outcomes and pulmonary function in addition to the harms related to breathing exercises in the treatment of asthma.

1. In adults and children 5 years of age and older with asthma, does the use of breathing exercises and/or retraining techniques[a] improve health outcomes, including: symptoms (e.g., cough, wheezing, dyspnea); health-related quality of life (general and/or asthma-specific); acute asthma exacerbations; reduced use of quick-relief medications or reduced use of long-term control medications, when compared with usual care and/or other breathing techniques alone or in combination with other intervention strategies?
    a. Does the efficacy and/or effectiveness of breathing techniques for asthma health outcomes differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?
    b. Does the efficacy and/or effectiveness of breathing techniques for asthma health outcomes differ according to variations in implementation (e.g., trainer

[a]For example: the Buteyko breathing technique; inspiratory muscle training (IMT); breathing physical therapy including paced and pursed lip breathing exercises; the Papworth method; biofeedback- and technology-assisted breathing retraining; and yoga breathing exercises.

experience) and/or nonbreathing components of the intervention (e.g., anxiety management)?

2. In adults and children 5 years of age and older with asthma, does the use of breathing exercises and/or retraining techniques improve pulmonary function or other similar intermediate outcomes when compared with usual care and/or other breathing techniques alone or in combination with other intervention strategies?
    a. Does the efficacy and/or effectiveness of breathing techniques for other asthma outcomes differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?
    b. Does the efficacy and/or effectiveness of breathing techniques for other asthma outcomes differ according to variations in implementation (e.g., trainer experience) and/or nonbreathing components of the intervention (e.g., anxiety management)?
3. What is the nature and frequency of serious adverse effects of treatment with breathing exercises and/or retraining techniques, including increased frequency of acute asthma exacerbations?
    a. Do the safety or adverse effects of treatment with breathing techniques differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?

Methods

The Agency for Healthcare Research and Quality (AHRQ) requested a Comparative Effectiveness Review on the effectiveness of breathing exercises and/or retraining for the treatment of asthma as part of its Effective Health Care (EHC) program. The Oregon Evidence-based Practice Center (EPC) established a team and a protocol to develop the evidence report.

Topic Development and Refinement

The topic for this report was nominated through a public process. The Scientific Resource Center (SRC) for the AHRQ Effective Health Care Program compiled information about this topic to evaluate its priority for a comparative effectiveness review. This information was evaluated and discussed by staff of the EHC and was approved for a full review.[32]

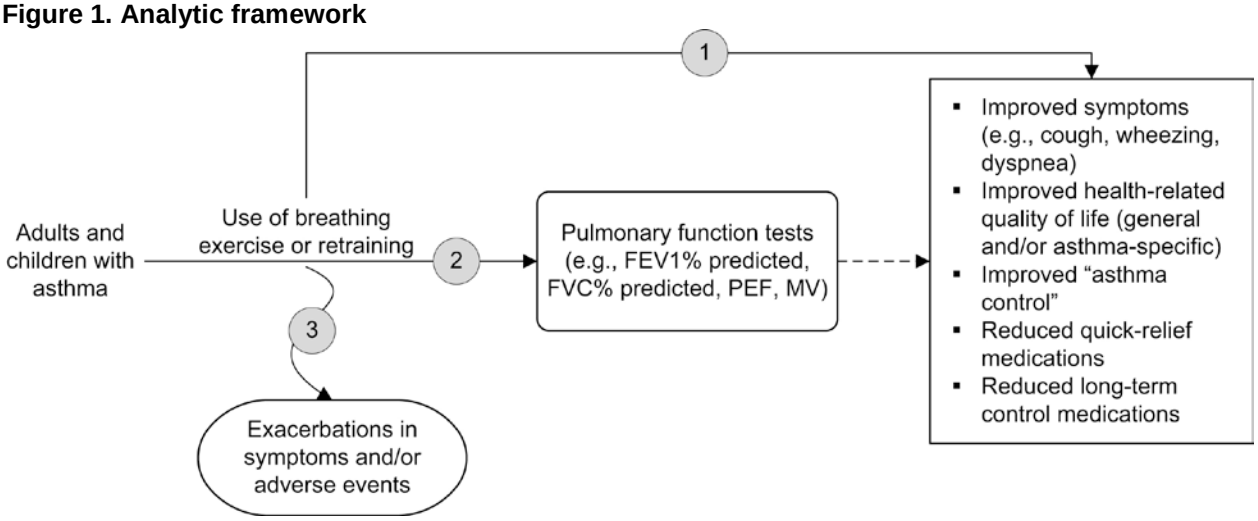
The Oregon EPC drafted a topic refinement document with proposed Key Questions after consulting with seven Key Informants. Key Informants included Western allopathic and alternative medical providers and representatives of patient advocacy groups. The alternative medical practitioners covered the areas of Buteyko breathing technique, yoga breathing techniques, and the Papworth breathing retraining method.

The Key Questions were posted on AHRQ's website for public comment in August and September of 2010 for 4 weeks and were revised as needed. We then drafted a protocol for the comparative effectiveness review and recruited a technical expert panel (TEP) to provide high-level content and methodological expertise throughout the review. The TEP was comprised of five individuals who specialize in asthma management from the fields of family medicine, community health and nursing, psychology, physical therapy, and pediatrics. The TEP was set up to ensure the scientific rigor, reliability, and methodological soundness of the research. The TEP provided comments on the methods protocol and provided input on substantive issues such as typical use of asthma medication, clinical value of outcomes, and clinical importance of effect sizes.

Analytic Framework

The analytic framework for evaluating the comparative effectiveness of breathing exercises and/or retraining for the treatment of asthma is shown in Figure 1. In general, the figure illustrates how the use of breathing exercises or retraining may result in intermediate outcomes (e.g., FEV_1 or PEF, and/or ultimate health outcomes (e.g., reduced symptom severity and improved quality of life). The figure also depicts the possibility of adverse events occurring after treatment. We did not systematically review the association between pulmonary function test results and asthma symptoms, along with other health outcomes.

Figure 1. Analytic framework



FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MV: minute volume; PEF: peak expiratory flow

Literature Search Strategy

A research librarian performed comprehensive literature searches in the following databases:

- MEDLINE accessed via PubMed
- PsycInfo
- EMBASE
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Physiotherapy Evidence Database (PEDro)
- Cochrane Central Register of Controlled Trials (CCRCT)
- AltHealthWatch
- Allied and Complementary Medicine (AMED)
- Manual, Alternative and Natural Therapy Index System (MANTIS)
- Indian Medical Journals (IndMED)

Appendix B outlines our search strategy for each database. These searches were used to locate relevant studies related to all three Key Questions. Searches were restricted to the time period of1990 to December 8, 2011. While we did not have translation services available to review non-English papers, we were able to find English-language abstracts or use electronic translation tools on non-English abstracts for all non-English articles that may have met inclusion criteria, based on the title of the article. Only two trials possibly appeared to meet our inclusion/exclusion criteria, based on the abstracts, but were not reviewed further because we did not have translation services available.[33,34] Titles and abstracts of these studies are presented in Appendix C.

In addition, because the Buteyko methods were developed in Russia, there may be relevant early research published only in Russian and not included on the databases we searched. Therefore, we searched Buteyko websites for reference to non-English studies that might meet our inclusion criteria.[35,36] One website listed 73 publications by Buteyko himself or his collaborators in Russian, and while it is possible that there was a trial listed among then, none included the word "trial" in the title and all appeared to be studies of pathophysiology, case series, or instructions in the use of the Buteyko method.[35]

Searches of these databases were supplemented with manual searching of reference lists contained in all included articles and in relevant review articles. We specifically examined reviews of asthma education programs for trials with any mention of breathing techniques for asthma management published during our search window (1990 to present).[37-42] Grey literature searches were also performed by the research librarian. For the purposes of this review, grey literature refers to any information that is not controlled by commercial publishing and included regulatory documents (e.g., U.S. Food and Drug Administration Medical and Statistical Reviews and Authorized Medicines for the European Union); clinical trial registry entries (e.g., ClinicalTrials.gov, the World Health Organization International Trials Registry Platform, and Current Controlled Trials Register); and conference abstracts (e.g., CSA's Conference Papers Index, Scopus conference papers, ProceedingsFirst, and PapersFirst). Upon receipt of the grey literature search results, we reviewed abstracts and/or full-text results according to the methods described below. We matched abstracts to any published studies and reviewed them in conjunction with the full text of these studies. In addition, a Scientific Information Packet (SIP) was requested from one relevant organization that produces materials and educational training for one intervention of relevance to this review (Buteyko Institute of Breathing and Health, Manuka, Australia). However, we did not receive a SIP.

The results of our searches were downloaded and imported into version 11.0.1 of Reference Manager® (Thomson Reuters, New York, NY), a bibliographic management database. We manually scanned for duplicates. Reference Manager was used to track the search results at the levels of title/abstract review and article inclusion/exclusion.

Process for Study Selection

A two-step process was used for study selection. First, two members of the research team independently reviewed each title and abstract (if available) to determine if an article met the broad inclusion/exclusion criteria for study design, population, and intervention (Table 1). Each title/abstract was coded as: potentially included, excluded, or background. Next, we retrieved full-text articles for all potentially included studies, including those that were questionable or unclear at the abstract stage. Two reviewers independently assessed each full-text article using a standard form that detailed the predetermined inclusion and exclusion criteria. Disagreements were resolved through discussion.

Table 1. Inclusion and exclusion criteria

Category	Inclusion Criteria	Exclusion Criteria
Population	• Humans, all races, ethnicities, cultural groups • Adults aged ≥ 18 years with asthma of any type and severity, symptomatic or using asthma medication • Children ≥ 5 years with asthma of any type and severity, symptomatic or using asthma medication • Asthma diagnosis by medical practitioner (self-report of physician diagnosis acceptable)	• Children < 5 years • Individuals with comorbid chronic obstructive pulmonary disease, emphysema, chronic bronchitis or any other chronic disease that affects pulmonary function (e.g., heart disease, thyroid disease)
Interventions	Interventions in which breathing retraining/exercises are a primary component. Such exercises include: • Buteyko breathing technique (including those focused only on mouth taping • Inspiratory muscle training • Expiratory muscle training • Diaphragmatic breathing techniques • Breathing physical therapy (e.g., paced and pursed lip breathing exercises) • Papworth method • Biofeedback- and other technology-assisted breathing retraining • Yoga breathing exercises • Other breathing exercises	• Interventions that do not focus primarily on asthma • Interventions whereby breathing techniques are not a primary treatment • In-hospital management of acute exacerbations • Physical fitness training • Alexander Technique
Comparator	• Other breathing techniques alone or in combination with other intervention strategies • Usual care as standard for the setting (e.g., asthma self-management education, control of environmental factors, pharmacologic therapy) • Technology-supported placebo device • Attention controls (receiving similar time and attention as the intervention group on another topic unrelated to breathing retraining) • Wait-list controls • No treatment offered (outside care is assumed)	• Other alternative or complementary methods that are potentially efficacious for asthma and are not focused on breathing retraining [e.g., relaxation techniques (e.g., progressive muscle relaxation), acupuncture, herbal therapies, chiropractic] • Physical activity or exercise

Table 1. Inclusion and exclusion criteria (continued)

Category	Inclusion Criteria	Exclusion Criteria
Outcomes	Key Question 1: • Symptoms (e.g., cough, wheezing, dyspnea, nocturnal symptoms) • Health-related quality of life (general and/or asthma-specific) • Asthma control (e.g., acute exacerbations, hospitalizations for asthma, urgent or emergent clinic or hospital visits for asthma (including unscheduled doctor visits), nocturnal control, missed school/work, daily activity tolerance or restrictions) • Exercise tolerance (e.g., 6-minute walk, shuttle run) • Quick-relief medication use (e.g., short-acting beta$_2$-agonists, anticholinergics) • Long-term control medications (e.g., inhaled corticosteroids, long-acting immunomodulators) Key Question 2: • Pulmonary function tests: FEV_1 % predicted; FVC % predicted; PEF; MV, exhaled nitric oxide, methylcholine challenge and/or responsiveness, sputum eosinophil markers of inflammation, other measures of CO_2, other spirometry measures Key Question 3: • Increased asthma symptoms or acute asthma exacerbations • Adverse reactions to therapies • Reduction in/negative influences on quality of life	• Costs • During or post-exercise breathlessness or pulmonary function (considered too highly correlated with fitness)
Time period	1990 to present	Before 1990
Setting	All settings	Not applicable
Study geography	All locations	
Publication language	English	All other languages

Table 1. Inclusion and exclusion criteria (continued)

Category	Inclusion Criteria	Exclusion Criteria
Study design	Key Questions 1, 2 and 3: • Randomized controlled trials • Controlled clinical trials • Comparative observational studies (prospective and retrospective cohort studies; case-control studies); including only those controlling for medication use and health care use with long-term (≥ 6 month) outcomes, with some validity of case ascertainment or in those with broadly representative samples Key Questions 1a and 2a: • Randomized controlled trials • Controlled clinical trials • Comparative observational studies (prospective and retrospective cohort studies; case-control studies); including cohort of patients who have undergone breathing retraining, reliably divided into subgroups of interest, adequately powered to detect differences in outcomes between groups, and adequately controlling for confounders Key Questions 1b and 2b: • Randomized controlled trials • Controlled clinical trials	Key Questions 1, 2 and 3: • Editorials, letters, nonsystematic literature reviews • Noncomparative observational studies (e.g., case-series, case reports, cross-sectional studies) • Comparative observations trials not meeting all inclusion criteria Key Questions 1a and 2a: • Editorials, letters, nonsystematic literature reviews • Noncomparative observational studies (e.g., case-series, case reports, cross-sectional studies) • Comparative observations trials not meeting all inclusion criteria Key Questions 1b and 2b: • Editorials, letters, nonsystematic literature reviews • Observational studies
Intervention duration	All	Not applicable
Follow-up duration	≥ 4 weeks post intervention	< 4 weeks post intervention
Sample size	N ≥ 10	N < 10

CO_2: carbon dioxide; FEV_1: forced expiratory flow in 1 second; FVC: forced vital capacity; MV: minute volume; PEF: peak expiratory flow

Data Abstraction and Data Management

We abstracted data from all included studies with a quality rating of "fair" or "good" (see section below on individual study quality assessment) into a standard evidence table. One investigator abstracted the data and a second checked the data. Discrepancies regarding data abstraction were resolved by re-review, discussion, and comments from others. The following information was obtained from each study, where available: author identification; year of publication; study location; study design; recruitment setting and approach; inclusion/exclusion criteria; demographic and health characteristics of the sample including baseline asthma; description of the intervention and control arms; any co-intervention components (e.g., advise about diet, relaxation training); compliance with treatment; and sample retention. Outcomes included: asthma symptoms; medication and health care use; quality of life and functioning; pulmonary function; and adverse outcomes. We also recorded the instruments used to measure each outcome, where available. We contacted authors of included studies if clarification of methods (e.g., randomization methods) or results (e.g., providing missing data or verifying the data) was needed.

Individual Study Quality Assessment

We used predefined criteria developed by the U.S. Preventive Services Task Force to assess the methodological quality of included studies.[43] Two independent reviewers assigned a quality rating of the internal validity for each study. Disagreements were resolved by discussion and consensus. A rating of "good," "fair," or "poor" was assigned using the predefined criteria for studies meeting inclusion criteria. For randomized controlled trials (RCTs), specific areas assessed included:

- The presence of adequate randomization methods (use of computer-generated random number tables or other process considered truly random);
- Allocation concealment;
- Similarity of groups at baseline;
- The specification of eligibility criteria;
- Reliable and valid diagnosis or asthma (optimal assessment included use of pulmonary function testing to confirm reversible component);
- Retention (retention of 90% or more overall was considered good; 60 to 89% was adequate, and less than 60% was considered a fatal flaw; differential attrition of 10 to 19 percentage points was considered potentially problematic and 20 percentage points or more was considered a fatal flaw);
- Time to followup (6 months or more was preferable, fewer than 6 weeks was potentially problematic)
- Equal, reliable and valid measurements;
- Blinding of outcome assessors; and
- Appropriate analyses (e.g., analyzing all participants in the treatment group to which they were initially assigned, use of conservative data substitution [preferably multiple imputation, imputation based random effects regression or similar models, or use of baseline values] when retention was below 90%, adjustment for potential confounders, no use of statistical tests that were inappropriate for the type of data analyzed).

All of these items were used to evaluate the risk of bias. Generally, a good-quality study met all major criteria, though it was possible to get a "good" rating if an item was not reported (so could not be assessed) if the rest of the methods were judged to be "good." A fair-quality study did not meet all criteria, but was judged to have no flaw so serious that it invalidated its results. A poor-quality study contained a serious flaw in design, analysis, or execution, such as differential attrition as described above, or some other flaw judged to be so serious as to cast doubt on the validity of the results. Examples of serious flaws include very large baseline group differences that were not or could not be adjusted for in an analysis, no information about followup and assumption of 100 percent followup was not tenable, or insufficient information was provided to determine the risk of bias.

We did not include studies rated as poor-quality in this review.

Data Synthesis

We summarized all included studies in narrative form as well as in summary tables that present the important features of the study populations, design, intervention, outcomes, and results. We divided comparisons into five groups based on the primary intervention focus and control group: (1) interventions focused on hyperventilation reduction breathing training versus control, (2) yoga breathing methods versus control, (3) IMT versus control, (4) breathing

approaches that did not focus on hyperventilation reduction versus control, and (5) hyperventilation reduction versus nonhyperventilation reduction breathing training approaches. Outcomes are discussed separately for each of the five groups.

To facilitate comparison of effect sizes across studies reporting different outcomes, when possible we calculated a standardized effect size (Hedges g) for group differences in change from baseline using Stata 11.2® (Stata Corp, College Station, TX), where sufficient data were available for calculation. In calculating standardized effect sizes for asthma symptom outcomes, all scores were coded so that a higher score indicated more symptoms (worse outcome). For quality of life measures, all scores were coded so that a higher score indicated higher quality of life (better outcome). Random effects meta-analyses were conducted where there were at least three trials within a group. Meta-analyses were always conducted within groups because of the high degree of clinical and methodological heterogeneity across group. Statistical heterogeneity was evaluated using the I^2 statistic. When trials reported multiple followup assessment, we pooled data from the assessment that was closest to the followup time reported by the other trials in the analysis to maximize consistency between studies. For trials with more than one control arm, we included the control group most similar in intensity to the intervention group that was included in the meta-analysis, thus choosing intensity-matched comparators wherever possible. We did not perform funnel plots or Egger's test of small study effects to assess for publication bias because of the small number of trials included in each meta-analysis.

We used effect size as one method to judge the importance of an effect. Effect sizes larger than 0.80 were considered large effects.[44] In addition, commonly used asthma scales have been examined to determine thresholds for clinically significant change in health status.[45] A change of 0.05 has been suggested for the Juniper Asthma Quality of Life Questionnaires (AQLQ).[46,47] For the St. George's Respiratory Questionnaire (SGRQ), the threshold for clinical significance is estimated to be 4 units, and patients whose treatment was judged to have been "very effective" showed an average change of 8.1 units.[45]

In a separate exploratory qualitative analysis for Key Questions 1b and 2b, we stratified all trials (regardless of group) by a series of study characteristics of interest and examined the proportion of trials reporting positive results in trials with and without the pertinent characteristic. Characteristics examined included study quality rating (substantial quality concerns vs. average quality concerns), whether the comparator included a breathing or relaxation component, whether the intervention involved the use of a device, and whether the two groups being compared involved the same number of hours of contact and homework. We examined outcomes, including: asthma symptoms, reliever medication use, quality of life, and pulmonary function.

Grading the Strength of Evidence

We graded the strength of evidence for primary outcomes using the standard process of the EPCs as outlined in the Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[48] Specifically, we assessed the strength of evidence for the major outcomes in each of the Key Questions. These outcomes included: (1) asthma symptoms and control, (2) asthma medication use, (3) quality of life and function for Key Question 1; and (4) pulmonary function test results for Key Question 2. The grade of evidence was based on four major domains: (1) risk of bias (low, medium, high), (2) consistency (no inconsistency present, inconsistency present, unknown or not applicable), (3) directness (direct, indirect), and (4) precision (precise, imprecise). Risk of bias is the degree to which the included studies for a given outcome or

comparison has a high likelihood of adequate protection against bias. We evaluated risk of bias considering both study design and aggregate quality of the studies. Consistency refers to the degree to which reported effect sizes from included studies appear to have the same direction and magnitude of effect. We assessed the sign of the effect sizes (i.e., effects have the same direction) and whether the range of effect sizes was narrow. When only a single study was included, consistency could not be judged. Directness relates to whether the evidence links the interventions directly to health outcomes. For a comparison of two treatments, directness implies that head-to-head trials measure the most important outcomes. Precision refers to the degree of certainty surrounding an effect estimate with respect to a given outcome.

We assigned an overall strength of evidence grade based on the total number of studies addressing the outcome and the ratings for these four individual domains for each key outcome, and for each comparison of interest. The overall strength of evidence was rated using four basic grades (as described in the AHRQ *Methods Guide*): high, moderate, low, and insufficient (Table 2).[48] We rated the evidence as insufficient when no studies were available for an outcome or comparison of interest, or the evidence is limited to small trials that are methodologically flawed and/or highly heterogeneous. Ratings were assigned based on our judgment of the likelihood that the evidence reflected the true effect for the major comparisons of interest.

Table 2. Strength of evidence grades and definitions

Grade	Definition
High	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low	Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
Insufficient	Evidence is unavailable or does not permit a conclusion

Applicability

To assess applicability, we used data abstracted on the population studied, the intervention and comparator, the outcomes measured, settings (including cultural context), and timing of assessments to identify specific issues that may limit the applicability of individual studies or the body of evidence to U.S. health care settings, as recommended in the Methods Guide.[49] We used these data to evaluate applicability, paying special attention to study eligibility criteria, recruitment strategies, baseline demographic features (e.g., age, smoking status, and comorbid conditions) and the intervention characteristics (whether there were multiple interventionists, level/degree of training among interventionists, whether there was a clearly defined protocol).

Review Process

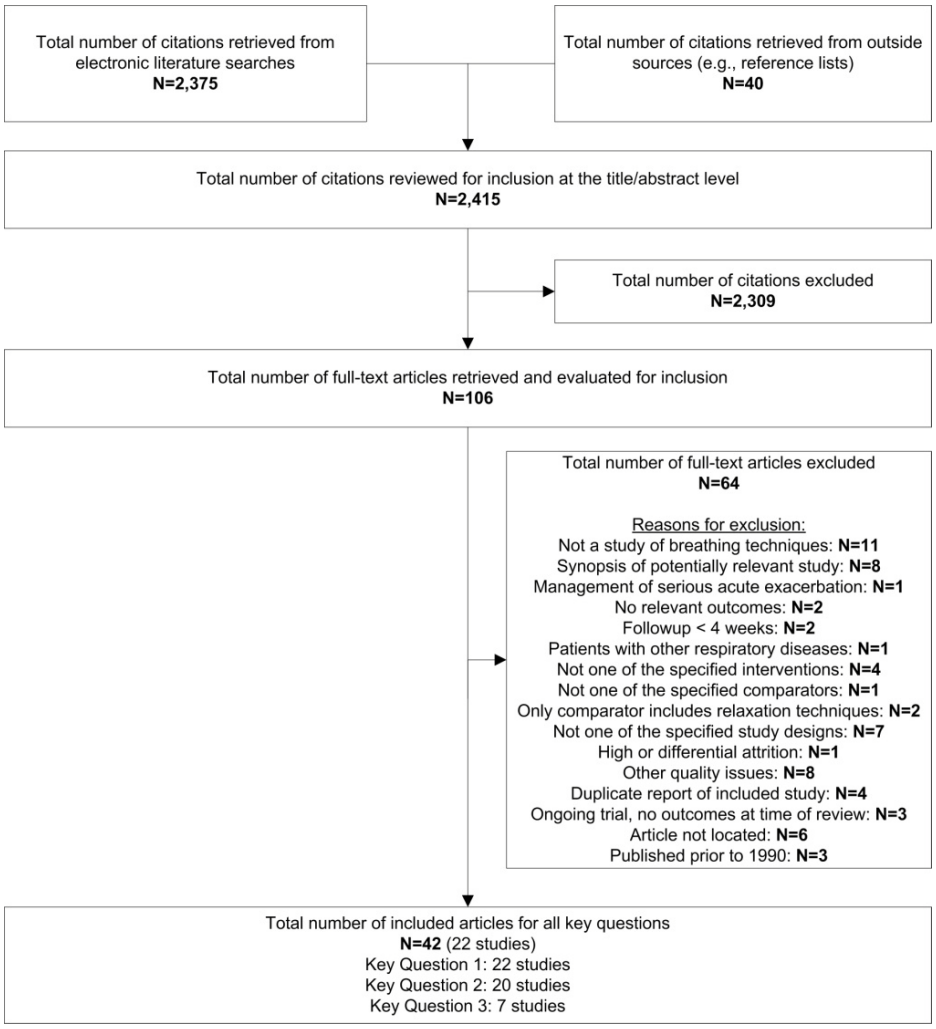
A full draft report was reviewed by experts and posted for public commentary from November 9, 2011, through December 5, 2011. Comments received from either invited reviewers or through the public comment website were compiled and addressed. A disposition of comments will be posted on the Effective Healthcare Program Web site 3 months after the release of the evidence report.

Results

Literature Search

Our literature search yielded 2,415 citations. From these, we provisionally accepted 106 articles for review based on abstracts and titles (Figure 2). After screening their full texts, 22 studies,[50-71] published in 42 articles,[50-91] were judged to have met the inclusion criteria (Appendix D). All of these studies were RCTs except one, which was a randomized crossover trial.[51] The remaining 64 full-text articles were excluded (Appendix E). The primary reasons for exclusion included not studying breathing techniques, not providing primary data, not using one of the specified study designs, and being rated as poor quality. The eight publications excluded for quality concerns represented six unique studies. Most were excluded because they failed to describe multiple important areas of their methods (e.g., randomization methods and followup rates and inclusion/exclusion rules and assessment methods were all missing) and the remaining were very small trials (n=12 and 17) that either lacked comparability between groups at baseline[92-94] or did not report acceptable measurement or analysis methods.[95]

Figure 2. Literature flow diagram



All trials were conducted with people with symptomatic asthma. Most were limited to those with stable asthma (e.g., stable dose of asthma medication, no recent use of oral steroids, and/or no recent hospitalization for asthma). Some trials were limited to people with a certain level of beta$_2$-agonist use (e.g., twice daily,[50,69] twelve times per week,[56] four times per week,[51,58] or twice weekly[52]), suggesting their asthma was not well controlled. Most trials confirmed reversibility of respiratory symptoms through pulmonary function testing. Trials primarily included adults; only one trial of IMT targeted children (ages 8 to 12 years),[65] and only four other trials included people younger than 16 years of age.[50,53,56,58] Trials used a variety of breathing retraining techniques (Table 3), including interventions that targeted hyperventilation reduction (e.g., Buteyko breathing technique, Papworth method),[50-59,71] yoga breathing techniques,[60-64] IMT,[65-69] and other controlled breathing approaches using prolonged exhalation or abdominal breathing.[52,70,71] Four of the trials of hyperventilation reduction used alternate breathing techniques for comparison[50,52,53,58] and seven used some kind of usual care, placebo, wait list, or attention control group.[51,52,54-57,59] One trial had two study arms with different treatments in addition to a placebo-control group. Comparisons from this study will be discussed in multiple sections of this report.[52]

Table 3. Included breathing retraining Interventions and comparisons

Intervention	Description/ Examples	Comparator	Number of Included Trials
Hyperventilation reduction breathing techniques	Nasal breathing, eliminating "overbreathing," end-tidal breath-holding. Examples include the Buteyko and Papworth methods.	Control	8*[50-59,71]
Hyperventilation reduction breathing techniques	Nasal breathing, eliminating "overbreathing," end-tidal breath-holding. Examples include the Buteyko and Papworth methods.	Another breathing technique	4*[50-59]
Yoga breathing	Diaphragmatic/ abdominal breathing, slowing and regularizing breathing, prolonging expiratory phase, using manual methods or the tongue and throat muscles to impose resistance. Also known as Pranayama.	Control	5[60-64]
Inspiratory muscle training	Use of exercises or device to increase strength of breathing muscles.	Control	5[65-69]
Other non-hyperventilation reduction breathing techniques	Slowed breathing.	Control	2*[52,70,71]

*One study with three treatment arms is included in each of these groups[52]

Thirty-two percent of the trials described allocation as concealed. Asthma symptoms, medication use, and quality of life were usually based on self-report, and only 41 percent of the trials reported that outcomes assessments were conducted blindly. Lack of blinding may be especially problematic for pulmonary function testing, which is effort-dependent and involves coaching to get an optimal performance. Lack of blinding may also be problematic for self-reported outcomes, where social desirability could introduce bias. Most trials were small, with 68 percent including only 30 or fewer participants per treatment arm. Only a single trial included more than 100 participants per treatment arm.[56] Trials were also inconsistent the degree to which they ensured the sample was limited to asthmatics: 42 percent did not report the use of pulmonary function testing to confirm an asthma diagnosis and 39 percent did not describe limiting excluding participants with other respiratory disorders or people at high risk for other respiratory disorders (e.g., smokers).

Results of Included Studies

We discuss results for the five different types of comparisons separately: hyperventilation reduction breathing techniques compared with control groups (Table 4) or with other nonhyperventilation reduction breathing techniques (Table 5); yoga breathing compared with control groups (Table 6); IMT compared with control groups (Table 7); and other nonhyperventilation reduction breathing techniques compared with control groups (Table 8). Table 9 briefly describes the instruments, including directionality, to aid in the interpretation of standardized scales (see end of chapter for all tables).

Key Question 1. In adults and children 5 years of age and older with asthma, does the use of breathing exercises and/or retraining techniques improve health outcomes, including: symptoms (e.g., cough, wheezing, dyspnea); health-related quality of life (general and/or asthma-specific); acute asthma exacerbations; reduced use of quick-relief medications or reduced use of long-term control medications, when compared with usual care and/or other breathing techniques alone or in combination with other intervention strategies?

Hyperventilation Reduction Breathing Techniques Versus Control Group

Key Points:

- We found moderate evidence that hyperventilation reduction breathing technique interventions with 5 or more hours of direct instruction may reduce asthma symptoms and the use of reliever medication in adults, though evidence was limited to a fairly small number of trials, most of which were at moderate risk of bias due to factors such as small sample sizes, high or differential attrition, and lack of appropriate blinding.
- Evidence is low or insufficient that hyperventilation reduction training affects controlled medication use, quality of life, or functioning in adults and children.

Eight trials (n=1,088) compared breathing retraining targeting hyperventilation reduction with a control group. Seven were RCTs[52,54-57,59,71] and one was a randomized crossover trial[51] (Table 4; Appendix D, Evidence Table 1a). The 4-week cross-over trial focused only on one component of the Buteyko breathing technique, specifically mouth-taping,[51] while the remaining provided broader instruction in modification of breathing (Appendix D, Evidence Table 1b). Interventions generally involved controlled, shallow breathing, and encouraging diaphragmatic breathing over chest breathing, with a breath-hold at the end of the exhalation. They advocated breathing through the nose at all times, and in some trials participants were encouraged to use a porous tape to hold the mouth closed at night while sleeping. They trained users to limit what they term "overbreathing" with sighs, yawns, and gasps. They encouraged clients to use breathing techniques when they experienced asthma symptoms for 5 to 10 minutes before using bronchodilators.

Four of these trials involved fairly extensive interventions, reporting 6 to 12 months of followup.[52,54-56] These trials provided 5 to 13 hours of contact with instructors, encouraged daily practice at home, and two of these included additional lifestyle components beyond breathing retraining, of dietary and sleep advice[52] and stress management.[52,55] Only one of these four trials

included a control group with matching treatment intensity,[56] the others compared hyperventilation reduction breathing training to usual care,[54,55] or a sham breathing training device.[52] One trial was limited to people with dysfunctional breathing, according to the Nijmegen questionnaire.[71] This instrument was designed to identify patients with chronic or habitual breathing patterns that induce hyperventilation, and assesses symptoms purported to identify hyperventilation (some of which may also be related to asthma symptoms) such as accelerated or deepened breathing, being unable to breathe deeply, palpitations, tightness around the mouth, tingling fingers, and dizzy spells.

Three lower-intensity interventions targeted breathing retraining only (i.e., included no co-interventions that were not directly targeting breathing retraining), but did attempt to provide comprehensive training rather than focusing only on a single aspect of the training. One trial used a video for both instruction and daily practice,[57] and the two others, conducted by the same researcher using very similar interventions, offered 1 to 2 hours of direct instruction.[59,71] Interventionists in all of these trials encouraged daily practice at home. One trial reported only 4-week outcomes,[57] and the other had 26-week followup for some or all outcomes.[59,71] Both trials attempted to provide attention-control comparators, one with relaxing landscape videos[57] and the other with general asthma education.[59]

Among all of the hyperventilation reduction trials with control group comparators, three used the Buteyko method,[52,56,57] three used the Papworth method or were described as similar to the Papworth method,[55,59,71] and one did not identify its methods as being either Buteyko or Papworth, but the description of the intervention was consistent with Buteyko and Papworth breathing methods,[54] and one addressed only a single, narrow aspect of the Buteyko method (mouth taping).[51]

All trials were rated as fair quality (Table 10). Two of the trials suffered from fairly high attrition[52,59] and three had greater attrition in the intervention group by at least ten percentage points at one or more followups.[52,55,59,71] Allocation concealment was reported in only three trials,[54,56,59] and outcomes assessment was clearly blinded in only four of the trials.[51,52,54,56] Only two of the RCTs randomized more than 50 participants per group,[56,59] and three trials had only 1-month of followup for some or all outcomes.[51,57,59]

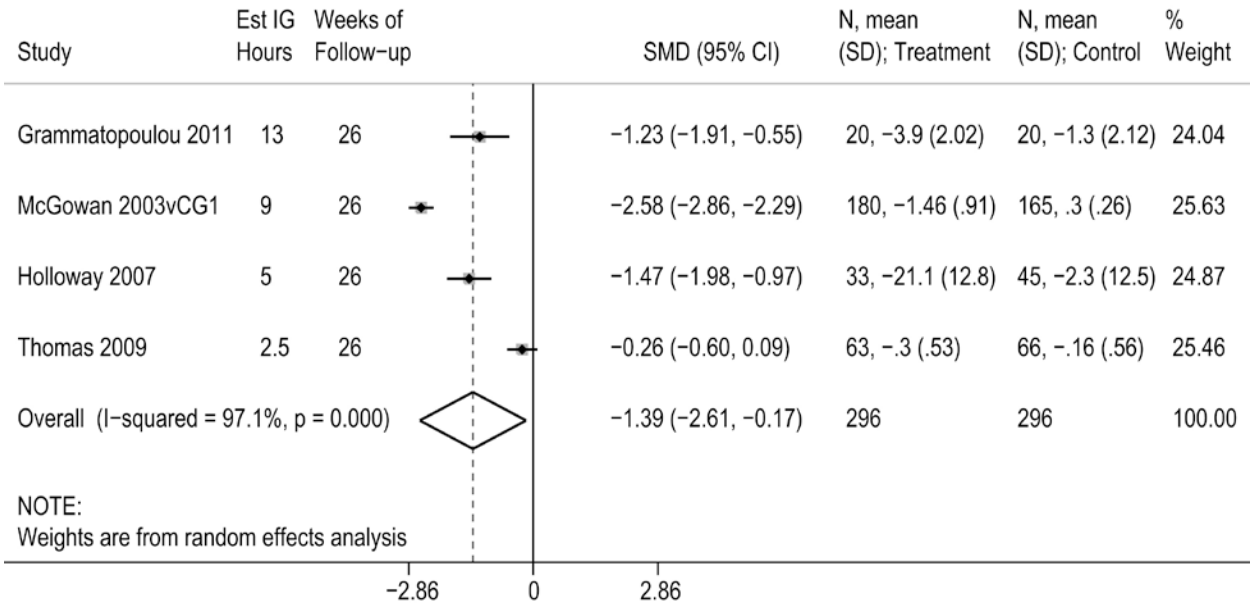
Six of these trials were conducted in the United Kingdom,[51,52,55,56,59,71] one in was conducted in Greece,[54] and one was conducted in Australia.[57] All trials were conducted in health care settings. The minimum ages of included participants ranged from 14 to 18 years, and most trials included adults up to ages 60 to 72 years. The average baseline reliever used in most trials was one to two puffs per day, generally along with 400 to 600 mcg of ICS use daily (in beclomethasone equivalent), and FEV_1 between 80 percent and 89 percent. The Australian trial had somewhat higher reliever medication use than the other four, with an average of 404 mcg per day at baseline (along with an average 430 mcg of ICS daily).[57]

Asthma Symptoms

All eight trials reported some type of asthma symptom outcome, which was usually a standardized questionnaire (Table 4; Appendix D, Evidence Table 1c). All four of the most-intensive and comprehensive interventions reported improvements in asthma symptoms at 6- to 12- months of followup.[52,54-56] Only four of the trials provided sufficient information to pool in a meta-analysis of asthma symptom scores, three of the four most intensive trials,[54-56] and one lower-intensity trial comparing 2 to 2.5 hours of Buteyko training with 2 to 2.5 hours of asthma education.[59] The standardized pooled effect size (or standardized mean difference [SMD]) for the

four trials with sufficient data to be included in a meta-analysis was -1.39 (95% confidence interval [CI], -2.61 to -0.17, Figure 3).[54-56,59] This analysis had very high statistical heterogeneity (I^2=97.1) and a wide range of effect sizes. However, because the pooled effect is very similar to effect seen in two of the trials, and the other two are approximately equidistant from the pooled estimate in opposite directions, the pooled effect may be a reasonable estimate for an average effect despite the high heterogeneity.

Figure 3. Effect of hyperventilation reduction techniques on asthma symptoms at 6 to 12 months



CI: confidence interval; CG: control group; est: estimated; IG: intervention group; N: sample size; SD: standard deviation; SMD: standardized mean difference

The largest trial showed the largest effect, with SMD of -2.58 (95% CI, -2.86 to -2.29). Symptom ratings on a scale of 0 (no symptoms) to 3 (severe symptoms) dropped from an average of 2.2 at baseline for all groups to 0.7 in the Buteyko group, while the control groups slightly increased to 2.4 to 2.5.[56] This was one of the relatively few trials reporting both allocation concealment and blinding of outcome assessors, although retention was somewhat lower in both control groups (82.5% and 73%) than the Buteyko group (90%).

Two other trials, both with fairly intensive interventions, reported standardized effect sizes greater than 1.2, which would generally be considered large.[54,55] In the trial by Holloway and colleagues, for example, the Papworth intervention group participants showed 18- to 21-point improvements on the 100-point SGRQ symptom subscale, compared with two-point improvements in the control group at 6 and 12 month followup.[55] This change is even greater than the change on the SGRQ seen in patients whose treatment was judged to be “very effective” in other research.[45] Outcomes assessment was not blinded in this trial, which may have artificially increased the effect size if intervention participants were more prone to demand characteristics. On the other hand, this trial relied on an asthma registry to recruit patients and did not independently verify the asthma diagnosis with pulmonary function testing. As such, if some of the patients were misdiagnosed and actually had chronic obstructive pulmonary disease or another respiratory condition, then this would likely attenuate the intervention’s effect. The asthma registry approach likely increases the applicability to typical clinical settings.

Similarly, the trial conducted in Greece by Grammatopoulou and colleagues[54] showed intervention participants moving from a score consistent with uncontrolled asthma to one in a range similar to those with completely controlled asthma at 26-week followup.[96,97] The average control group score, on the other hand, remained below the average score of someone with well-controlled asthma.

The other fairly intensive trial, which was not included in the meta-analysis, reported mixed results, found differences in symptom scores from daily diaries, but no group differences in a standardized symptom scale.[52] This was a fairly small trial (n=30 per group) with fairly low followup at 6 months (77% retention in the intervention group vs. 80% in the control group), using a last-observation-carried-forward (LOCF) data substitution method.

Of the remaining trials, which were all fairly low intensity, only one reported statistically significant improvements in symptoms, and only at four weeks.[71] The other trials did not find improvements in asthma symptoms after 1 to 6 months.[51,57,59] Other than the mouth-taping cross-over trial, these trials showed effect sizes consistent with small beneficial effects, but group differences were not statistically significant.

Medication Use

Medication use was reduced in three[52,56,57] of the six trials reporting these outcomes (Table 4; Appendix D, Evidence Table 1d).[51,52,56,57,59,71] However, medication use was reported in only two of the four higher-intensity trials.[52,56] In the largest trial, reliever medication use dropped from 18 puffs per week at baseline in all groups to less than one puff per week in the intervention group, compared with no change in either of the control groups at 6-month followup.[56] Although specific data were not shown, this trial also reported greater reductions in the use of controller medication. Although the data were self-reported, and may be subject to demand characteristics (since Buteyko participants were encouraged to delay bronchodilators), they were gathered by blind outcome assessors.

Reliever medication use was reduced at 6-month followup in the trial by Cooper and colleagues comparing a Buteyko intervention with a sham breathing retraining device.[52] SABA use was reduced by a median of two puffs per day in the intervention group, compared to no change in the control group. Neither ICS use nor prednisone use differed at 6-month followup in this trial. After 6-month followup, 60 of the 69 participants completing the first phase of the trial took part in a steroid-reduction phase. Intervention participants in this phase reduced ICS use by a median of 41 percent, compared with no reduction in the control group. However, this difference was not tested directly; instead, the authors report only the results of the three-way comparison between the Buteyko group and another treatment arm (a device to control the pace of breathing), which was not statistically significant (p=0.70). This is the trial with fairly low and differential retention that used LOCF as a data substitution method. Medication use was not reported in the two other higher intensity trials that showed large positive effects on asthma symptoms.[54,55]

Medication outcomes were reported in the mouth-taping trial[51] and the other three lower-intensity trials.[57,59,71] Reductions in bronchodilator use in the trial of video-based instruction[57] were similar to those seen in the trial by Cooper and colleagues.[52] This was a small trial (n=36) with only 4 weeks of followup, but did have fairly high retention (89% in each group). This trial reported no group differences in ICS use. No group differences in medication use were seen in the mouth-taping trial[51] or the lower-intensity Papworth-style interventions.[59,71]

Quality of Life and Functioning

Seven of the trials[51,52,54,55,57,59,71] reported measures of asthma-related quality of life, functioning, or mental health symptomatology at 1 to 12 months post-baseline, and all but the one study[51] (which focused only on mouth-taping) reported group differences in some measures (Appendix D, Evidence Table 1e).

Asthma-Related Quality of Life

Six trials[51,52,55,57,59,71] reported asthma-specific quality of life using standardized measures, including only two of the higher-intensity trials (Table 4; Appendix D, Evidence Table 1e).[52] Four reported statistically significant group differences at one or more time points. The trial with the higher-intensity Papworth intervention[55] reported improvements on the SGRQ one year after the end of the intervention, however the differences appeared to be driven by the "symptoms" subscale, since neither the "impacts" nor the "activities" subscales showed group differences at either followup. Thus, improvements were seen in symptoms, but did not appear to affect other areas of day-to-day life. The remaining higher intensity trials either found no differences between groups[52] or did not report this outcome.[54,56] The three lower-intensity trials that reported group differences in a measure of quality of life up to 6 months post-baseline were the video-based treatment trial and both of the lower-intensity Papworth-style trials.[57,59,71]

Functioning and Mental Health

Changes in Short-Form Health Survey (SF-36) scores were reported in two trials, and although many SF-36 subscale outcomes were reported in these two trials, group differences were rarely seen (Appendix D, Evidence Table 1e).[52,54] Two trials, including the Papworth intervention trial with a large effect on asthma symptoms,[55] reported improvements in mental health outcomes of depression and anxiety at 26 weeks.[55,59] Anxiety and depression scales scores indicated that participants were not, on average, anxious or depressed either before or after treatment. Reductions were small in magnitude (e.g., group differences of 1.6 on a 68-point rating scale). Group differences were maintained in one of these trials to 1 year.[55]

Hyperventilation Reduction Breathing Techniques Versus Other Breathing Techniques

Key Points:

- Hyperventilation reduction breathing techniques may be more likely to reduce reliever medication use than other breathing techniques in adults, but strength of evidence is low.
- Hyperventilation reduction training is no more likely to improve symptoms, controller medication use, or quality of life than other breathing techniques functioning in adults, but strength of evidence is low.

Four RCTs (n=285) directly compared the use of breathing techniques targeting hyperventilation reduction with another breathing technique that did not target hyperventilation reduction. Three of these trials used the Buteyko approach[50,52,53] and one was modeled after the Papworth method (Table 5; Appendix D, Evidence Tables 2a and 2b).[58] One of these involved a 10-hour Buteyko intervention and was described above, compared to the use of a device to modify breathing to achieve a typical yoga inspiration-to-expiration cycle of 1:2 with minimal one-on-one instruction and no components addressed other than the breathing technique.[52]

The three remaining trials employed comparators targeting controlled or paced breathing, but did not encourage the use of slow, nasal, shallow breathing with breath-holding or other techniques focused on reducing hyperventilation.[50,53,58] All of these trials involved at least five contacts, usually face-to-face. Two trials used an approach that was initially intensive, meeting every day for 5 to 7 days for training.[50,53] All three trials attempted to provide the same frequency and hours of treatment in both treatment groups. However, in one trial more than half of the Buteyko participants received additional instruction sessions and the average number of followup phone calls was seven in the Buteyko group, compared to one in the comparison group.[50]

In addition to some kind of breathing retraining in the nonhyperventilation reduction groups, one trial also included general asthma education and relaxation techniques,[50] and another included shoulder and upper arm stretches.[58]

All four trials were rated as fair quality (Table 11). One trial had a number of quality-related issues, despite having followup on 95 percent of participants, including only a small number of participants randomized (n=20 or fewer per group), a very wide age range (age 12 to 70 years), no information on blinding of outcomes assessment, and reliance on self-report of variability in breathing symptoms that improve with beta$_2$-agonist use for asthma diagnosis.[50] Additionally, the Buteyko intervention was more intensive than the comparator.

Another trial reported good measurement and randomization procedures, but was rated as "fair" quality because of the small number of participants (n=57 total) and retention below 90 percent.[58] The remaining two failed to report either allocation concealment or blinding of outcomes assessment, and had either fairly high attrition overall[52] or higher attrition in the Buteyko breathing technique group than the other intervention group,[53] in addition to other minor issues.

These trials were conducted in Australia,[50,58] the United Kingdom,[52] and Canada.[53] Average age ranged from 44 to 47, and all but one had a wide age range from 12 to 18 years up to 65 or older. Asthma severity was quite high in one trial, where participants were using an average of almost 900 mcg of reliever medication per day and 1,250 mcg of ICS (in beclomethasone equivalents).[50] Baseline FEV_1 was 74 percent in this trial. Participants in the remaining trials were using two to three puffs of reliever medication per day along with 650 to 850 mcg of ICS, with an average FEV_1 around 80 percent.[52,53,58]

Asthma Symptoms

Two trials reported no group differences in asthma control, with little improvement in either group at 13 and 26 weeks (Table 5; Appendix D, Evidence Table 2c).[50,53] Two reported no or minimal group differences but did report improvement in both treatment groups for either the asthma control questionnaire and physician global rating at 28 weeks[58] or median change in the symptoms subscale of the Mini-AQLQ at 26 weeks.[52] Within-group change in the latter was not tested statistically, but both groups showed a median improvement of more than 0.5, which is considered a clinically significant difference.[98] The best quality trial in this group showed almost no group differences on five additional symptom scales; both groups improved on two of the additional symptom scales.[58]

Medication Use

Two[50,52] of the three[50,52,58] trials reporting reliever medication use found greater reductions with Buteyko breathing technique than either abdominal breathing[50] or a device to train in the

use of prolonged exhalation after 13 to 26 weeks (Table 5; Appendix D, Evidence Table 2d).[52] The trial with the greatest baseline asthma severity (and the most quality concerns, including more intensive intervention contacts in the hyperventilation reduction group than the comparison breathing intervention) showed the greatest improvements in reliever use, reporting median reductions of 904 mcg per day in bronchodilator use at 3-month followup in the Buteyko group, compared with a 57 mcg reduction in the abdominal breathing group.[50] The Buteyko group went from using approximately 9 to 10 puffs of $beta_2$-agonist per day to approximately one puff every other day. The trial showing no group differences reported reductions in reliever medication by almost two puffs per day in both the hyperventilation-reduction group and the controlled breathing with stretching group.[58]

All four trials reported results for controller medication. Two trials reported little change in ICS use for either group,[50,52] including the trial with the most dramatic results for $beta_2$-agonists.[50] Of the remaining trials, one reported that ICS use was reduced by 50 percent in both the Buteyko and the controlled breathing groups,[58] and other trial reported greater reductions in ICS use and a greater likelihood of discontinuing long-acting $beta_2$-agonists with hyperventilation reduction techniques than with a more typical physical therapeutic approach.[53] In this trial, ICS use was reduced by an average of 317 mcg in the hyperventilation-prevention group and only 56 mcg in the physical therapy group. Two trials reported no differences between groups in prednisone use.[50,52]

Quality of Life and Functioning

All four trials reported an asthma-specific quality of life outcome, and none found that any group showed greater improvement than another group (Table 5; Appendix D, Evidence Table 2e). In two trials, both groups showed increases of more than 0.5 on the Juniper quality of life scales,[52,53] which is the threshold for clinically significant change.[45] However, the changes over time were statistically significant in only one of these two trials.[53]

One trial reported functioning outcomes and found that scores on the subscale role limitation due to physical problems improved by a median of 25 points on a 100-point scale at 3 months in the hyperventilation-prevention group, while the median change in the device-assisted yoga-style breathing was zero.[52] Other functioning subscales showed little improvement in either group.

Yoga Breathing Versus Control

Key Points:

- Yoga breathing may improve asthma symptoms and quality of life in adults, but strength of evidence is low due to concerns about the methodological quality of the trials.
- Evidence is insufficient to determine whether yoga can reduce asthma medication use in adults and children.

Five trials (n=360) compared the yoga group with a control group (Table 6; Appendix D, Evidence Table 3a).[60-64] All were fairly to highly intensive interventions and all required daily practice at home in addition to supervised sessions (Appendix D, Evidence Table 3b). Two programs conducted in India were very intensive.[60,64] One included 4-hour sessions daily for 2 weeks covering yoga practice, lectures, group discussions, diet (including a study-provided breakfast), and stress management, followed by an additional 4 weeks of home practice.[64] Another trial involved a 70-minute-long daily yoga session for 6 months and all patient were hospitalized initially to facilitate training.[60] The duration of the inpatient stay was not specified. This trial was limited to male vegetarians aged 25 to 50 years.

A third trial in India was focused specifically on yoga breathing exercises among people with at least 6 months of prior yoga experience, compared with the use of meditation.[63] Both treatment arms involved 20 minutes of practice twice daily for 12 weeks, although the number of these sessions that were supervised versus those conducted at home was not described. In this study, the authors reported that participants "had no history of regular medication and they were advised to discontinue if on any medication." It was unclear if this is referring to all medication, or only asthma medication. No age limits were reported and the average age in this trial was 29 years.

The final two trials were conducted in the United States.[61,62] One compared an eight-session yoga class with a stretching class.[62] This trial was limited to participants aged 18 and over, with an average age of 51 years. The other trial involved a comprehensive naturopathic treatment program that included yoga as well as dietary restriction, nutritional supplements, and a guided journaling session.[61] Participants in this trial were predominantly female and the average age was 44 years.

All trials were rated fair quality and three had substantial quality issues that limit our confidence in results (Table 12).[60,61,63] Two of these trials were quite intensive and conducted in India.[60,63] These trials included only 17 to 25 people per group, failed to report both allocation concealment and blinding of outcomes assessment, and provided no information on refusals or exclusions prior to randomization. In addition, one did not indicate how they divided the participants into groups and failed to report the use of pulmonary-function testing to confirm reversibility for asthma diagnosis.[60] Also, the usual-care group in this trial received only bronchodilators, antibiotics, and expectorants, but not ICS. The other trial did not report the proportion of participants with followup, and it was unclear if their group assignment was truly random.[63] The third trial was conducted in the United States and involved a comprehensive naturopathic intervention, which did not allow us to determine the effect of yoga breathing techniques specifically.[61] Outcomes assessment in this trial was not blinded, and it was unclear whether those assigning participants to groups had access to intake assessment data. This trial also did not report the use of pulmonary function testing in the diagnosis of asthma, number of refusals or exclusions prior to randomization, nor did they describe whether they excluded people with other respiratory disorders or recent use of oral steroids from their sample.

The Indian trial of daily 4-hour sessions also failed to report both allocation concealment and blinding of outcomes assessment, but had retention above 90 percent in both groups and good assessment procedures.[64] The U.S.-based yoga class trial had the best methods of the group, but had low and somewhat differential retention (79% in the intervention group vs. 67% in the control group).[62]

Asthma severity was not consistently described in this subgroup of studies, but average severity would likely be considered to be moderate according to National Asthma Education and Prevention Program (NAEPP) as based on either daily reliever use[62] or FEV_1 in the "moderate asthma" range.

Asthma Symptoms

All but one trial[62] showed greater improvement in the yoga groups on at least one measure of asthma symptoms, including all three trials conducted in India (Table 6; Appendix D, Evidence Table 3c).[60,61,63,64] The U.S.-based trial of an eight-session yoga class reported no group differences in asthma symptoms.[62] Although it was difficult to compare effect sizes across different measures, the largest effect size appeared to be found in one of the lower quality trials

based in India, comparing yoga breathing exercises with meditation.[63] This trial reported a 64 percent reduction in symptoms in the intervention group at 12 weeks, compared with a six percent reduction in symptoms in the meditation group.

Another trial with a very intensive intervention reported a very large effect size at 2- and 4-week followup, but the effect was attenuated (yet still statistically significant) after 8 weeks.[64] In this trial and the U.S.-based trial of a comprehensive naturopathic intervention,[61] both groups showed improvements in a Juniper symptom subscale well beyond the level of clinical significance (i.e., improvement of 0.5 points).[45] Greater improvements were apparent, however, in those participating in the yoga interventions than those in the control groups.

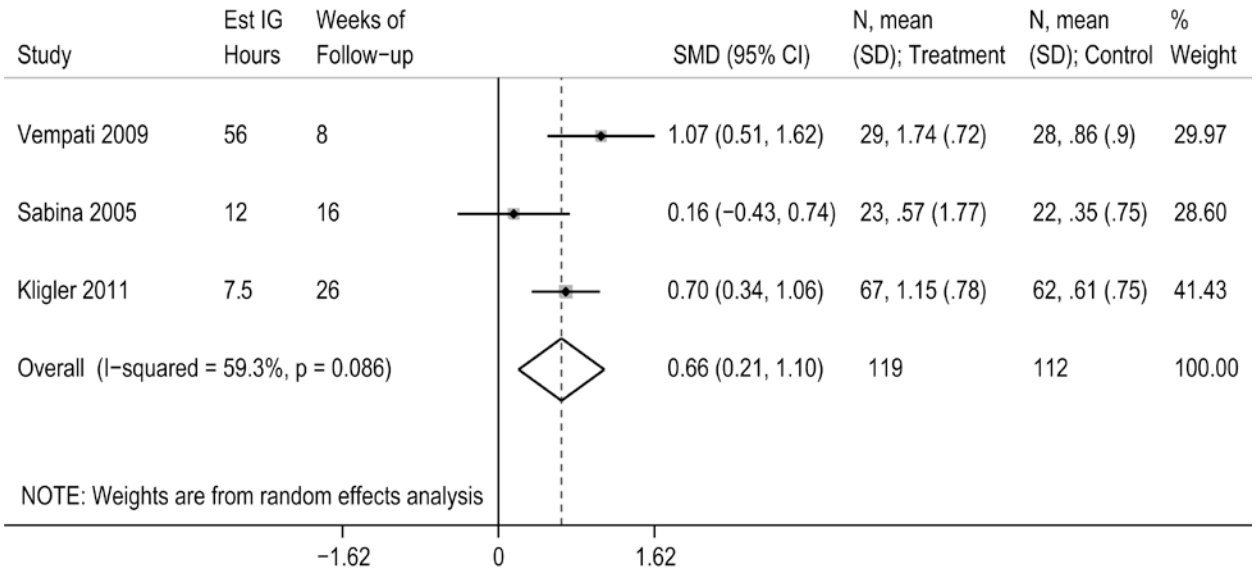
Medication Use

Three trials reported medication use,[60,62,64] including two trials conducted in India (Table 6; Appendix D, Evidence Table 3d).[60,64] One trial found that 53 percent of yoga participants reduced medication required to control their dyspnea, compared with 18 percent in the control group after 26 weeks, but the specific type of medication was not reported.[60] In the trial of daily 4-hour yoga sessions, as with asthma symptoms, both groups showed improvement in medication use: yoga participants reduced rescue medication use by an average of 1.5 puffs per day after 8 weeks compared with a reduction of 0.5 puffs per day among control participants.[64] There were no statistically significant group differences between those taking the yoga class and those on the waiting list after 16 weeks.[62]

Quality of Life and Functioning

Three of the trials reported functioning or quality of life outcomes (Appendix D, Evidence Table 3e).[61,62,64] The pooled standardized effect size for overall asthma-related quality of life in these three trials was 0.66 (95% CI, 0.21 to 1.10, I^2=59.3%, Figure 4), consistent with improved asthma-related quality of life in yoga breathing groups compared to controls.

Figure 4. Effect of yoga breathing techniques on quality of life at 2 to 6 months



CI: confidence interval; est: estimated; IG: intervention group; N: sample size; SD: standard deviation; SMD: standardized mean difference

The eight-session yoga class did not lead to greater improvement in overall asthma-related quality of life than being on a waiting list after 16 weeks.[62] Participants in both the comprehensive naturopathic intervention[61] and the daily 4-hour sessions[64] showed greater improvement overall asthma-related quality of life (again exceeding the threshold for clinically significant improvement) as well as the "activities" and "emotions" subscales than the usual care groups after 8[64]and 26 weeks.[61] As before, however, the usual-care participants also showed clinically and statistically significant improvement in both of these trials. There were also group differences on the SF-36 subscales of physical and social functioning, role limitations due to physical limits, and both of the summary component scores (physical and mental) in the trial involving a comprehensive naturopathic treatment program.[61]

Inspiratory Muscle Training Versus Control

Key Points:

- Evidence is insufficient to draw conclusions about the effect of IMT on asthma symptoms, medication use, or quality of life in adults and children.

Five small trials (n=169) examined the effect of IMT on asthma (Table 7; Appendix D, Evidence Tables 4a and 4b) after 8 to 26 weeks.[65-69] Three of these trials, all conducted by the same researcher in Israel, compared the use of a training device that controlled the level of resistance associated with inhalation with a sham device that provided no resistance.[67-69] Level of resistance was gradually increased over the course of training with the active device, but the sham device provided no resistance at any setting. Participants' average age ranged from 34 to 40 years, and no age limitations were listed for any of these trials. One trial was limited to women categorized as being in the mild-persistent to moderate range of asthma. Participants used an average of 3.2 puffs per day of reliever medication and had a baseline FEV_1 of 83 percent.[68] The second trial was limited to those using two or more puffs of SABA daily, with an average use of 2.7 puffs of reliever per day and a baseline FEV_1 of 91 percent.[69] The third trial

was limited to people with severe asthma. Participants in this trial used an average of six puffs of reliever medication per day and had an average baseline FEV_1 of 59 percent, the lowest of all included trials.[67]

The fourth trial was conducted among children in Brazil who had previously received no treatment for asthma and whose asthma was poorly controlled.[65] Baseline FEV_1 was not reported in this trial. The trial compared a 14-session program that included one-on-one instruction as well as IMT with the use of a breathing training device that built up inspiratory muscles through gradually increasing the resistance required for inspiration, plus medication (rescue and preventive) and three monthly medical visits for medication monitoring and general asthma education. This was compared with asthma education and medication alone.

The final trial was conducted in South Africa among inactive nonsmokers with moderate-persistent asthma and an average age of 22 years.[66] This trial instructed participants in diaphragmatic breathing. Participants were told to hold a weight on their abdomen while breathing through a 1 centimeter wide tube. Control group participants received no breathing training.

All trials were rated fair quality, and all but one[67] had fairly substantial quality issues (Table 13).[65,66,68,69] The trials conducted in Israel included 15 or fewer participants per treatment group in all cases,[67-69] although followup rates where high in two of the three trials.[67,69] None of these trials reported whether allocation was concealed or whether they excluded participants with other respiratory disorders. None of these trials provided detailed inclusion/exclusion criteria and two them also failed to report information on baseline comparability of the treatment groups.[68,69]

The trials in South Africa[66] and Brazil[65] were also fairly small including 22 to 25 participants per treatment arm with 100 percent followup. Neither trial, however, reported allocation concealment or blinding of outcomes assessment. In addition, the Brazilian trial did not appear to use pulmonary testing to confirm asthma diagnosis, provided little detail on their outcomes assessment methods, and they did not report whether IMT trainers were in contact with the larger asthma treatment team (and perhaps providing advice or support for general asthma management and medication use such as encouraging patients to use controllers consistently) as part of the fourteen IMT-focused sessions.[65] In addition, children receiving only asthma education and medication showed little improvement, which suggests these treatments were suboptimal. The South African trial did report the use of pulmonary testing to confirm asthma diagnosis, but provided no description of refusals and exclusions prior to randomization.[66] They also reported no information on changes in asthma symptoms, medication use, or quality of life, but only reported pulmonary function outcomes.

Asthma Symptoms

Only two of the trials reported asthma symptoms at followup (Table 7; Appendix D, Evidence Table 4c).[65,67] The Brazilian trial reported that all of the children in the control group regularly experienced daytime symptoms after 3 months, compared with none of the children receiving IMT.[65] Similarly, 22 of the 25 control group children experienced frequent asthma attacks, compared with only two of the 25 IMT participants.[65] Large group differences were also found for nighttime symptoms. The fact that the children receiving only medication management and asthma education were still experiencing high levels of asthma symptoms suggests that their treatment was not effective and may not have been comparable to treatment in the United States.

The Israeli trial with the fewest quality concerns reported greater improvement in morning chest tightness, cough, daytime asthma symptoms, and nighttime asthma symptoms after 6

months in IMT participants as recorded in daily diaries, compared with those using a sham device.[67]

Medication Use

Four trials reported some kind of group difference in change in bronchodilator use (Table 7; Appendix D, Evidence Table 4d).[65,67-69] As with asthma symptoms, medication effects were large in the Brazilian trial: at 3-month followup 16 percent of the children in the IMT group were using bronchodilators compared with 84 percent of the control group children.[65] They did not report on controller medication use, which is unfortunate since the children in both groups were previously untreated, initiating both rescue and controller medication in this trial, and we cannot tell if the level of recommended controller medication use was comparable between groups.

All three Israeli trials reported statistically significant reduction in beta$_2$-agonist use at final followup in those using the active training device, but no such change in those who used the sham device after 13 to 26 weeks.[67-69] Groups were not statistically compared directly with each other in two cases,[68,69] however, and in one of these that provided sufficient data to calculate a standardized effect size, the effect was not statistically different from zero.[69]

Quality of Life

Two trials reported functioning outcomes (Appendix D, Evidence Table 4e).[65,67] The Brazilian trial reported that none of the children undergoing IMT had difficulty with activities of daily living at 3-months followup, but all of the control children did.[65] One of the Israeli trials reported an average decline of 1.7 days of missed work in the prior three months, compared with almost no change in the control group participants.[67]

Other Nonhyperventilation Reduction Breathing Techniques Versus Control

Key Points:

- Evidence is insufficient to draw conclusions about the effect of other nonhyperventilation reduction breathing techniques on asthma symptoms, medication use, or quality of life in adults and children.

Two heterogeneous trials (n=153) compared a nonhyperventilation reduction breathing technique with a control group (Table 8; Appendix D, Evidence Tables 5a and 5b).[52,70] One trial, conducted in the United States with paid volunteers, examined the use of biofeedback for breathing retraining.[70] The intervention group engaged in biofeedback targeting respiratory resistance, respiratory reactance, and HRV as well as training in pursed-lip abdominal breathing with prolonged exhalation. This trial had three different control groups: biofeedback targeting only HRV, placebo biofeedback involving bogus "subliminal suggestions designed to help asthma," and waiting list. The first three groups involved weekly biofeedback sessions for 10 weeks, plus the request to practice at home 20 minutes twice daily with a home-training unit. The trial did not report baseline medication use or FEV_1 values, but reported that participants' asthma was most commonly rated as being in the moderate persistent range based on medication level according to National Health, Lung and Blood Institute (NHLBI) criteria.[1]

The other trial compared the use of a device to modify breathing to achieve an inspiration-to-expiration cycle of 1:2 with a sham device that did not modify breathing.[52] Comparisons involving other treatment arms in this trial were included above under hyperventilation reduction techniques. Participants were expected to practice using the device at home twice a day for six

months. The average age of participants for this trial was 44 years, and was limited to participants aged 18 to 70 years. Both trials were rated as fair quality (Table 14). The main concerns of the biofeedback trial included lack of information on allocation concealment, higher retention in the wait list group than all other groups (92% vs. 74% to 79%), and fairly small sample size (22 to 25 per group), although they did report blinded outcomes assessment.[70] The trial examining the breathing device had fairly low and somewhat differential retention (73% in the intervention group vs. 83% in the control group), conducted many statistical comparisons for the relatively small sample, and did not clearly describe whether baseline differences were controlled for, but did report blinded outcomes assessment.[52] Both trials reported pulmonary function testing to confirm asthma diagnosis.

The comparison between the active biofeedback groups targeting breathing in addition to HRV versus HRV-only tests the unique contribution of breathing retraining.[70] No differences were found between these groups on either asthma symptoms or controller medication use at 12 weeks. Both of these two groups, however, did show greater reductions in number of asthma exacerbations and controller medication use than the placebo and waitlist groups, suggesting biofeedback targeting HRV may have contributed to improvement in asthma. This trial did not examine quality or life or functioning.[70]

No differences on asthma symptoms, medication use or quality of life were noted at 6-month followup in the trial comparing the device to train prolonged exhalation with a placebo device.[52]

Key Question 1a. Does the efficacy and/or effectiveness of breathing techniques for asthma health outcomes differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?

Key Points:

- Evidence is insufficient to determine whether patient characteristics influence treatment effect in adults and children.

The trials were heterogeneous on too many factors and reporting was too inconsistent to allow us to assess the impact of population characteristics such as demographic characteristics or baseline asthma severity on effect size across studies. However, three trials did report results of subgroup analyses examining differential effects of treatment by different characteristics.[51,59,90] It was unclear if these analyses were planned *a priori*, but they do target subgroups hypothesized to gain the greatest benefit from the specific interventions of their trials, based on the physiologic models of action for their interventions or prior research. None of the trials reported conducting tests for interactions before exploring subgroup analyses. The United Kingdom trial that compared a relatively low-intensity Papworth-style intervention with an asthma education comparator of comparable intensity found that results were consistent between those who scored in the "disordered breathing" range on the Nijmegen questionnaire and those who did not.[59] Similarly, the trial of nighttime mouth-taping did not find larger effect among the subgroup of people who were rated as being "mouth breathers" at baseline.[51] Finally, the trial using biofeedback for breathing retraining found that there were no differences in response between those older than 40 years of age and those younger than 40 years of age.[90]

Key Question 1b. Does the efficacy and/or effectiveness of breathing techniques for asthma health outcomes differ according to variations in implementation (e.g., trainer experience) and/or nonbreathing components of the intervention (e.g., anxiety management)?

Key Points:

- Evidence is insufficient to determine whether certification and/or training of the provider affects effect size in hyperventilation reduction trials in adults and children.
- Exploratory analyses suggest that comprehensive approaches, especially those including additional, nonbreathing components may be more likely to show a benefit than approaches that isolate a single aspect of breathing in adults.
- Exploratory analyses suggest that intensity-matched control groups and control groups that involved either an alternate breathing approach or a technique to reduce autonomic arousal may reduce the likelihood of finding group differences in adults.

Among the 11 hyperventilation reduction trials, the expertise of the trainer may have had an impact on medication use, but not on self-reported symptoms. Four of the hyperventilation reduction trials reported using providers with specific training or certification in the Buteyko breathing technique, three trials described their intervention as Buteyko, but did not involve a practitioner, either because they used video tapes to deliver the intervention[57,58] or limited the intervention to mouth-taping.[51] Four trials used physical therapists without describing further certification, and did not describe their method as Buteyko.[54,55,59,71] All four hyperventilation reduction trials using specially training or certified providers showed reductions in medication use.[50,52,53,56] Only one other trial showed reduction in medication use and only for controller use.[57] However, the effect of practitioner training was not evident for self-reported symptoms: two[52,56] of the four using Buteyko practitioners reported positive or mixed findings, compared with three[54,55,71] of the seven trials that did not. Also, of the two trials reporting large improvements in asthma symptoms, one used certified Buteyko practitioners and one did not. Interestingly, the only trials reporting improvements in quality of life did not involve certified Buteyko practitioners.[57,59]

Looking across all trials, we compared the proportion of trials reporting benefits of treatment with and without several treatment components. First, interventions that included co-interventions in addition to breathing retraining[52,55,61,64] (e.g., dietary advice, relaxation training) were likely to show a benefit, and interventions that provided comprehensive training and education on breathing retraining were more likely to show a benefit than interventions that isolated one aspect of breathing retraining (e.g., prolonged exhalation,[52,70] mouth taping,[51] strengthening inspiratory muscles[67-69]), which generally showed no benefit. For example, 83 percent of trials reporting extra non-breathing components reported a positive effect on asthma symptoms and 100 percent reported reductions in reliever medication use (of those reporting these outcomes), compared with 36 and 33 percent respectively among trials that restricted their interventions to breathing training. However, as discussed next, intensity of intervention (measured in hours of contact) and comprehensiveness (measured in number of intervention components) are likely confounded.

More comprehensive programs were also more likely to offer more hours of exposure to interventionists, and data were insufficient to truly tease apart the effects of hours of contact from the effects of the content that was presented. However, we were able to compare patterns of results among the 13 trials that had the same number of contact hours in the treatment and

comparator groups[52,53,56-59,62,63,67-71] with the 10 trials in which intervention participants received more hours of contact than those in the comparator group.[50-52,54,55,60,61,64-66] Based on the number of trials reporting positive results (and not magnitude of effects), trials that matched intensity between treatment groups were less likely to show reductions in reliever medication use (83% of trials with more intensive intervention than control groups showed reductions in reliever use, compared with 30% of those with matching intensity in the two groups). However, comparable differences were not seen for asthma symptoms or quality of life outcomes. This exploratory analysis is limited by incomplete and perhaps selective reporting of these major outcomes.

Trials that compared any breathing retraining with either another breathing technique or an intervention likely to induce relaxation or a reduced state of autonomic arousal[50,52,53,57,58,62,63,70] (k=8) were less likely to show group differences on asthma symptoms and quality of life compared with trials containing control groups that did not include either of these components (k=15).[51,52,54-56,59-61,64--69,71] Seventy-five percent of trials with a nonbreathing or nonrelaxation comparator showed greater improvement on a measure of asthma symptoms in the intervention than the control group, compared with 12.5 percent of those with breathing or relaxation comparators. Similar results were seen for quality of life in these trials (20% showing benefit when compared with another breathing technique and/or relaxation vs. 57% showing benefit when compared with nonbreathing/ relaxation control). We saw no qualitative relationship between likelihood of effect and study quality rating or whether the treatment involved the use of a device. These data are purely exploratory and do not account for magnitude or precision of effect, and they do not consider the impact of incomplete and perhaps selective reporting. As such, these data must be interpreted cautiously.

Key Question 2. In adults and children 5 years of age and older with asthma, does the use of breathing exercises and/or retraining techniques improve pulmonary function or other similar intermediate outcomes when compared with usual care and/or other breathing techniques alone or in combination with other intervention strategies?

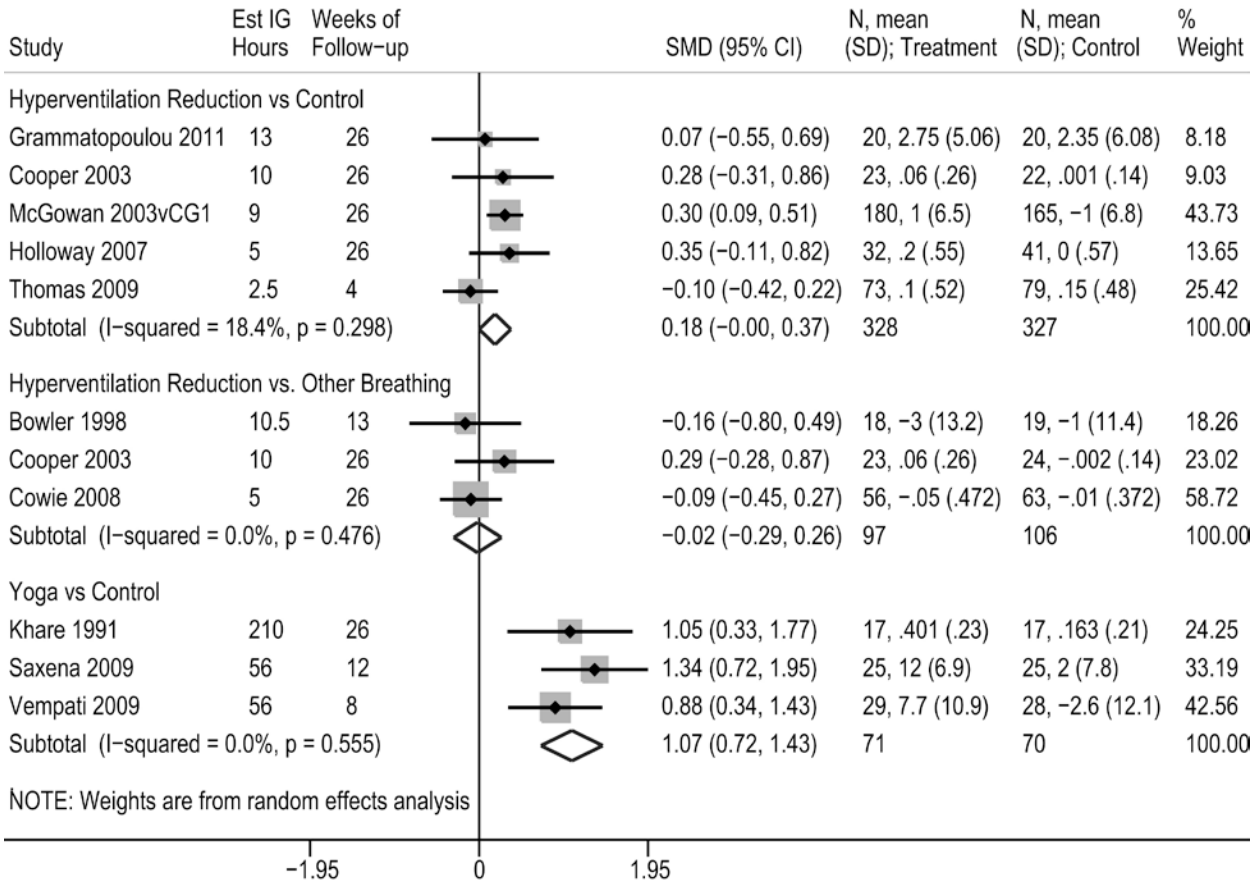
Hyperventilation Reduction Breathing Techniques Versus Control Group

Key Points:

- Evidence is moderate that hyperventilation reduction breathing techniques do not improve lung function in adults.

Seven of the eight hyperventilation reduction trials reported one or more pulmonary function outcomes, primarily FEV_1, FVC, and PEF at 4 to 52 weeks (Table 4; Appendix D, Evidence Table 1f).[51,52,54-57,59] The standardized pooled effect size of five trials that could be combined showed minimal impact of hyperventilation reduction techniques on FEV_1 (SMD=0.18, 95% CI, 0.00 to 0.37, I^2=18.4%, Figure 5).[52,54-56,59] Absolute changes in the interventions in these groups were small, for example improvements of 20 milliliters or less in FEV_1 or less than 2 percent improvement in percent predicted of FEV_1. The two trials that could not be pooled were the video-based interventions with matched-intensity control video for comparison, and the mouth-taping trial. Both found no effect of the intervention on FEV_1.[51,57]

Figure 5. Effect of breathing retraining for asthma on pulmonary function at 1 to 6 months



CG: control group; CI: confidence interval; est: estimated; IG: intervention group; N: sample size; SD: standard deviation; SMD: standardized mean difference

Group differences were only found in one trial, and only when compared to one of the two control groups.[56] In this trial, percent predicted FEV_1 increased from 80 to 81 percent in the Buteyko group while dropping from 75 to 74 percent in the nurse education control group. However, the lower-intensity control group of asthma education only (which was not included in the meta-analysis) did not show a drop and did not differ from the Buteyko group in change from baseline.

Three trials measured end-tidal CO_2,[54,55,59] which is a specific target of interventions to reduce hyperventilation. Only one trial found group differences, reported at 4, 12, and 26 weeks.[54] Breathing rate was reduced in two of these trials, which suggests that participants did modify their breathing as instructed, but that modification did not always alter the CO_2 levels as hypothesized by the Buteyko method proponents.[54,55]

Hyperventilation Reduction Breathing Techniques Versus Other Breathing Techniques

Key Points:

- Hyperventilation reduction breathing techniques do not differ from other breathing techniques in terms of effect on pulmonary function in adults, but the evidence to support this is low.

All four trials in this group reported on change in FEV_1 at 13 to 28 weeks (Appendix D, Evidence Table 2f). None found group differences, and there was little change within groups in any trials. The standardized pooled effect size of the three trials that provided sufficient data for analysis was -0.02 (95% CI, -0.29 to 0.26, I^2=0.0%, Figure 5).[50,52,53] Only one trial reported PEF, and found no group differences.[50] Other measures of pulmonary function similarly showed no group differences including end-tidal CO_2,[50,58] provocative dose of methacholine causing 20 percent reduction in FEV_1,[52] and FVC.[58] One trial did find that those undergoing Buteyko breathing technique had lower minute volume, a specific target of hyperventilation-reduction approaches, than those being trained in abdominal breathing.[50] Thus, participants did modify their breathing in a manner consistent with the Buteyko breathing technique approach, but this change did not alter the amount of CO_2 in their exhalation, which suggests that CO_2 levels may not be an important trigger for asthma as suggested by Buteyko breathing technique proponents.

Yoga Breathing Versus Control

Key Points:

- Yoga breathing techniques may improve pulmonary function in adults, but the evidence to support this is low.

Neither of the U.S.-based trials improved pulmonary function outcomes,[61,62] despite the positive effects on other outcomes for the comprehensive naturopathic treatment program (Table 6; Appendix D, Evidence Table 3f).[61] However, intensive yoga training in India resulted in substantial improvements in pulmonary function with a standardized pooled effect size for these three trials of 1.07 (95% CI, 0.72 to 1.43 I^2=0.0%, Figure 5).[60,63,64] The trial with the largest effect (and the greatest quality concerns) showed improvement in percent predicted FEV_1 of 12 percentage points, compared with only two percentage points in the control group.[63] The best-quality trial of the three Indian trials reported improvements of 7.7 percentage points in the intervention group on percent predicted FEV_1 compared with a 2.6 percentage point reduction in the control group at eight-week followup.[64] Group differences were also found on FVC,[60] FEV_1/vital capacity (VC) ratio,[60,64] and PEF readings[60,63,64] in the trials conducted in India, but not in those conducted in the United States.[61,62] Only one of the trials reported that outcomes assessment was blinded.[62] None of the trials described training or quality assurance measures for the spirometry technicians, and only one provided any detail about spirometry procedures beyond naming the machine that was used. The best-quality intensive India-based trial[64] reported taking the best of three FEV_1 readings, in accordance with ATS standards.[11]

Inspiratory Muscle Training Versus Control

Key Points:

- Evidence is insufficient to determine whether IMT improves pulmonary function in adults and children.

Results from IMT trials were mixed and could not be pooled due to substantial differences in population, setting, and treatment approach in the three trials reporting the same outcome. Treatment-naïve Brazilian children with previously uncontrolled asthma improved PEF readings by an average of 80 percent after 3 months of IMT training along with asthma medication management and education, compared to almost no change on average in those receiving medication and asthma education alone (Table 7; Appendix D, Evidence Table 4f).[65] Lack of improvement in the control group suggests that medication management may have been suboptimal in this group. Among adults, two trials showed improvements in both FEV_1 and FVC, one with the use of an IMT device,[67] and the other using weights placed on the abdomen while in a semi-recumbent position.[66] Another trial found no differences in FEV_1.[68]

Other Nonhyperventilation Reduction Breathing Techniques Versus Control

Key Points:

- Evidence is insufficient to determine whether other nonhyperventilation reduction techniques improve pulmonary function in adults and children.

Spirometry results did not change over time in either the trial of prolonged exhalation using a training device[52] or in any of the treatment groups in the biofeedback trial (Appendix D, Evidence Table 5f).[70]

Key Question 2a. Does the efficacy and/or effectiveness of breathing techniques for other asthma outcomes differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?

Key Points:

- Evidence is insufficient to determine whether patient characteristics influence the effect of treatment on pulmonary function in adults and children.

The best-quality trial of yoga conducted in India displaying large benefits of treatment reported that participants with exercise-sensitive asthma showed a greater improvement on FEV_1 than those whose asthma was not sensitive to exercise.[64] This analysis did not appear to be planned a priori, nor did the intervention particularly target factors that purported to differentially affect those with exercise-sensitive asthma. No other trials reported subgroup analyses for any pulmonary function outcomes.

Key Question 2b. Does the efficacy and/or effectiveness of breathing techniques for other asthma outcomes differ according to variations in implementation (e.g., trainer experience) and/or nonbreathing components of the intervention (e.g., anxiety management)?

Key Points:

- Evidence is insufficient to determine whether certification and/or training of the provider affects effect size in hyperventilation reduction trials.

- Exploratory analyses suggest that control groups that involved either an alternate breathing approach or a technique to reduce autonomic arousal may reduce the likelihood of finding group differences in adults.

Benefits were more likely to be seen if the control group did not involve breathing training of any kind or relaxation techniques (42% positive vs. 14% positive with breathing/relaxation comparison group). These data are preliminary, however, and only valid for hypothesis generation and did not account for effect size.

Key Question 3. What is the nature and frequency of serious adverse effects of treatment with breathing exercises and/or retraining techniques, including increased frequency of acute asthma exacerbations?

Key Points:

- Hyperventilation reduction breathing techniques do not appear to be associated with any harms in adults, other than minor annoyances associated with mouth taping at night, but the evidence to support this is low.
- Yoga breathing techniques do not appear to be associated with any harms in adults, but the evidence to support this is low.
- There was no evidence on harms associated with IMT or other non-hyperventilation reduction approaches in adults or children.

Seven trials reported on adverse events,[51,53,55,57,58,61,62] five of which examined a hyperventilation reduction approach compared with either a control or another breathing retraining approach,[51,53,55,57,58] and two examined yoga interventions.[61,62] Three of the seven studies (including one yoga trial[62]) noted that there were no adverse events or harms that occurred in either the intervention or control group over 16 to 52 weeks of intervention and followup.[53,55,62] One study of a Buteyko breathing technique intervention, compared to a relaxation control group, noted that one hospitalization occurred with one member of the control group.[57] Another study comparing a Buteyko breathing technique intervention delivered by video with a placebo intervention involving nonspecific upper body mobility exercises reported 138 adverse events in the Buteyko breathing technique group and 121 in placebo group, none of which was considered to be related to treatment.[58] The trial of comprehensive naturopathic treatment reported mild headache, fatigue, and/or nausea, which they attributed to the use of the supplements and not yoga.[61] In the study focused on the effect of a nighttime mouth-taping intervention, participants reported problems related to the intervention including it being uncomfortable, causing sore lips, making breathing more difficult, feeling unnatural, decreasing sleep quality, causing a feeling a suffocation, or was embarrassing.[51]

Key Question 3a. Do the safety or adverse effects of treatment with breathing techniques differ between different subgroups (e.g., adults/children; males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions)?

Key Points:

- There was no evidence on whether patient characteristics influenced the likelihood of experience harm in adults or children from any treatment included in the review.

No trials examined harms of treatment within subgroups or compared subgroups on likelihood of harms.

Table 4. Overview of results: hyperventilation reduction breathing techniques versus control

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma sx	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality¶	Applicability to U.S. Health Care Setting
Grammatopoulou 2011[54]	26w	IG	20	Diaphragm, nasal breathing; short pause	13	NR	NR	83.7	↓				↔		++	Conducted in Greece, limited to those with mild or moderate asthma
		CG	20	Usual care	NR											
Cooper 2003[52]	26w	IG1	30	BBT†	10	2 puffs/d‡	657	80	↓ ↔	↓	↔	↔	↔		++	Conducted in the UK, used certified BBT practitioner
		CG	29	Sham device	NR, 1 session											
McGowan[56,99]	26w	IG	200	BBT	2h + 7 sessions	18 puffs/w	NR	76.7	↓↓ (vs each group)	↓↓ (vs each group)	↓↓ (vs each group)		↑ ↔		++	Conducted in Scotland, used certified BBT practitioner
		CG1	200	Nurse education	2h + 7 sessions											
		CG2	200	Brief asthma education	2h											
Holloway 2007[55,72]	52w	IG	39	Papworth§	5	NR	NR	89.6	↓↓				↔	↔	++	Conducted in the UK, used respiratory therapist
		CG	46	Usual care	NR											
Opat 2000[57,77]	4w	IG	18	BBT video	19.8	404 mcg/d	430	NR	↔	↓	↔	↑		↔	++	Conducted in Australia, all-volunteer sample
		CG	18	Landscape video	18.6											

Table 4. Overview of results: hyperventilation reduction breathing techniques versus control (continued)

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma sx	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality¶	Applicability to U.S. Health Care Setting
Thomas 2009[59,79-81]	26w	IG	94	HRBT	2-2.5	1.4 dose/d	400‡	89.5	↔	↔**	↔**	↑	↔ **		++	Conducted in the UK
		CG	89	Asthma education	2-2.5											
Thomas 2003[71,78,82]	26w	IG	17	HRBT	1.25	1.5 can/ 3m	600	NR	↓ ↔ ††	↔	↔	↑ ↔ ††			++	Conducted in the UK, limited to those with Nijmegen scores suggestive of dysfunctional breathing
		CG	16	Asthma education session	1											
Cooper 2009‖[51,75,89]	4w	IG	51	Mouth-taping	NA	10 puffs/w‡	567	86.2	↔	↔		↔		↔	++	Conducted in the UK
		CG		Usual care	NA											

BBT: Buteyko breathing technique; can: canister(s); CG: control group; d: day(s); FEV_1: forced expiratory volume in 1 second; h: hour(s); ICS: inhaled corticosteroids; IG: intervention group; mcg: microgram(s); med: medication; NA: not applicable; NR: not reported; PEF: peak expiratory flow; QoL: quality of life; SABA: short-acting $beta_2$-agonists; sx: symptoms; UK: United Kingdom; w: week(s)

*Time to longest followup

†Also included dietary restrictions, stress management and instruction to avoid oversleeping

‡Median

§Also includes stress management

‖Crossover study design, mouth-taping and control phases¶All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

**Outcome was assessed at 4 weeks only

††Statistically significant only at 4w followup

↑: Intervention group shows greater improvement than control group, small to moderate effect

↑↑: Intervention group shows greater improvement than control group, large effect (standardized ES >0.8, absolute change from baseline of 50% or more in intervention group and 10% or less in the control group, or comparable)

↔: Trial shows no consistent differences between groups

↑↔: Mixed results

Table 5. Overview of results: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma Sx or Control	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality	Applicability to U.S. Health Care Setting
Cooper 2003[52]	26w	IG1	30	BBT†	10	2 puffs/d‡	657	80	↔	↓BBT	↔	↔	↔		++	Conducted in the UK, used certified BBT practitioner, used device that may not be widely available
		IG2	30	Yoga breathing device	NR, 1 session, practice 6m											
Bowler 1998[50,73,88]	13w	IG1	19	BBT sessions	7-10.5 or more	892 mcg/d	1250	74	↔	↓BBT	↔	↔	↔	↔	+	Conducted in Australia, all volunteer sample, used certified BBT practitioner, high levels of baseline asthma medication use
		IG2	20	Abdominal breathing, asthma education	7-10.5											
Cowie 2008[53]	26w	IG1	65	BBT sessions	NR, 5 sessions	NR	840	81	↔		↓BBT	↔§	↔		++	Conducted in Canada, university setting, used certified BBT practitioner, used certified physical therapist
		IG2	64	Physical therapy sessions	NR, 5 sessions											

Table 5. Overview of results: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques (continued)

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma Sx or Control	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality	Applicability to U.S. Health Care Setting
Slader 2006[58]	28w	IG1	28	BBT video	90	3 puffs/d	NR	80	↔§	↔§	↔§	↔	↔		+++	Conducted in Australia, limited to those with moderate to severe asthma, low baseline scores on mood domains on QoL questionnaire, conducted in research setting
		IG2	29	Video-based controlled breathing, mobility and stretching	90											

BBT: Buteyko breathing technique; CG: control group; d: day(s); FEV_1: forced expiratory volume in 1 second; h: hour(s); ICS: inhaled corticosteroids; IG: intervention group; mcg: microgram(s); med: medication; NA: not applicable; NR: not reported; PEF: peak expiratory flow; QoL: quality of life; SABA: short-acting $beta_2$-agonists; sx: symptoms; UK: United Kingdom; w: week(s)

*Time to longest followup

†Also included dietary restrictions, stress management and instruction to avoid oversleeping

‡Median puffs per day, typical dose per puff = 100 mcg

§No difference between groups but both groups showed improvement

‖All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

↑: Intervention group shows greater improvement than control group, small to moderate effect

↑↑: Intervention group shows greater improvement than control group, large effect (standardized ES >0.8, absolute change from baseline of 50% or more in intervention group and 10% or less in the control group, or comparable)

↔: Trial shows no consistent differences between groups

↑↔: Mixed results

Table 6. Overview of results: yoga breathing techniques versus control

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma Sx	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality	Applicability to U.S. Health Care Setting
Khare 1991[60]	26w	IG	17	Daily yoga	210	NR	NR†	NR	↓		↓‡		↑	↑↑	+	Conducted in India, limited to male vegetarians age 25 to 50, standard of care did not include ICS
		CG	17	Usual care	NR											
Vempati 2009[64,74,83-87]	8w	IG	30	Yoga practice and lectures§	56	2.1 puffs/d¶	339**	66	↓	↓↓		↑↑	↑↑	↑	++	Conducted in India, mild to moderate asthma only
		CG	30	Usual care	NR, 1 session											
Kligler 2011[61]	26w	IG	77	Yoga breathing††	6-9	NR	NR	NR	↓			↑	↔		+	Self-identified sample, intervention included dietary change, supplements and journaling
		CG	77	Usual care	NR											

Table 6. Overview of results: yoga breathing techniques versus control (continued)

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma Sx	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality	Applicability to U.S. Health Care Setting
Saxena 2009[63]	12w	IG	25	Yoga breathing exercise	56	NR	NR	72	↓↓				↑↑	↑↑	+	Conducted in India, limited to those with 26w experience with yoga and no regular use of medication (or advised to discontinue medication if using)
		CG	25	Meditation	56											
Sabina 2005[62]	16w	IG	29	Yoga class	12	1 puffs/d	NR	NR	↔	↔		↔	↔	↔	++	Mild to moderate asthma only, all self-identified sample, conducted in research setting
		CG	33	Stretching class	12											

CG: control group; d: day(s); FEV_1: forced expiratory volume in 1 second; h: hour(s); ICS: inhaled corticosteroids; IG: intervention group; mcg: microgram(s); med: medication; NA: not applicable; NR: not reported; PEF: peak expiratory flow; QoL: quality of life; SABA: short-acting $beta_2$-agonists; sx: symptoms; w: week(s)

*Time to longest followup

†19/34 (56%) "disturbed sleep and dyspnea on daily routine work which was relieved by oral drugs"; 8/34 (24%) "asthma required injection frequently to control dyspnea or admission to hospital"

‡Reduction in dose to "control dyspnea," type of medication not specified

§Also includes dietary advice, instruction on cleansing techniques, meditation and relaxation

‖All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

¶Includes 11 with missing data, unclear if nonusers or simply missing

**Includes 25 with missing data, unclear if nonusers or simply missing
††Also include dietary advice
↑: Intervention group shows greater improvement than control group, small to moderate effect
↑↑: Intervention group shows greater improvement than control group, large effect (standardized ES >0.8, absolute change from baseline of 50% or more in intervention group and 10% or less in the control group, or comparable)
↔: Trial shows no consistent differences between groups
↑↔: Mixed results

Table 7. Overview of results: inspiratory muscle training versus control

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma sx	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality†	Applicability to U.S. Health Care Setting
Lima 2008[65]	13w	IG	25	IMT, meds and asthma education	14.6	NR	NR	NR	↓↓	↓↓				↑↑	+	Conducted in Brazil, limited to 8- to 12-year-old children with untreated, uncontrolled asthma
		CG	25	Meds, asthma education	3											
Shaw 2011[66,91]	8w	IG	22	Abdominal strengthen-ing	NR	NR	NR	NR					↑↑		+	Conducted in South Africa, only moderate-persistent asthma
		CG	22	Usual care	NR											
Weiner 1992[67]	26w	IG	15	IMT	60	6 puffs/d	NR	59	↓	↓↓			↑↑		++	Conducted in Israel, moderate to severe asthma only
		CG	15	Sham device	60											

Table 7. Overview of results: inspiratory muscle training versus control (continued)

Study	Followup*	Group	N Randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma sx	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality†	Applicability to U.S. Health Care Setting
Weiner 2002[68]	20w	IG	11	IMT	60	3.2 puffs/d	NR	83		↔ ↓			↔		+	Conducted in Israel, limited to females with mild to moderate asthma
		CG	11	Sham device	60											
Weiner 2000[69]	13w	IG	12	IMT	36	2.7 puffs/d	NR	91		↔ ↓					+	Conducted in Israel
		CG	11	Sham device	36											

CG: control group; d: day(s); FEV_1: forced expiratory volume in 1 second; h: hour(s); ICS: inhaled corticosteroids; IG: intervention group; IMT: inspiratory muscle training; mcg: microgram(s); med: medication; NA: not applicable; NR: not reported; PEF: peak expiratory flow; QoL: quality of life; SABA: short-acting $beta_2$-agonists; sx: symptoms; w: week(s)

*Time to longest followup

†All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

↑: Intervention group shows greater improvement than control group, small to moderate effect

↑↑: Intervention group shows greater improvement than control group, large effect (standardized ES >0.8, absolute change from baseline of 50% or more in intervention group and 10% or less in the control group, or comparable)

↔: Trial shows no consistent differences between groups

↑↔: Mixed results

Table 8. Overview of results: nonhyperventilation reduction breathing techniques versus control

Study	Followup*	Group	N randomized	Description	Intensity (Total Hours)	Baseline SABA Use	Baseline ICS Use (mcg/d)	Baseline FEV_1 (L)	Asthma sx	Reliever Med Use	Controller Med Use	QoL	FEV_1	PEF	Quality¶	Applicability to U.S. Health Care Setting
Lehrer 2004[70,76,90]	12w	IG	23	Prolonged exhalation with HRV biofeedback	NR, 10 sessions	NR	NR	NR	↔ §		↔ §		↔ ‖		++	All volunteer sample, strict adherence to NAEPP guidelines with monthly visits, conducted in research setting
		CG1	22	HRV biofeedback	NR, 10 sessions											
		CG2	24	Sham device†	NR, 10 sessions											
		CG3	25	Waitlist	Waited for 30w											
Cooper 2003[52]	26w	IG2	30	Prolonged exhalation device	NR, 1 session, 6m practice	2 puffs/d ‡	657	80	↔	↔	↔	↔	↔		++	Conducted in the UK, used device that may not be widely available
		CG	29	Sham device	NR, 1 session											

CG: control group; d: day(s); FEV_1: forced expiratory volume in 1 second; h: hour(s); HRV: heart rate variability; ICS: inhaled corticosteroids; IG: intervention group; mcg: microgram(s); med: medication; NA: not applicable; NAEPP: National Asthma Education and Prevention Program; NR: not reported; PEF: peak expiratory flow; QoL: quality of life; SABA: short-acting $beta_2$-agonists; sx: symptoms; UK: United Kingdom; w: week(s)

*Time to longest followup

†Includes practice (but with no instruction) of maintaining a state of relaxed alertness, classical music tapes

‡Median

§No differences between biofeedback groups with and without breathing retraining component; both of these groups did differ from either the sham device and waitlist groups

‖No differences in "spirometry", specific measures NR

¶All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

↑: Intervention group shows greater improvement than control group, small to moderate effect

↑↑: Intervention group shows greater improvement than control group, large effect (standardized ES >0.8, absolute change from baseline of 50% or more in intervention group and 10% or less in the control group, or comparable)

↔: Trial shows no consistent differences between groups

↑↔: Mixed results

Table 9. Instruments used for measuring asthma symptoms, control, quality of life, or related outcomes

Outcome Measure	Instrument	Number of Items	Range	Directionality (Higher score = better or worse)	Constructs Measured, Subscales	Number of Included Studies Using Instrument
Symptom, Severity, or Control	Asthma Control Questionnaire (ACQ)[100]	7	0-6	Worse	Symptoms, beta$_2$-agonist use, pulmonary function (FEV_1)	3
	Asthma Control Diary (ACD)[101]	8	0-6	Worse	Morning score: PEFR, awakenings, symptom severity; Bedtime score: activity limitations, shortness of breath, wheezing, bronchodilator use, PEF	1
	Physician / Patient Global Assessment for Asthma Control	NR	0-100	Better	Not described	1
	Asthma Control Test (ACT)[96]	22	1-5	Worse	Symptoms and control, activity, health care use	1
Asthma-Related Quality of Life	St. George's Respiratory Questionnaire (SGRQ)[102]	76	0-100	Worse	Symptoms, activity, impacts	1
	Asthma Quality of Life Questionnaire (AQLQ-Marks)[103]	20	0-4	Worse	Breathlessness and physical restriction, mood disturbance, social disruption, concern for health	5
	Mini-Juniper Quality of Life Questionnaire (Mini-Juniper)[46]	15	1-7	Better	Overall quality of life, symptom severity, environment impact on asthma, emotional impact of asthma, activity limitations	5
	Asthma Quality of Life Questionnaire (AQLQ-Juniper)[47]	32	1-7	Better	Symptoms, emotions, environment, physical activities, practical problems	3
Dysfunctional Breathing	Nijmegen Questionnaire[104]	16	1-5	Worse	Hyperventilation syndrome (chest pain, feeling tense, blurred vision, dizzy spells, feeling confused, faster or deeper breathing, short of breath, tight feelings in chest, bloated feeling in stomach, tingling fingers, unable to breathe deeply, stiff fingers or arms, tight feelings round mouth, cold hands or feet, palpitations, feeling of anxiety)	5
General Functioning and Quality of Life	Short-form (SF-36) Health Survey[105]	36	0-100	Better	Vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health	3*
Mental Health	Hospital Anxiety and Depression Scale (HADS)[106]	14	0-3	Worse	Anxiety, depression	2

FEV_1: forced expiratory volume in 1 second; PEF: peak expiratory flow: PEFR: peak expiratory flow rate
*Includes one study that used the SF-12

Table 10. Quality and applicability issues: hyperventilation reduction breathing techniques versus control

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applic-ability to U.S. Health Care Settings
Cooper 2003[52]	RCT	26w	IG1 (BBT)	30	77%	NR	Yes	Yes	Likely*	LOCF	++	Unclear which baseline differences were controlled for, many comparisons on small number of participants	Conducted in the UK, used certified BBT practitioner
			CG	30	80%								
Grammato-poulou 2011[54]	RCT	26w	IG (HRBT)	20	100%	Yes	Yes	NR	NR	NA	++	Assessment of asthma dx not described; Exclusion for other respiratory d/o NR, but did exclude smokers and those age ≥60	Conducted in Greece, only 14% of those sent invitation were randomized (recruited from attendees of asthma department)
			CG	20	100%								
Holloway 2007[55,72]	RCT	26w	IG (Pap-worth)	39	85%	NR	No	U	Likely*	None	++	More smokers in IG but smoking not controlled for in analysis; PFT for confirmation unclear, recruited from registry	Conducted in the UK, used respiratory therapist
			CG	46	98%								
		52w	IG	39	82%								
			CG	46	87%								

Table 10. Quality and applicability issues: hyperventilation reduction breathing techniques versus control (continued)

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applic-ability to U.S. Health Care Settings
McGowan 2003[56,99]	RCT	26w	IG (BBT)	200	90%	Yes	Yes	Yes	Yes	None	++	Specific use of spirometry to determine asthma dx not described; no description of refusals or exclusions prior to randomization	Conducted in UK, used Registered BBT practitioner
			CG1 (Nurse Ed)	200	82.5%								
			CG2 (Intro ed)	200	73.0%								
Opat 2000[57,77]	RCT	4w	IG (BBT)	18	89%	U	NR	No	NR, but age limited to ≤50	None	++	Allocation concealed from participant, NR if concealed from research staff	Conducted in Australia, all-volunteer sample
			CG	18	89%								
Thomas 2009[59,79-81]	RCT	4w	IG (HRBT)	94	78%	Yes	U	NR	Yes	LOCF	++	Blinding of nonself-report outcomes NR	Conducted in the UK
			CG	89	89%								
		26w	IG	94	67%‡								
			CG	89	74%‡								

Table 10. Quality and applicability issues: hyperventilation reduction breathing techniques versus control (continued)

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applic-ability to U.S. Health Care Settings
Thomas 2003[71,78,82]	RCT	26w	IG (HRBT)	17	94%	NR	NR	Yes	NR	None	++		Conducted in the UK, limited to those with Nijemegen scores suggestive of dysfunctional breathing
			CG	16	75%								
Cooper 2009[51,75,89]	Cross-over RCT	4w	IG (mouth-taping)	51‖	98%	NR	Yes	Yes	Likely*	None	++	Handling of other respiratory illness NR, but did exclude those with	Conducted in the UK
			CG										

BBT: Buteyko breathing technique; CG: control group; d/o: disorder(s); HRBT: hyperventilation reduction breathing technique; IG: intervention group; LOCF: last observation carried forward; NR: not reported; PFT: pulmonary function test; RCT: randomized controlled trial; resp: respiratory; U: unclear; UK: United Kingdom; US: United States; w: week(s)

*Did not specifically report excluding those with other respiratory disorders, but did report excluding those with other disorders without listed the specific disorders excluded.

† All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

‡Followup at 26w only measured for quality of life

‖Crossover study design, mouth-taping and control phases

Table 11. Quality and applicability issues: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applicability to U.S. Health Care Settings
Bowler 1998[50,73,88]	RCT	13w	IG1 (BBT)	19	95%	Yes	NR	No	Likely*	None	+	IG1 more intensive	Conducted in Australia, all volunteer sample, used certified Buteyko practitioner, high levels of baseline asthma medication use
			IG2 (abdom. breathing)	20	95%								
Cooper 2003[52]	RCT	26w	IG1 (BBT)	30	77%	NR	Yes	Yes	Likely*	LOCF	++	Unclear which baseline differences were controlled for	Conducted in the UK, used certified Buteyko practitioner for BBT intervention, used device that may not be widely available for yoga breathing device comparator
			IG2 (yoga breathing device)	30	73%								

Table 11. Quality and applicability issues: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques (continued)

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applicability to U.S. Health Care Settings
Cowie 2008[53]	RCT	26w	IG1 (BBT)	65	86%	Yes	NR	Yes	Yes	None	++	Did not report $beta_2$-agonist, use as outcome, but did report other medications; concern about reporting bias	Conducted in Canada, university setting, used certified Buteyko practitioner for BBT intervention, certified physical therapist of physical therapy intervention
			IG2 (physio-therapy)	64	98%								
Slader 2006[58]	RCT	28w	IG (BBT)	28	82%	Yes	Yes	Yes	No, but limited to non-smokers with ≤ 10 pack-years	None for 28w	+++		Conducted in Australia, limited to those with moderate to severe asthma, low baseline scores on mood domains on quality of life questionnaire, conducted in research setting.
			IG2 (controlled breathing)	29	86%								

abdom: abdominal; BBT: Buteyko breathing technique; d/o: disorder(s); IG: intervention group; LOCF: last observation carried forward; NR: not reported; PFT: pulmonary function test; RCT: randomized controlled trial; UK: United Kingdom; US: United States; w: week(s)

*Did not specifically report excluding those with other respiratory disorders, but did report excluding those with other disorders without listed the specific disorders excluded.

†All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

Table 12. Quality and applicability issues: yoga breathing techniques versus control

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applicability to U.S. Health Care Settings
Khare 1991[60]	RCT	26w	IG (yoga breathing)	17	100%	NR	NR	NR	Yes	NA	+	No description of refusals or exclusions prior to randomization	Conducted in India, limited to male vegetarians age 25 to 50, standard of care did not include ICS
			CG	17	100%								
Kligler 2011[61]	RCT	26w	IG (yoga)	77	87	U	No	NR	NR	Yes, RER	+	Did not limit to those without recent oral steroid use, no description of refusals or exclusions prior to randomization	Self-selected participants, Included dietary and journaling treatment components
			CG	77	80								
Sabina 2005[62]	RCT	16w	IG (yoga breathing)	29	79%	Yes	Yes	Yes	Yes	Yes, Method NR	++	None	Mild to moderate asthma only, self-selected sample, conducted in research setting
			CG	33	67%								
Saxena 2009[63]	RCT	12w	IG (yoga breathing)	25	NR	NR	NR	Yes	Yes	NR	+	Randomization procedures likely not truly random, no description of refusals or exclusions prior to randomization	Conducted in India, limited to those with 26w experience with yoga, limited to those with no regular use of medication or advised to discontinue medication if using
			CG	25	NR								

Table 12. Quality and applicability issues: yoga breathing techniques versus control (continued)

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applicability to U.S. Health Care Settings
Vempati 2009[64,74,83-87]	RCT	8w	IG (yoga breathing)	30	97%	NR	NR	Yes	Yes	None	++	None	Conducted in India, mild to moderate asthma only
			CG	30	93%								

CG: control group; d/o: disorder(s); ICS: inhaled corticosteroids; IG: intervention group; LOCF: last observation carried forward; NA: not applicable; NR: not reported; PFT: pulmonary function test; RCT: randomized controlled trial; RER-Random Effects Regression model; UK: United Kingdom; US: United States; w: week(s)
*Did not specifically report excluding those with other respiratory disorders, but did report excluding those with other disorders without listed the specific disorders excluded.
†All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

Table 13. Quality and applicability issues: inspiratory muscle training versus control

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applicability to U.S. Health Care Settings
Lima 2008[65]	RCT	13w	IG (IMT)	25	100%	NR	NR	No	NA	NA	+	Assessment of symptoms and medication use not described	Conducted in Brazil, limited to 8- to 12-year-old children with untreated, uncontrolled asthma
			CG	25	100%								
Shaw 2011[66,91]	RCT	8w	IG (abdom-inal strength-ening)	22	100%	NR	NR	Yes	NR	NA	+	Did not report asthma sx or medication use, no description of refusals or exclusions prior to randomization	Conducted in South Africa, did not describe recruitment source, did not describe baseline asthma sx, or med use, University setting with average age 21
			CG	22	100%								
Weiner 1992[67]	RCT	26w	IG (IMT)	15	100%	NR	Yes	Yes	NR	NA	++	Did not provide detailed inclusion /exclusion rules; noted that "most patients in the control group became gradually aware of the fact that they were using a sham device," no description of refusals or exclusions prior to randomization	Conducted in Israel, limited to those with moderate to severe asthma
			CG	15	100%								

Table 13. Quality and applicability issues: inspiratory muscle training versus control (continued)

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those With Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns or Clarifications	Factors Limiting Applicability to U.S. Health Care Settings
Weiner 2000[69]	RCT	26w	IG (IMT)	12	92%	NR	NR	Yes	NR	None	+	Did not provide detailed inclusion /exclusion rules; no information on baseline comparability of groups	Conducted in Israel, limited to those with > 1 puff/d beta$_2$-agonist consumption
			CG	11	100%								
Weiner 2002[68]	RCT	20w	IG (IMT)	11	91%	NR	Yes	Yes	NR	None	+	Did not provide detailed inclusion /exclusion rules; no information on baseline comparability of groups, no description of refusals or exclusions prior to randomization	Conducted in Israel, limited to females with mild to moderate asthma
			CG	11	82%								

*Did not specifically report excluding those with other respiratory disorders, but did report excluding those with other disorders without listed the specific disorders excluded.
†All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw
abdom: abdominal; CG: control group; d/o: disorder(s); IG: intervention group; IMT: inspiratory muscle training; NA: not applicable; NR: not reported; PFT: pulmonary function test; RCT: randomized controlled trial; US: United States; w: week(s)

Table 14. Quality and applicability issues: other nonhyperventilation reduction breathing techniques versus control

Study	Study Design	Followup	Group	N Randomized	Retention	Allocation Concealment	Blinding of Outcomes Assessment	PFT for Asthma Confirmation	Excluded Those w/ Other Resp. d/o	Handling of Missing Data	Overall Quality Rating†	Other Quality Concerns Or Clarifications	Factors Limiting Applicability to U.S. Health Care Settings
Cooper 2003[52]	RCT	26w	IG2 (yoga breathing device)	30	73%	NR	Yes	Yes	Likely*	LOCF	++	Unclear which baseline differences were controlled for	Conducted in the UK, used device that may not be widely available
			CG	30	80%								
Lehrer 2004[70,76,90]	RCT	12w	IG (abdom. breathing with biofeed-back	23	74%	NR	Yes	Yes	Yes	LOCF	++	No description of refusals or exclusions prior to randomization	All volunteer sample, might have higher standard of care since research protocol stipulated strict adherence to NAEPP guidelines with monthly visits, conducted in research setting
			CG1 (biofeed-back)	22	77%								
			CG2 (placebo)	24	79%								
			CG3 (waitlist)	25	92%								

abdom: abdominal; CG: control group; d/o: disorder(s); IG: intervention group; LOCF: last observation carried forward; NAEPP: National Asthma Education and Prevention Program; NR: not reported; RCT: randomized controlled trial; PFT: pulmonary function test; UK: United Kingdom; US: United States; w: week(s)

*Did not specifically report excluding those with other respiratory disorders, but did report excluding those with other disorders without listed the specific disorders excluded.

†All trials were rated "Fair"; further gradation is provided as follows: +++ = Minor quality issues, but not meeting criteria for "Good" quality; ++ = Between +++ and + trials in quality; + = Substantial quality issues, but no clear fatal flaw

Summary and Discussion

Overview of Main Findings

Available evidence suggests that selected intensive behavioral approaches that include breathing retraining exercises may improve asthma symptoms and reduce reliever medication use in motivated adults with poorly controlled asthma. This suggestion, however, was based primarily on evidence from small, methodologically limited trials with widely heterogeneous samples. The evidence was further compromised by the relatively short followup and inconsistent outcome reporting (Table 15). Primary outcomes (symptom reduction and reliever medication use) were also self-reported, making them susceptible to social desirability bias. The largest, most coherent body of evidence for a specific breathing training technique assessed hyperventilation reduction techniques and showed they reduced asthma symptoms and reliever medication use.

Hyperventilation reduction techniques were not found to improve pulmonary function tests as measured by FEV_1 or PEF. Yoga was the only technique with evidence that it may improve pulmonary function and symptoms. However, quality issues in these trials limit confidence in results and applicability to the U.S. health care system was very low. The yoga practiced in these trials was likely more intensive than would available to most patients in the United States, for example 4 hours per day for 2 weeks, or daily 70-minute sessions for 6 months. Additionally, yoga may not have the same cultural significance in the United States as it does in India. Available research on IMT and other breathing retraining techniques was limited to a heterogeneous group of small trials that are best characterized as pilot studies, which provided insufficient evidence to draw conclusions on these interventions' effectiveness.

Programs that included more hours of contact (e.g., 5 or more hours) and that also offered intervention components beyond breathing retraining or advice appeared more likely to be found effective. Trials that matched treatment groups for number of hours of contact were less likely to show benefit than those providing extra hours of contact for the intervention group. This suggests that generic benefits of therapeutic contact (e.g., empathy, encouragement, and self-monitoring techniques) may be important components of treatment. These observations, however, should be considered hypothesis-generating rather than definitive for numerous reasons, including the lack of accounting for effect size and the high heterogeneity on numerous dimensions in these trials, which precludes clear isolation of the effects of any specific elements. Specific mechanisms of action for breathing training may be less important than enhanced self-efficacy, self-monitoring, and anxiety management.

Although interventions could be quite intensive, there was no evidence that breathing techniques are harmful besides minor annoyances associated with mouth taping. Although asthma medications associated with NAEPP guidelines are generally safe and effective, they can be associated with unpleasant or even harmful side effects,[1] so breathing retraining may be worth trying for some patients who are highly motivated to manage asthma symptoms with minimal use of reliever medication. In the United States, results of these trials would likely be most applicable to patients with a high level of motivation, given the fairly high attrition rates in several trials and, in some cases, selected samples.

Evidence was primarily applicable to adults; only a single trial of IMT targeted children (ages 8 to 12 years),[65] and only four other trials included people younger than 16 years of age,[50,53,56,58] all addressing hyperventilation reduction training. It is unlikely that many teens were

included in these trials, however, since, where it was reported, the average participant age was in the forties in these studies. Subgroup analyses of teens and/or emerging adults were not reported.

Hyperventilation Reduction Breathing Retraining Techniques

Hyperventilation reduction techniques had the best evidence base, with 11 efficacy or comparative effectiveness trials. Almost all trials had very small samples, and all had some methodological limitations. The only relatively large-scale trial of any breathing retraining method (n=600 randomized into three groups) investigated the effects of Buteyko techniques and showed substantially larger reductions in both asthma symptoms and reliever medication use in the treatment group, compared to either of two control groups. Retention in the two control groups in this trial, however, was lower in the two control groups than the Buteyko group (90% retention in the Buteyko group vs. 82% in the intensity-matched group vs. 73% in the low-intensity control group at 6 months).[56]

Five of the seven trials that compared comprehensive hyperventilation reduction training with a control or placebo reported reductions in asthma symptoms.[54-56,59,71] The pooled estimate suggested a large effect on asthma symptoms, although only four trials provided sufficient data to be included in the meta-analysis, and statistical heterogeneity was very high. In general, pooled estimates based on few trials are likely to overestimate true effects,[107] and including four trials will provide an estimate that is within 10 percent of the true estimate of effect in only about 50 percent of cases, according to a recent analysis.[108] Thus, the pooled estimate in this case may overestimate the true effect. Of the four trials in the meta-analysis, one was the large trial described above and the other three were limited by either low retention,[59] no report of pulmonary function testing to confirm asthma,[54,59] no report that allocation was concealed,[55] and lack of blinding of outcomes assessment.[55]

Hyperventilation reduction interventions did not show greater reduction in asthma symptoms than interventions involving other breathing techniques. In some cases, both the intervention and controls groups improved, while in others neither group showed improvement.

All but one of the trials that showed improvements in asthma symptoms involved at least 5 hours more of intervention contact for study subjects in the treatment group(s), compared with usual care or control groups. Two trials included additional components not related to breathing.[52,55] As hyperventilation reduction techniques required substantial practice on the part of asthma patients, it is not surprising that extra support was important for patients to master the techniques and maintain their use. On the other hand, greater general support could also explain between-group differences.

Most trials (five of the nine trials reporting reliever medication use) showed greater reductions in reliever medication use with hyperventilation reduction breathing training, compared with either a control group or another breathing approach.[51,52,56,57,59] In most cases, reductions in bronchodilator use generally amounted to an average of 1.5 to 2.5 puffs per day, apparently almost eliminating the use of bronchodilators in two trials.[52,56] In one trial of patients with high medication use (median baseline use was 8.5 to 9.5 puffs per day), intervention participants reduced reliever use by a median of approximately nine puffs/day, compared with a change in only one-half of a puff per day among those using a competing breathing approach.[50] While this finding would be strengthened if the investigators had also demonstrated improvement in asthma symptoms, this trial did not report changes in asthma symptoms in any peer-reviewed publications. Internet-based material identified through our grey literature search, however, qualitatively suggest symptoms improvement in this trial.[109-111] We have concerns that

these data may not be treated as rigorously in internet-based reports as they would be in a peer-reviewed journal, where methods are carefully assessed and statistical significance is generally presented. Regardless of whether these studies found an improvement in daily symptoms, participants were able to dramatically reduce reliever medication use without increasing the risk of a severe exacerbation.[50] One other high-intensity trial reported both symptom medication outcomes and found reductions in both symptoms and reliever medication use.[56] The three trials of the lower-intensity interventions all reported these outcomes and found no consistent group differences for either asthma symptoms or reliever medication use.[57,59,71]

Practitioners that trained patients in hyperventilation-reduction techniques generally coached patients to delay using reliever medication until they tried breathing methods and these techniques failed. Thus, reductions in reliever medication use may reflect intervention compliance or reduction in unnecessary use and may not be the result of improved pathophysiology. Despite uncertainty about causal factors or about coherence of medication and symptom-based outcomes, however, a reduction of 1.5 to 2.5 puffs of reliever medication per day, maintained for up to 6 months, would likely be viewed as clinically significant by most asthma patients. A reduction of nine puffs per day of reliever medication would be considered a large improvement by any standards, although our understanding of the true clinical significance is limited by the fact that they only reported short-term (3-month) outcomes.

Changes in controller medication use and asthma-related quality of life were rarely seen in the hyperventilation reduction trials, and none of these trials consistently reported improvement in pulmonary function, compared with usual care, attention control, or another breathing technique.

The BTS recommends that Buteyko breathing techniques be considered to help patients control asthma symptoms, which would be consistent with our findings.[22] This recommendation was based on three of the trials included in our review,[50,52,57] along with one additional trial that we excluded because it used a relaxation training comparison group.[112] We included seven additional published trials and one unpublished trial, all of which were rated as fair quality, adding 1,145 additional participants. These include trials using hyperventilation reduction techniques that are not specifically limited to Buteyko methods, while the BTS guideline evidence base only included trials of Buteyko breathing training. The additional trials in our review had mixed findings, but generally supported the possible effectiveness of hyperventilation reduction techniques when compared with usual care, but not when compared with two other breathing techniques.

Yoga Breathing Techniques

The breathing techniques used in yoga are different from hyperventilation reduction methods. The techniques studied in the trials of yoga breathing involved deep breathing, sometimes with mechanically narrowed air passages and prolonged exhalation. In contrast, hyperventilation reduction breathing techniques advocate quiet, shallow breathing with breathing-holding. Both yoga and hyperventilation reduction methods, however, advocate the use nasal breathing rather than mouth breathing, and both appear to have the effect of slowing the passage of air in and out of the lungs. It is unclear if the two approaches have similar physiologic effects, so we elected to analyze these interventions separately.

We identified five trials examining yoga breathing techniques. Three very intensive trials were conducted in India, one of which also included dietary advice, cleansing techniques, and meditation. All three reported improvements in asthma symptoms, reductions in medication use,

and improved pulmonary function.[60,63,64] These trials had limited applicability to the U.S. health care system due to cultural differences and populations targeted. All three of these were small studies, one of which included only 8-week outcomes[64] and two trials that included substantial methodological flaws.[60,63] Since pulmonary function tests require maximal effort from the patient to get accurate results, and since technician behavior may affect the likelihood of maximal effort, high-quality training and monitoring of these tests are critical to protect against bias and type I error. Only one of the three studies reporting beneficial effects described pulmonary function test procedures in sufficient detail to provide assurance that test results were reliable.[64]

Of the two trials conducted in the United States,[61,62] one included substantial components in addition to breathing techniques, which makes it impossible to determine the role of yoga breathing methods in the improvements in asthma outcomes.[61] The other trial with good applicability to the United States reported on the efficacy of an eight-session yoga class and showed no differences between those randomized to yoga class compared with those randomized to a stretching class of the same intensity.[62] Based on these findings, yoga does not appear to improve asthma as one might be typically introduced to yoga in the United States.

One trial designed to isolate the effects of yoga breathing exercises (as opposed to a comprehensive yoga program) showed reductions in asthma symptoms and improvement in pulmonary function, but this study had substantial methodological limitations and very limited applicability to the United States as it was conducted in people with at least 6 months of experience with yoga who were not using medications.[63] Two additional trials focused exclusively on using a device to enhance prolonged exhalation, which is consistent with yoga breathing.[52,70] Neither of these trials showed that this breathing approach without any other components improves asthma symptoms, reduces medication use, or improves pulmonary function. This suggests that a broader yoga program is needed to produce a benefit for asthma. How comprehensive of a program is needed to produce an effect, however, remains an open question.

A recent review studies employing yoga for asthma found evidence to be inconclusive among seven included trials. They reported mixed results in trials that were plagued by methodological limitations. We included only two of the trials from their review.[62,64] The remaining trials were excluded because they did not meet our minimum quality criteria,[95,113] were not published in English,[33] used a form of yoga did not appear to include breathing exercises,[114] or were published prior to 1990.[115] The three additional trials that we included were two of the intensive India-based trials[60,63] and one comprehensive program conducted in the United States,[61] all of which did show benefits of treatment.

Some yoga practitioners have emphasized the need for individualized treatment, and that there can be no “asthma” treatment that could be broadly applied.[116] Further, isolating elements such as breathing exercises only may be discouraged by many practitioners. Most of the trials in this review did have a specific protocol of breathing exercise and postures used by all participants, often performed in a group setting. Thus, these trials may underestimate the effect that might be possible if practitioners were able to individualize the treatment.

Inspiratory Muscle Training and Other Nonhyperventilation Reduction Breathing Techniques

This body of evidence does not allow us to draw conclusions about the effectiveness of IMT or nonhyperventilation reduction breathing techniques (three small heterogeneous trials). We only identified five IMT trials,[65-69] three of which were conducted by the same researcher,[67-69]

and all but one[67] had substantial methodological limitations. The best evidence comes from a small trial of 30 Israeli adults with moderate to severe asthma, who averaged six puffs of asthma medication per day at baseline.[67] IMT participants showed greater improvements than those using a sham device, but no differences were seen in the two very similar trials in participants with lower baseline reliever medication use.[68,69] A separate trial by the same author did show that improvements in inspiratory muscle strength, as measure by maximal inspiratory mouth pressure, were correlated with reductions in SABA use, among those undergoing IMT. This trial was not included in this review because it did not report group-specific outcomes.[117]

While the remaining IMT trials showed large group differences for some outcomes, but these were relatively small trials with substantial methodological limitations and low applicability to the United States.[65,66] Our conclusions are consistent with a Cochrane review that concluded evidence was insufficient to determine whether IMT provides clinical benefit to asthma patients.[118]

Specific Versus Nonspecific Effects of the Breathing Techniques

Asthma control may be affected by numerous factors including, psychological (e.g., stress, anxiety, suggestion),[30] physiological (e.g., respiratory infections, exercise), and environmental factors (e.g., allergens, weather). While training in hyperventilation reduction techniques may help improve asthma symptoms and reduce asthma reliever medication use, it is difficult to determine whether improvements could be attributed to the use of the specific techniques espoused for these interventions. Instructing patients to delay the use of reliever medication may be sufficient to reduce reliever medication use, since symptoms may sometimes resolve spontaneously. Thus, rather than directly improving asthma, trials might help participants eliminate unnecessary use of reliever medications, which is still an important positive outcome. Subjective assessment of asthma symptoms is responsive to placebo interventions (e.g., sham acupuncture or a placebo inhaler),[119] and this may be sufficient to improve asthma symptoms in some cases, in addition to the enthusiastic advocacy by a treatment professional and dramatic testimonials. Some trials attempted to control the enthusiastic advocacy of the treatment modality by including comparison groups that involved other, plausible breathing retraining. However, it is difficult to say whether the treatment providers were comparable in their conviction that the techniques would be successful.

Another possibility is that these techniques improved asthma through reduction in anxiety or autonomic arousal. Asthma patients are more likely to have co-morbid anxiety disorders than those in the general population. They are also more likely to show greater bronchoconstriction in response to stress than health controls.[30] Case-series in patients with co-morbid asthma and panic disorder suggest that asthma education plus psychological panic control approaches can reduce asthma symptoms.[120] Participants in the two trials of hyperventilation reduction techniques in this review that measured anxiety did show greater reductions in anxiety scores than control participants.[55,59] However, the clinical significance of these results was questionable because reductions in anxiety were small, participants averaged in the normal range of anxiety at both baseline and followup, and these studies were mixed with regard to asthma outcomes.[55,59] Thus, it seems unlikely that reductions in anxiety in reported in these trials had a substantial impact on the reported asthma outcomes.

Regarding autonomic arousal, a Cochrane review of psychological interventions for adults with asthma included nine trials examining some form of relaxation training, including the trial of biofeedback included in this review.[70] This review's overall conclusion was that there was

insufficient evidence to determine whether psychological therapies improve asthma. A closer look at the subset of trials reporting relaxation training, however, showed reductions in asthma medication use without improvements in asthma symptoms or pulmonary function in a number of trials. Thus, another possibility is that the reductions in reliever medication use that was found in our included trials may be related to reductions in level of autonomic arousal or anxiety, which may also be achieved through the use of relaxation techniques. Another trial (not included in the current review because the intervention was not a breathing retraining technique) using a "Senobi" stretch, which was designed to lower the level of autonomic arousal, similarly found a greater reduction in reliever medication use in participants doing the Senobi stretch three times daily (reduction from baseline of 1.7 uses per week), compared with those doing a forward bend three times daily (reduction of 0.4 uses per week).[121] Many of the hyperventilation reduction trials in this review, however, reported reductions in asthma symptoms as well as medication use, at least among those offering more intensive interventions (5 hours or more of direct instruction). In contrast, the relaxation trials generally only reported improvements in medication use. A small trial (n=34) comparing Buteyko training with relaxation training offers further evidence that hyperventilation reduction methods may provide effects beyond reductions in autonomic arousal. This trial found that while both groups had symptom improvement, these improvement was greater in the Buteyko group.[112] Although this is only a single, small trial, it suggests that Buteyko may have a greater effect than reduced autonomic arousal alone.

While there is some evidence that suggests that the specific effects of hyperventilation reduction techniques may outstrip the non-specific effects of the interventions, alternate hypotheses cannot be definitively ruled out. In particular, the effects of recommending delaying reliever medication use for 5 to 10 minutes while using methods that may reduce anxiety or arousal, bias in outcomes reporting, and the placebo effect. The last is the most troublesome because sources of information widely available via the internet present dramatic claims with great conviction, making the placebo effect difficult to minimize.

It can be very difficult to isolate critical treatment elements in complex interventions, and use of some elements in isolation may underestimate their importance if the components are dependent on each other or interact with each other, or if individuals vary in the degree to which specific components are necessary or sufficient to gain improvements. Thus, critical intervention components often cannot be elucidated, especially in this relatively flawed and heterogeneous body of research.

Strength of Evidence

The strength of the evidence for each outcome is presented by intervention group in Table 15. In most cases, the strength of evidence was insufficient or low. The evidence that hyperventilation reduction breathing techniques can reduce asthma symptoms and reliever medication use was judged to be moderate, as was evidence that hyperventilation reduction techniques are unlikely to improve pulmonary function.

Applicability of the Evidence to U.S. Health Care System

The included trials' applicability to the U.S. setting and health care system was generally low, with trial-specific limitations listed in Tables 4 through 8. Only three of the trials were conducted in the United States.[61,62,70] The hyperventilation reduction trials were primarily conducted in the United Kingdom and Australia, yoga trials were primarily conducted in India, and IMT trials were conducted in Israel, Brazil, and South Africa. Many of these countries have

substantial cultural or economic differences from the United States, and the standard of usual asthma care may differ, as well as availability of practitioners. While having trials conducted in a number of different countries can improve cross-cultural applicability, in this case there are too many competing sources of heterogeneity to be able to identify which components may be transferable across cultures.

Some yoga and IMT trials were even further limited in their applicability to the general U.S. population by limiting samples to males[60] or females only,[68] vegetarians within a fairly narrow age range,[60] people with 6 months of yoga experience and not using medications,[63] and children with untreated asthma.[65] Further, the standard of usual care in some of these trials also appeared to be different from the current U.S. standard of care due to nonuse of controller medications[60,63] or poor success in managing asthma, further limiting our confidence in reported between-group differences.[65]

The hyperventilation reduction trials were primarily conducted in the United Kingdom[51,52,55,56,71] and Australia,[50,57,58] with the addition of one trial conducted in Canada[53] and one trial conducted in Greece.[54] As few studies reported outcomes beyond 6 months, results can only be generalized to short-term outcomes. One trial was limited to participants with dysfunctional breathing,[71] which limits applicability to persons with asthma in general. This was a pertinent subgroup to the intervention offered, however, which provided physical therapy to reduce dysfunctional breathing.

While the included trials were generally conducted in health care settings, these countries have very different health care systems from the United States. Despite the differences in health care systems, however, the BTS guidelines[22] and the NAEPP guidelines[1] both have similar goals for asthma patients in that they advocate the use of controller medications to minimize the use of reliever medication for people with persistent asthma, so asthma treatment is likely fairly similar in the United Kingdom and the United States. Patients with poorly controlled asthma who are motivated to use complementary and alternative methods to minimize their use of medication and avoid overuse of reliever medications may be good candidates to try these techniques, if they can find a practitioner with the requisite expertise.

Finding a qualified provider, however, may not be a straightforward process. The Buteyko breathing technique is the most widely known of the hyperventilation reduction approaches, and is the only one specifically endorsed by the BTS.[22] Additionally, several of the trials of hyperventilation reduction used certified Buteyko practitioners. Websites listing Buteyko practitioners indicate that there were only approximately 50 certified Buteyko practitioners in the United States, practicing in 21 states as of December 2011, and most worked in complementary and alternative medical settings.[122-124]

While many Buteyko providers emphasize the importance of proper training in practitioners, there appears to be some disagreement among practitioners about what constitutes necessary and sufficient training. For example, one group claims to be the only certifying group with the rights to teach the patented Buteyko method outside of Russia and included a warning that practitioners who were not on their list may not be qualified.[122] Indeed, Konstantin Buteyko himself apparently did not approve all training and certifying organizations, and his supporters denounced two of the included trials[50,53] as not using his techniques correctly, despite their report of using trained Buteyko practitioners.[125] The single trial that used interventionists trained by Konstantin Buteyko himself did show the largest effects on medication use and was one of only two trials[55,56] reporting a large effect on asthma symptoms.[56] Regardless of Konstantin Buteyko's opinions, while trials that used certified Buteyko practitioners were more likely to show

reductions in medication use, they were also slightly *less* likely to show improvements in quality of life, compared with hyperventilation reduction trials that did not use certified Buteyko practitioners. Thus, while Buteyko-affiliated organizations strongly advocate for the importance of certification, the evidence does not unequivocally support this.

The evidence supporting yoga breathing techniques is not as strong as that for hyperventilation reduction techniques, and applicability of the evidence is also lower. Thus, there is no evidence to suggest that a typical person in the United States who does not have a strong interest in yoga would be likely to benefit from a yoga-based intervention. However, patients with asthma who are students of yoga and willing to undertake intensive training may find benefits of asthma-targeted practice with a trained yoga practitioner. Evidence for IMT or other breathing retraining approaches is too scant and low in applicability to suggest that asthma patients in the United States would likely find them beneficial.

Limitations

Potential Limitations of Our Approach

A potential limitation of our review is that we limited included studies to English language publications. Previous research has suggested that evidence for complementary and alternative treatments may be biased if non-English publications are excluded.[126] We did examine the abstracts of any non-English publications identified in our searches that may have met inclusion criteria for our review, based on titles. We found only two trials that appeared that they could possibly meet inclusion criteria.[33,34] One of the trials (published in German) compared breathing exercises, yoga, and usual care in 28 participants, finding that breathing exercises improved lung function (FEV_1 and VC), while yoga and usual care did not. Effects on asthma symptoms, medication use, or quality of life were not reported in the abstract, nor in the tables or figures in the full text article.[33] The other study (published in French) examined the effects of physical respiratory rehabilitation and physical training in the form on swimming on lung function, compared with a control group described as "immunotherapy alone." The authors reported greater reduction in bronchial obstruction in children in the active treatment group, but did not report effects on asthma symptoms, medication use, or quality of life.[34]

Some proponents of Buteyko breathing techniques suggested that relevant early studies conducted by Buteyko himself may be only published in Russian. However, we did not find any Russian-language studies with descriptions or titles indicating that they were likely controlled trials conducted by Buteyko on websites devoted to his research. We feel it is very unlikely that the results of this review would be different if we had included trials published in other languages.

Another potential criticism is our exclusion of trials rating as having "poor" methodological quality. While some reviewers may believe that it is important to present all trials of any quality, we felt that if study results did not meet some minimal standard of internal validity then those results could be misleading and should not be presented. We found nine trials that were not included because they did not meet our minimal standards for quality or reporting (Appendix D).[92-95,113,127-130] These trials assessed the effects of hyperventilation reduction breathing techniques,[92-94] nonhyperventilation reduction breathing techniques,[127-130] and yoga.[95,113] One of these trials was a mere mention of a trial of biofeedback involving asthma patients with no actual data.[93] Only three of the trials compared treatment groups statistically[92,95,128] and one of these reported group differences.[92] Threats to validity in these three trials included lack of baseline

comparability, differential dropout between groups, very small numbers of participants, and lack of important information such as assessment methods and dropout. These trials were consistent with the included body of literature in that most trials reported a benefit of some kind on at least one outcome, though a variety of outcomes were reported and preferential reporting of statistically significant outcomes was possible.

We were unable to locate seven articles that may have met inclusion criteria (Appendix D).[131-137] We believe it is likely that most if not all would not have met inclusion criteria for several reasons. None of these trials were included in other reviews of breathing retraining, despite the fact that most of them fell in the search window of at least one other review on this topic. Two were conference abstracts published by authors of trials that were included in this review, so conference abstracts could represent early reports on trials that were already included.[134,135] Another study listed "Anonymous" as the author, so was likely a synopsis of another trial rather than original research.[132] We believe the fact that we found these studies at all is testimony to the thoroughness of our grey literature searching.

We excluded trials that used relaxation training as a comparison group, since the efficacy of relaxation training for asthma is plausible but not established,[138] so interpretation may have been difficult, particularly in the case of no differences between groups. A number of included trials had comparators that could plausibly induce a state of relaxation, such as meditation, stretching, and landscape videos with instruction to use "relaxed breathing." We decided to err on the side of inclusion, which may have biased our review on the side of reduced effect sizes. Others may have chosen to exclude these trials. Also, we included trials that included a relaxation component along with the breathing training intervention, and possibly as a result we could not clarify the role of relaxation or reduced autonomic arousal vs. the role of the breathing training specifically in improving asthma outcomes.

When we had insufficient information to fully evaluate a trial, but had enough information to determine that it would likely meet inclusion criteria, we contacted authors and asked for the specific information we needed in order to complete our inclusion/exclusion determination and quality rating. Thus, we included information received through personal communication with authors, including extensive data received on the large Buteyko trial, which had only been published as a conference abstract at the time of this review.[56] These data did not appear in peer-reviewed publications and are not widely available for verification. However, we felt that it was important to attempt to include all pertinent literature, both published and unpublished, to minimize publication bias and provide the most complete picture of the evidence possible. Quality standards were consistently applied to published and unpublished data. We did not contact authors who provided sufficient data to assign a quality rating and determine pertinent results, even if some data were missing, so these trials might have been at a slight disadvantage when assigned quality ratings. When we contacted authors, we asked only about information necessary to complete our quality rating or clarify data that were unclear to us.

Limitations of the Literature

Clinical and methodological heterogeneity was substantial across the entire body of literature, but in some cases a majority of the trials examining the same treatment approach were similar enough to consider combining them statistically. Due to heterogeneity of outcomes reported and lack of important outcomes in many trials, however, we were only able to perform meta-analyses for selected (not all) intervention approaches and for a limited number of outcomes. Even when comparable outcomes were reported, some trials were left out of the meta-

analysis due to lack of necessary data (usually measures of variability such as standard deviations or confidence intervals). In the end, we were able to combine trials of only two interventions (hyperventilation reduction and yoga breathing training) for only three outcomes: asthma symptoms (hyperventilation reduction approaches vs. control only), quality of life (yoga vs. control only), and pulmonary function testing (for hyperventilation reduction and yoga trials). All pooled data are based on just three to five trials, so pooled results have a high probability of being more the 10 percent off from the true effect estimate.[108]

Finally, there was minimal comparative effectiveness research. Most trials compared a breathing retraining approach with some kind of control group. This was appropriate, given that effectiveness has not been well established for any treatment approaches. Nevertheless, once effectiveness is better established, the ability to compare approaches with each other on effectiveness and acceptability to asthma patients will be useful.

Clinical Implications

NAEPP guidelines advocate a stepwise approach to asthma management, with the goal "to maintain control of asthma with the least amount of medication and hence minimal risk for adverse effects."[1] One of the specific goals of the approach is to have people with asthma require a reliever medications no more than twice per week. Participants in the hyperventilation reduction trials were on average using relievers more frequently than twice per week at the beginning of the trial, generally averaging about two puffs per day or more. While there are flaws in the research, participants were generally successful in reducing reliever medication to a level consistent with NAEPP guidelines, at least in the short term, in most trials that provided a comprehensive approach to hyperventilation reduction breathing retraining, particularly those involving at least five hours of direct instruction. This was achieved without increases in asthma symptoms, exacerbations, or declines in lung function. For people whose asthma is not well-controlled, hyperventilation reduction techniques may provide a low-risk approach to achieve better control and avoid overuse of reliever medications. Participants in the trials were told only to reduce the use of controller medications after consulting their medical providers, and this is a very important safety consideration for all users of these techniques. Inflammation may increase with reduction in controlled medications without the patient realizing it, and lead to exacerbations in the longer term. Hyperventilation reduction techniques may be a useful tool in the larger asthma management toolbox, which also includes medication and other components as needed, such as environmental controls, symptom monitoring, and a plan for handling exacerbations.

While the available evidence base for yoga is not as strong in terms of quality and quantity, there is a small body of evidence suggesting that intensive yoga training may reduce asthma symptoms and improve lung function. Patients who would like to undertake intensive asthma-focused training need not be discouraged, but again should not change their use of asthma medication without consulting with their medical provider.

Evidence Gaps

Evidence gaps for all treatment approaches were substantial. For hyperventilation reduction techniques, there was only a single large trial, and it had not yet been published in a peer-reviewed journal.[56] A fully published account of another large trial of at least fair-quality is crucial to confirm the effects seen in this review. None of the trials were conducted in the United States, which would be important if it is to be considered for wide-spread adoption here. Once

replication has established its effectiveness more firmly, examination of components of care can be undertaken. We found little evidence that was clearly and directly applicable to non-Caucasian adults.

No large-scale trial of yoga training was found, and little evidence was found that was applicable to the United States.

No trials of IMT have been conducted in the United States, and all trials we found were small, including no more than 25 participants per treatment arm, and most had serious methodologic limitations. Only one investigator in this area has undertaken a systematic program of research to examine effects in different populations, and this work is still in the early stages.

The literature for other nonhyperventilation reduction breathing techniques is in its infancy, and a strong theoretical basis is needed to support further research in these and the other techniques examined.

Future Research

In general, there was little consistency of asthma-related terms used in these trials, and terms were sometimes used vaguely or differently, making it difficult to characterize interventions.

Bruton and colleagues suggest components that should be described when characterizing breathing retraining, and we strongly support their recommendations to improve our understanding of the interventions and to provide a framework for exploring differential effects of different components of breathing training.[139] They suggest including information on route (nasal or oral), rate (breaths per minute), depth (e.g., shallow, normal.), inspiratory and expiratory flow speed, region (e.g., abdominal), timing, regularity (of volume, timing, rate), breath holds, repetitions, and whether manual assistance was involved. Careful and consistent descriptions of specific techniques used would allow exploration of effectiveness of specific elements.

All intervention types would benefit from additional studies and evidence. In addition to detailing breathing retraining techniques as described by Bruton and colleagues, future studies should include outcomes of asthma symptoms, reliever medication use, quality of life, and pulmonary function at minimum.[139] In addition, controller medication use should always be described. Best practices regarding randomization, blinding, and followup are also crucial to any further research in this area. Trials should include asthma treatment with medications and education that is consistent with the standard of care in the United States.

Because asthma control fluctuates and many factors can affect asthma control (psychological, environmental, physiological), it is important to have large enough samples to capture appropriately diverse groups or asthmatics, with long enough followup to ensure that changes are stable. Outcome measurements should be repeated over time with follow-up through at least 6 months, and preferably through12 months, to capture ensure effects remain through all seasons.

Further examination of the impact of targeting autonomic arousal in controlling asthma may be helpful. Trials should compare a relaxation-only arm with relaxation plus a breathing technique to determine if the breathing technique adds to the benefit of relaxation alone.

Given that the current state of the evidence differed across intervention approaches, specific suggested next steps by intervention approach include:

- Hyperventilation reduction breathing techniques:
    - Replication of results of the large, good-quality trial with intensity-matched comparator and valid, blinded outcome assessment

    - In addition to matching treatment intensity between treatment and control groups, researchers should also attempt to match the groups in terms of what kind of change in asthma the patient is told they can expect. The internet is replete with dramatic testimonials as to the effectiveness of Buteyko breathing methods, and researchers should attempt to provide comparable levels of confidence in their techniques for treatment and control groups
    - Test the effects of delaying reliever medication use for 5 to 10 minutes while using techniques designed to reduce anxiety and autonomic arousal, compared with delay of reliever use for 5 to 10 minutes while using hyperventilation reduction techniques in order to examine the effects of reliever medication delay separate from breathing techniques.
    - Trials focused on hyperventilation reduction techniques in children and older adults
    - Trials that include substantial numbers of non-Caucasian participants
    - Trials that attempt to isolate the necessity or efficacy of other specific components of treatment
- Yoga breathing techniques
    - Well-designed and executed replication of a high-intensity approach in the United States, without additional non-yoga components
- IMT
    - Well-designed and executed trial comparing a training device with a sham device, with larger n, in the United States, such as that used in the Weiner study[67]

Table 15. Strength of evidence

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: asthma symptoms (global symptom severity or control, specific symptoms, exacerbations)	Hyperventilation reduction breathing technique versus control	8	Medium	Consistent	Direct	Imprecise	Moderate	Range of effects in 7 comprehensive interventions none to large, 5 of 7 reported benefit; 1 narrowly-focused trial showed no benefit for mouth-taping
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	4	Medium	Consistent	Direct	Imprecise	Low	No trial found a benefit of one approach over another; both groups improved in 2 trials, neither group improved in 2 trials
	Yoga breathing technique versus control	5	Medium-High	Consistent	Direct	Imprecise	Low	4 of 5 trials report benefit, three with substantial quality concerns
	IMT versus control	2	Medium-High	Consistent	Direct	Imprecise	Insufficient	2 small trials with different populations and methods, both show benefit, one with high risk of bias
	Non-hyperventilation reduction breathing technique versus control	2	Medium	Consistent	Direct	Imprecise	Insufficient	No benefit in trials using biofeedback or breathing device, mixed results in 1 trial of physical therapy

Table 15. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: medication use (reliever)	Hyperventilation reduction breathing technique versus control	6	Medium	Consistent	Direct	Imprecise	Moderate	3 trials found reduction in reliever medication and the 3 lowest-intensity trials did not.
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	3	Medium	Consistent	Direct	Imprecise	Low	Greater reduction in use with hyperventilation reduction breathing training in 2 of 3 cases, both groups improved in 1 trial
	Yoga breathing technique versus control	2	Medium	Inconsistent	Direct	Imprecise	Insufficient	2 trials with substantial differences in intensity, location, and population and reported contradictory results
	IMT versus control	4	High	Inconsistent	Direct	Imprecise	Insufficient	4 small trials, 3 by one author, 3 with high risk of bias, two shows probable benefit
	Nonhyperventilation reduction breathing technique versus control	1	Medium	N/A	Direct	Imprecise	Insufficient	No benefit of treatment

Table 15. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: medication use (controller)	Hyperventilation reduction breathing technique versus control	5	Medium	Inconsistent	Direct	Imprecise	Low	1 of 4 found large benefit, but raw data NR, remaining 3 found no group differences
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	4	Medium	Inconsistent	Direct	Imprecise	Low	No differences in effectiveness in 3 of 4 trials
	Yoga breathing technique versus control	1	High	N/A	Direct	Imprecise	Insufficient	1 trial with high risk of bias showed benefit of yoga, type of medication not listed, just that it was used "to control dyspnoea"
	IMT versus control	0	N/A	N/A	N/A	N/A	Insufficient	0 trials
	Nonhyperventilation reduction breathing technique versus control	2	Medium	Consistent	Direct	Imprecise	Insufficient	No benefit of treatment either trial
Key Question 1: quality of life	Hyperventilation reduction breathing technique versus control	6	Medium	Inconsistent	Direct	Imprecise	Low	Benefit found in 2 of 6, results mixed in another 2 trials
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	4	Medium	Inconsistent	Direct	Imprecise	Low	No differences in effectiveness in all cases, both groups met threshold for clinical improvement in 2 trials, but change only statistically significant in one of these trials
	Yoga breathing technique versus control	3	Medium-High	Consistent	Direct	Imprecise	Low	3 trials, large effect seen in trial with shortest followup. Pooled effect showed benefit.
	IMT versus control	0	N/A	N/A	N/A	N/A	Insufficient	0 trials
	Nonhyperventilation reduction breathing technique versus control	2	Medium	Inconsistent	Direct	Imprecise	Insufficient	2 trials with mixed results

Table 15. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 1: Functioning or mental health	Hyperventilation reduction breathing technique versus control	4	Medium	Consistent	Direct	Imprecise	Low	2 of 2 found small benefit for anxiety and depression, 2 of 2 found mixed results for functioning
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	1	Medium	N/A	Direct	Imprecise	Insufficient	Single study showing greater benefit of Buteyko breathing training than yoga breathing training via device on some functioning subscales
	Yoga breathing technique versus control	1	High	N/A	Direct	Imprecise	Insufficient	1 trial with substantial non-yoga components showed benefit
	IMT versus control	2	High	Consistent	Direct	Imprecise	Insufficient	2 trials with high risk of bias showing benefit, one in children, one in adults
	Nonhyperventilation reduction breathing technique versus control	1	Medium	N/A	Direct	Imprecise	Insufficient	1 trial with mixed results, benefit primarily seen on role limitations due to physical problems, not other subscales

Table 15. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 2: pulmonary function (FEV_1)	Hyperventilation reduction breathing technique versus control	5	Medium	Consistent	Indirect	Imprecise	Moderate	Small or no benefit found in all trials
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	4	Medium	Consistent	Indirect	Imprecise	Low	No benefit for FEV_1 in any trials
	Yoga breathing technique versus control	5	Medium-High	Consistent	Indirect	Imprecise	Low	3 of 5 show benefit of yoga, all 3 high-intensity interventions, 2 with large effects
	IMT versus control	3	High	Inconsistent	Indirect	Imprecise	Insufficient	2 of 3 trials showed benefit, two with high risk of bias
	Nonhyperventilation reduction breathing technique versus control	2	Medium	Consistent	Indirect	Imprecise	Insufficient	2 trials with different treatment approaches showing no benefit of treatment

Table 15. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 2: pulmonary function (PEF)	Hyperventilation reduction breathing technique versus control	3	Medium	Consistent	Indirect	Imprecise	Low	No benefit found in any trial
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	1	High	N/A	Indirect	Imprecise	Insufficient	1 trial showing no benefit in either group
	Yoga breathing technique versus control	4	Medium-High	Consistent	Indirect	Imprecise	Low	3 of 4 show benefit of yoga, all 3 high-intensity interventions, 2 with large effects
	IMT versus control	1	High	N/A	Indirect	Imprecise	Insufficient	Single trial with large effect, high risk of bias
	Nonhyperventilation reduction breathing technique versus control	0	N/A	N/A	Indirect	N/A	Insufficient	0 trials

Table 15. Strength of evidence (continued)

Outcome	Group	Number of Studies	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Comments
Key Question 3: harms	Hyperventilation reduction breathing technique versus control	3	Medium	Consistent	Direct	Imprecise	Low	None found adverse effects related to the intervention, one listed minor annoyances associated with mouth-taping
	Hyperventilation reduction breathing technique versus nonhyperventilation reduction breathing technique	2	Medium	Consistent	Direct	Imprecise	Low	No adverse effects related to interventions
	Yoga breathing technique versus control	2	Medium	Consistent	Direct	Imprecise	Low	No adverse effects related to yoga
	IMT versus control	0	N/A	N/A	N/A	N/A	Insufficient	N/A
	Nonhyperventilation reduction breathing technique versus control	0	N/A	N/A	N/A	N/A	Insufficient	N/A

FEV_1: forced expiratory volume in 1 second; IMT: inspiratory muscle training; N/A: not applicable; PEF: peak expiratory flow

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Abbreviations and Acronyms

AHRQ	Agency for Healthcare Research and Quality
AMED	Allied and Complementary Medicine
AQLQ	Asthma Quality of Life Questionnaire
ATS	American Thoracic Society
BTS	British Thoracic Society
CAM	complementary and alternative medicine
CCRCT	Cochrane Central Register of Controlled Trials
CI	confidence interval
CO_2	carbon dioxide
EPC	Evidence-based Practice Center
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
HRV	heart rate variability
ICS	inhaled corticosteroid(s)
IMT	inspiratory muscle training
IndMED	Indian Medical Journals
LOCF	last observation carried forward
MANTIS	Manual, Alternative and Natural Therapy Index System
mcg	microgram(s)
NAEPP	National Asthma Education Program and Prevention
PEDro	Physiotherapy Evidence Database
PEF	peak expiratory flow
RCT	randomized controlled trial
SABA	short-acting $beta_2$-agonists
SF	Short Form Health Survey (e.g., SF-36)
SGRQ	St. George's Respiratory Questionnaire
SIP	scientific information packet
SMD	standardized mean difference
TEP	technical expert panel
VC	vital capacity

Appendix A. Medications Recommended for Use in Treating Asthma

Medi-cation	Drug class	Product(s)	Indications	Mechanism	Potential adverse effects
Long-term control medi-cations	Inhaled cortico-steroids	Beclometha-sone dipropionate, budesonide, flunisolide, fluticasone propionate, mometasone furoate, triamcinolone acetonide	Long-term prevention of symptoms; suppression, control and reversal of inflammation. Reduce need for oral corticosteroids.	Anti-inflammatory, blocks late reaction to allergen and reduces airway hyper-responsiveness and inhibits cytokine production, adhesion protein activation and inflammatory cell migration and activation... Reverse $beta_2$-receptor downregulation. Inhibit microvascular leakage.	Cough, dysphonia, oral thrush (candidiasis). Systemic effects may occur with high doses (e.g., adrenal suppression, osteoporosis, skin thinning, and easy bruising). Suppression of growth velocity seen in children taking low to medium doses (transient effect).
	Systemic cortico-steroids	Methyl-prednisolone, prednisolone, prednisone	For short-term "burst" control and for long-term prevention of symptoms in severe persistent asthma (suppression, control, and reversal of inflammation).	Same as ICS.	Short term use: reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, hypertension, mood alteration, peptic ulcer, rarely aseptic necrosis. Long-term use: adrenal axis suppression, dermal thinning, growth suppression, hypertension, diabetes, Cushing's syndrome, muscle weakness, cataracts, impaired immune function (rare).
	Cromolyn sodium and nedocromil	NA	Long-term prevention of symptoms of mild persistent asthma. Preventive treatment prior to exercise or allergen exposure.	Anti-inflammatory, blocks early and late reaction to allergen, interferes with chloride channel function, and stabilizes mast cell membranes and inhibits activation and release of mediators from eosinophils and epithelial cells. Inhibits acute response to exercise, cold dry air and sulfuric dioxide.	Cough and irritation, unpleasant taste for nedocromil.

Medi-cation	Drug class	Product(s)	Indications	Mechanism	Potential adverse effects
	Immuno-modulators	Omalizumab	Long-term control and prevention of symptoms in moderate to severe persistent allergic asthmatics inadequately controlled by ICS.	Prevention of IgE binding to high-affinity receptors on basophils and mast cells. Decrease mast cell mediator from allergen exposure. Decrease number of high-affinity receptors in basophils and submucosal cells.	Pain and bruising at injection site, anaphylaxis, and malignant neoplasms (unclear relationship).
	Leukotriene receptor antagonists	Montelukast tablets and granules, zafirlukast tablets	Long-term control and prevention of symptoms in mild persistent asthma patients	Leukotriene receptor antagonists, selective competitive inhibition of $CysLT_1$ receptor.	No specific AEs reported for montelukast except Churg-Strauss (rare). Reversible hepatitis and rare irreversible hepatic failure (liver transplant and death) for zafirlukast.
	5-Lipo-oxygenase inhibitor	Zileuton tables	Long-term control and prevention of symptoms in mild persistent asthma patients aged ≥ 12 years	Inhibits production of leukotrienes from arachidonic acid	Elevation of liver enzymes and limited case reports of reversible hepatitis and hyperbilirubinemia.
	Long-acting $beta_2$-agonists	Inhaled formoterol and salmeterol; albuterol sustained-release tablets	Long-term prevention of symptoms in addition to ICS. Prevention of exercise-induced broncho-spasm.	Bronchodilation, smooth muscle relaxation following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction.	Tachycardia, skeletal muscle tremor, hypokalemia, prolongation of QT_c interval in overdose. Diminished bronchoprotective effects. Potential risk of uncommon, severe, life-threatening or fatal exacerbation.
	Methyl-xanthines	Theophylline sustained-release tablets and capsules	Long-term control and prevention of symptoms in mild persistent asthma or as adjunctive with ICS in moderate or persistent asthma.	Bronchodilation, smooth muscle relaxation from phosphodiesterase inhabitation and possible adenosine antagonism. May affect eosinophilic infiltration to bronchial mucosa as well as decrease in epithelial T-lymphocyte. Increases diaphragm contractility and mucociliary clearance.	Insomnia, gastric upset, ulcer aggravation or reflux, hyperactivity (children), urination difficulties (elderly men with prostatism). Dose-related acute toxicities (e.g., tachycardia, nausea, CNS stimulation, hyperkalemia SVT, seizures, vomiting, headache, hematemesis, and hyperglycemia).

Medi-cation	Drug class	Product(s)	Indications	Mechanism	Potential adverse effects
Quick-relief medi-cations	Short-acting $beta_2$-agonists	Inhaled albuterol, levalbuterol and pirbuterol	Relief of acute symptoms and preventive treatment for exercise-induced bronchospasm prior to exercise.	Bronchodilation, binds to the $beta_2$-adrenergic receptor producing smooth muscle relaxation following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction.	Tachycardia, skeletal muscle tremor, lactic acid increase, headache, hyperglycemia. Patients with cardiovascular conditions may have adverse cardiovascular reactions.
	Anti-cholinergics	Ipratropium bromide	Relief of acute broncho-spasm.	Bronchodilation, competitive inhibition of muscarinic cholinergic receptors. Reduced intrinsic vagal tone of airways may block reflex bronchoconstriction secondary to irritants or to reflux eosinophils. May decrease mucous gland secretion.	Dry mouth, wheezing, and blurred vision if sprayed in eyes.
	Cortico-steroids	Methylpredniso lone, prednisolone, prednisone	Prevent progression, reverse inflammation, speed recovery, and reduce relapse rate in exacerbations.	Same as ICS.	Reversible abnormalities in glucose metabolism, increased appetite, fluid retention, facial flushing, weight gain, hypertension, mood alteration, peptic ulcer, aseptic necrosis (rare).

Adapted from the National Asthma Education and Prevention Program's Prevention Guidelines for the Diagnosis and Management of Asthma (Figures 3-22 and 3-23)[1]

Abbreviations: AE: adverse effect; AMP: adeno monophosphate; CNS: central nervous system; ICS: inhaled corticosteroids; SVT: supraventricular tachycardia

Appendix B. Search Strategies

Database: **AltHealthWatch**

S16 S1 and S15
S15 S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14
S14 TI biofeedback or AB biofeedback
S13 TI diaphragmatic breath* or AB diaphragmatic breath*
S12 AB (diaphragm*) and AB (exercise* or training or retraining or pattern* or technique*)
S11 AB (breath* or respirat*) and AB (exercise* or training or retraining or pattern* or technique*)
S10 TI (breath* or respirat*) and TI (exercise* or training or retraining or pattern* or technique*)
S9 TI (breath* or respirat*) and TI (paced or pursed)
S8 AB (breath* or respirat*) and AB (paced or pursed)
S7 AB (breath* or respirat*) and AB (physiotherap* or physical therap*)
S6 TI (breath* or respirat*) and TI (physiotherap* or physical therap*)
S5 TI Pranayama or AB Pranayama
S4 TI Buteyko or AB Buteyko
S3 TI yogic OR AB yogic
S2 TI yoga OR AB yoga
S1 TI asthma* or AB asthma*

Database: **AMED** (Allied and Complementary Medicine) <1985 to December 2011>

---

1 asthma/
2 asthma$.ti,ab.
3 1 or 2
4 breathing exercises/
5 yoga/
6 Yoga.ti,ab.
7 yogic.ti,ab.
8 Buteyko.ti,ab.
9 Pranayama.ti,ab.
10 Papworth.ti,ab.
11 "inspiratory muscle training".ti,ab.
12 "expiratory muscle training".ti,ab.
13 ((breath$ or respirat$) adj5 (physiotherap$ or physical therap$)).ti,ab.
14 ((breath$ or respirat$) adj5 (paced or pursed)).ti,ab.
15 ((breath$ or respirat$) adj5 (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.
16 (diaphragm* and (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.
17 diaphragmatic breath$.ti,ab.

18 biofeedback/
19 biofeedback.ti,ab.
20 or/4-19
21 3 and 20
22 limit 21 to yr="1990 -Current"
23 limit 22 to english

Database: **CINAHL**

S27 S3 and S25 Limiters - Published Date from: 19900101-20111231
S26 S3 and S25
S25 S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24
S24 TI biofeedback or AB biofeedback
S23 (MH "Biofeedback") OR (MH "Biofeedback (Iowa NIC)")
S22 TI diaphragmatic breath* or AB diaphragmatic breath*
S21 TI diaphragm* and TI (exercise* or training or retraining or pattern* or technique*)
S20 AB diaphragm* and AB (exercise* or training or retraining or pattern* or technique*)
S19 AB (breath* or respirat*) and AB (exercise* or training or retraining or pattern* or technique*)
S18 TI (breath* or respirat*) and TI (exercise* or training or retraining or pattern* or technique*)
S17 TI (breath* or respirat*) and TI (paced or pursed)
S16 AB (breath* or respirat*) and AB (paced or pursed)
S15 AB (breath* or respirat*) and AB (physiotherap* or physical therap*)
S14 TI (breath* or respirat*) and TI (physiotherap* or physical therap*)
S13 TI "expiratory muscle training" or AB "expiratory muscle training"
S12 TI "inspiratory muscle training" or AB "inspiratory muscle training"
S11 TI Papworth or AB Papworth
S10 TI Pranayama or AB Pranayama
S9 TI Buteyko or AB Buteyko
S8 TI yogic or AB yogic
S7 TI yoga or AB yoga
S6 (MH "Yoga") OR (MH "Yoga Pose")
S5 (MH "Breathing Exercises (Saba CCC)")
S4 (MH "Breathing Exercises") OR (MH "Buteyko Method")
S3 s1 or s2
S2 TI asthma* or AB asthma*
S1 (MH "Asthma") OR (MH "Asthma, Exercise-Induced") OR (MH "Status Asthmaticus")

Database: **Cochrane Central Register of Controlled Trials**

#1 asthma*:ti,ab,kw
#2 "breathing exercises":ti,ab,kw

#3 yoga:ti,ab,kw
#4 yogic:ti,ab,kw
#5 Buteyko:ti,ab,kw
#6 Pranayama:ti,ab,kw
#7 Papworth:ti,ab,kw
#8 "inspiratory muscle training":ti,ab,kw
#9 "expiratory muscle training":ti,ab,kw
#10 breath*:ti or respirat*:ti
#11 physiotherap*:ti or physical therap*:ti
#12 (#10 AND #11)
#13 breath*:ab or respirat*:ab
#14 physiotherap*:ab or physical therap*:ab
#15 (#13 AND #14)
#16 paced:ti,ab or pursed:ti,ab
#17 ((#11 OR #14) AND #16)
#18 exercise*:ti or training:ti or retraining:ti or pattern*:ti or technique*:ti
#19 (#10 AND #18)
#20 exercise*:ab or training:ab or retraining:ab or pattern*:ab or technique*:ab
#21 (#13 AND #20)
#22 diaphragm*:ti,ab
#23 (#22 AND (#18 OR #20))
#24 diaphragmatic next breath*
#25 biofeedback:ti,ab,kw
#26 (#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #12 OR #15 OR #17 OR #19 OR #21 OR #23 OR #24 OR #25)
#27 (#1 AND #26), from 1990 to 2011

Database: **CSA**

KW=asthma AND KW=(Buteyko OR Pranayama OR Papworth OR yoga OR yogic OR biofeedback OR "inspiratory muscle training" OR "expiratory muscle training" OR "breathing physical therapy" OR "breathing physiotherapy" OR paced OR pursed OR "breathing exercise*" OR "breathing training" OR "breathing retraining" OR "diaphragmatic breathing" OR "breathing technique*")

Database: **EMBASE** <1988 to 2011 July 28>

---

1 asthma/ or allergic asthma/ or asthmatic state/ or exercise induced asthma/ or extrinsic asthma/ or intrinsic asthma/ or mild intermittent asthma/ or mild persistent asthma/ or moderate persistent asthma/ or nocturnal asthma/ or occupational asthma/ or severe persistent asthma/ (112140)
2 asthma$.ti,ab.
3 1 or 2
4 breathing exercise/
5 YOGA/

6 yoga.ti,ab.
7 yogic.ti,ab.
8 Buteyko.ti,ab.
9 Pranayama.ti,ab.
10 Papworth.ti,ab.
11 "inspiratory muscle training".ti,ab.
12 "expiratory muscle training".ti,ab.
13 ((breath$ or respirat$) adj5 (physiotherap$ or physical therap$)).ti,ab.
14 ((breath$ or respirat$) adj5 (paced or pursed)).ti,ab.
15 ((breath$ or respirat$) adj5 (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.
16 (diaphragm* and (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.
17 diaphragmatic breath$.ti,ab.
18 feedback system/
19 biofeedback.ti,ab.
20 or/4-19
21 3 and 20
22 limit 21 to yr="1990 -Current"
23 limit 22 to english language

Database: **IndMED**

---

asthma
AND
buteyko OR
yoga OR
yogic OR
papworth OR
pranayama OR
biofeedback OR
expiratory muscle training OR
inspiratory muscle training OR
breathing physical therapy OR
breathing physiotherapy OR
paced OR
pursed OR
breathing exercise OR
breathing exercises OR
breathing training OR
breathing retraining OR
diaphragm breathing OR
breathing technique OR
breathing techniques OR
breathing pattern OR
breathing patterns

Database: **Mantis** <1880 to December 2010>

---

1 asthma$.mp. [mp=title, abstract, descriptors]
2 yoga.mp. [mp=title, abstract, descriptors]
3 yogic.mp. [mp=title, abstract, descriptors]
4 Buteyko.mp. [mp=title, abstract, descriptors]
5 Pranayama.mp. [mp=title, abstract, descriptors]
6 Papworth.mp. [mp=title, abstract, descriptors]
7 "inspiratory muscle training".mp. [mp=title, abstract, descriptors]
8 "expiratory muscle training".mp. [mp=title, abstract, descriptors]
9 ((breath$ or respirat$) adj5 (physiotherap$ or physical therap$)).mp. [mp=title, abstract, descriptors]
10 ((breath$ or respirat$) adj5 (paced or pursed)).mp. [mp=title, abstract, descriptors]
11 ((breath$ or respirat$) adj5 (exercise$ or training or retraining or pattern$ or technique$)).mp. [mp=title, abstract, descriptors]
12 (diaphragm* and (exercise$ or training or retraining or pattern$ or technique$)).mp. [mp=title, abstract, descriptors]
13 diaphragmatic breath$.mp. [mp=title, abstract, descriptors]
14 biofeedback.mp. [mp=title, abstract, descriptors]
15 or/2-14
16 1 and 15
17 limit 16 to yr="1990 -Current"

Database: Ovid **MEDLINE**(R)

---

1 asthma/ or asthma, exercise-induced/ or status asthmaticus/
2 asthma$.ti,ab.
3 1 or 2
4 Breathing Exercises/
5 Yoga/
6 yoga.ti,ab.
7 yogic.ti,ab.
8 Buteyko.ti,ab.
9 Pranayama.ti,ab.
10 Papworth.ti,ab.
11 "inspiratory muscle training".ti,ab.
12 "expiratory muscle training".ti,ab.
13 ((breath$ or respirat$) adj5 (physiotherap$ or physical therap$)).ti,ab.
14 ((breath$ or respirat$) adj5 (paced or pursed)).ti,ab.
15 ((breath$ or respirat$) adj5 (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.
16 (diaphragm* and (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.
17 diaphragmatic breath$.ti,ab.
18 biofeedback, psychology/
19 biofeedback.ti,ab.
20 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19

21 3 and 20
22 limit 21 to yr="1990 -Current"
23 remove duplicates from 22
24 limit 23 to english language

Database: **PEDRO**

---

asthma
AND
buteyko OR
yoga OR
yogic OR
papworth OR
pranayama OR
biofeedback OR
expiratory muscle training OR
inspiratory muscle training OR
breathing physical therapy OR
breathing physiotherapy OR
paced OR
pursed OR
breathing exercise OR
breathing training OR
breathing retraining OR
diaphragm breathing OR
breathing technique OR
breathing pattern

Database: **PsychINFO**

---

1 asthma/
2 asthma$.ti,ab.
3 1 or 2
4 yoga/
5 yoga.ti,ab.
6 yogic.ti,ab.
7 Buteyko.ti,ab.
8 Pranayama.ti,ab.
9 Papworth.ti,ab.
10 "inspiratory muscle training".ti,ab.
11 "expiratory muscle training".ti,ab.
12 ((breath$ or respirat$) adj5 (physiotherap$ or physical therap$)).ti,ab.
13 ((breath$ or respirat$) adj5 (paced or pursed)).ti,ab.
14 ((breath$ or respirat$) adj5 (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.

15 (diaphragm* and (exercise$ or training or retraining or pattern$ or technique$)).ti,ab.
16 diaphragmatic breath$.ti,ab.
17 biofeedback/ or biofeedback training/
18 biofeedback.ti,ab.
19 or/4-18
20 3 and 19
21 limit 20 to yr="1990 -Current"
22 limit 21 to english language

Appendix C. Non-English Studies

Our literature search identified 248 unique articles published in a non-English language. The following articles appear to be relevant studies (only based on their title and/or abstract) to this comparative effectiveness review.

Reference	Abstract	Language
Fluge T, Richter J, Fabel H, et al. Long-term effects of breathing exercises and yoga in patients with bronchial asthma. Pneumologie 1994;48(7):484-90. PMID: 7937658.	To compare the effects of BE or Y on the course of bronchial asthma we studied 36 subjects with a mild disease. The patients were randomly divided into three groups. Two of them participated in a 3 weeks training program of BE or Y while the third group rested without any additional treatment. At the end of the training period the patients were asked to practice BE or Y on their own. Drug therapy and lung function parameters before and after a $beta_2$-agonist metered dose inhaler albuterol were recorded prior to the training program and in 4 weeks intervals for 4 months thereafter. The response to the $beta_2$-agonist was documented continuously in 28 patients. The mental state of the patients was elucidated by questionnaires. Prior to the study a significant effect of inhaled albuterol on the FEV_1 was shown without any significant between group differences. Both caused a significant amelioration of the mental state but only the BE induced a significant improvement of lung function parameters compared with the individual baseline values. The FEV_1 increased significantly by 356.3 ± 146.2 ml ($p<0.05$) and the VC by 225.0 ± 65.5 ml ($p<0.01$). These long-term changes were not significantly different from the actual response to albuterol. BE decreased the RV significantly by 306.3 ± 111.6 ml ($p<0.05$), an effect significantly higher compared with the $beta_2$-agonist ($p<0.01$). BE in combination with albuterol caused an additive effect.	German
Rocha EM. The effect of respiratory rehabilitation on the functional ventilation changes in the asthmatic child. Allerg Immunol 1993;25(1):26-8. PMID: 8471136.	The aim of this study was to evaluate the improvement of lung function abnormalities during asymptomatic periods in children with perennial atopic asthma after physical respiratory rehabilitation and swimming. 240 lung function tests were performed regularly by whole-body plethysmography during asymptomatic periods on 68 atopic asthmatic children aged 5 to 13 (mean 8.7 years), in a follow up 4 years study (1983 to 1987). Total lung capacity, VC, FEV_1, resistance, MEF_{50}, RV and TGV were recorded. We selected TGV for measured hyperinflation, resistance for bronchial obstruction and MEF_{50} for small airways obstruction. We divided these children population in two groups: group A control (20 subjects, mean 9.3 years age) immunotherapy alone; group B (48 subjects, mean 8.03 years age) immunotherapy and respiratory rehabilitation and swimming. Furthermore, we compared the evolution of the lung function according to the severity of asthma on B group alone. The number of hyperinflated or bronchial obstructed children who did RRS is significantly smaller than on the control group. Nevertheless, breathing exercises and swimming has no effect on peripheral airway obstruction. When we compared the effect of asthma on B group alone, we noted that the recovery of lung abnormalities were observed on the great majority of mild and moderate hyperinflated and bronchial obstructed asthma. In severe asthma, the results were not so good, particularly on bronchial and peripheral airway obstruction. In these last cases the functional prognosis will be uncertain. Respiratory rehabilitation and swimming have an unquestionable effect on improvement of hyperinflated asthmatic children, some effect on improvement on permanent bronchial obstruction, and without any benefit on permanent peripheral airway obstruction. Lung function tests might be monitored the RRS in all asthmatic children with lung function impairment.	French

Abbreviations: BE: breathing exercise; FEV_1: forced expiratory volume in 1 second; MEF_{50}: maximal expiratory flow at 50 percent; ml: milliliter; RRS: respiratory rehabilitation and swimming; RV: residual volume; TGV: thoracic gas volume (also known as functional residual capacity); VC: vital capacity; Y: yoga

Appendix D. Evidence Tables

Evidence Table 1a. Study characteristics: hyperventilation reduction breathing techniques versus control

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
Cooper 2003[52]	UK	IG1 (BBT)	30	44	44.9	2 puffs/d†	657 mcg/d	80	Aged 18 to 70y, non-smoking volunteers with stable asthma, taking an inhaled SABA at least 2 times/w and regular ICS w/ no change in dose in previous 4w, pre-bronchodilator FEV_1 of at least 50 percent predicted and 10 percent increase following 400mcg inhaled salbutamol, a PD_{20} of methacholine causing a 20 percent fall in FEV_1 of 10.24 µmol or less, mean daily sx score of 1 or more during run-in.	No other important illnesses, taking tx other than sodium cromoglycate.
		CG	30							
Grammato-poulou 2011[54]	Greece	IG (HRBT)	20	46.8	42.5	NR	NR	83.7	Aged 18 to 60y, adults diagnosed with asthma.	Aged < 60y, smokers, used oral corticosteroids in the previous 3m, suffered from heart failure, previously participated in a asthma education program.
		CG	20							
Holloway 2007[55,72]	UK	IG (Pap-worth)	39	49.7	57.6	NR	NR	89.6	Aged 16 to 70y, literate in English, commitment to participate for up to eight attendances, no serious comorbidity.	NR
		CG	46							

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
McGowan 2003[56]	Scotland	IG (BBT)	200	NR	50	18 puffs/w	NR	76.7	Age 14 to 69y; documented mild asthma with a total symptom score > 7 in the last 1w of run-in; asthma management requiring at least 12 bronchodilator dose units in the last 1w of run-in.	Previous BBT, Balanced Volitional Breathing or Eucapnic Breath training; unsafe asthma (requiring ≤ 500mcg/d ICS and use of $beta_2$-agonist > 5 times/d; or > 500mcg/d ICS and use of $beta_2$-agonist > 8 times percent predicted); significant other illness (including chronic pulmonary airways obstruction); exacerbation of asthma (e.g., hospitalization, major change in preventative therapy within last 4w); HR > 90 on two occasions prior to randomization.
		CG1 (nurse education)	200							
		CG2 (brief asthma education)	200							
Opat 2000[57,77]	Australia	IG (BBT)	18	32.2	58.3	404 mcg/d	430 mcg/d	NR	Aged 18 to 50y, diagnosed with asthma by a medical practitioner (self-reported physician diagnosis), ready access to a VCR throughout trial period.	Previously learned BBT; regularly taking oral corticosteroids or more than 1600mcg of inhaled steroid per day; taking < three doses of inhaled bronchodilator medication per week; experienced a severe asthma exacerbation within 6w of trial start date.
		CG	18							

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
Thomas 2009[59,79-81]	UK	IG (HRBT)	94	46.0*	61.2	1.4 doses/d	400 mcg/d*	89.5	Aged 17 to 65y treated for asthma in 10 primary care general practices in the UK, physician-diagnosed asthma, moderate impairment of asthma-related health status (AQLQ score < 5.5, "uncontrolled"), had < 10 pack-years, ≥ one anti-asthma medication Rx in the previous 1y, no COPD, and asthma not dangerously unstable and in need of urgent medical review (assessed by asthma nurse).	NR
		CG	89							
Thomas 2003[71,78,82]	UK	IG (diaph-ragm breathing)	17	48.8	78.8	1.5 canisters /3m	600 mcg/d	NR	Aged 17 to 65y with diagnosis of asthma who had received at least one Rx for an inhaled or oral bronchodilator or prophylactic anti-asthma medication in previous 1y, ≥ 23 on Nijmegen questionnaire (suggestive of dysfunctional breathing).	NR
Cooper 2009‡[51,75,89]	UK	IG (mouth-taping)	51	53	64	10 puffs /w†	567 mcg/d	86.2	Aged 18 to 72y with symptomatic asthma defined as taking at least four puffs/w of an inhaled short-acting bronchodilator, daily sx plus nocturnal or early morning sx or PEF of 10 percent or more on at least three nights/w during the run-in period.	FEV_1 below 50 percent predicted value, previous BBT training, unable to breathe through nose, diagnosed with sleep apnea, or history of smoking more than 10 pack years.
		CG								

*Median

†Median puffs/d, typical dose per puff = 100 mcg

‡Crossover study design, mouth-taping and control phases

Abbreviations: AQLQ: Asthma Quality of Life Questionnaire; BBT: Buteyko breathing techniques; CG: control group; COPD: chronic obstructive pulmonary disease; d: day(s); FEV_1: forced expiratory volume in 1 second; HR: heart rate; HRBT: hyperventilation reduction breathing technique; ICS: inhaled corticosteroids; IG: intervention group; m: month(s); mcg: microgram(s); NR: not reported; PD_{20}: provocative dose causing an decrease in FEV_1 of 20 percent; PEF: pulmonary expiratory flow; pred: predicted; Rx: prescription; SABA: short-acting $beta_2$-agonists; sx: symptoms; tx: treatment; UK: United Kingdom; µmol: micromole(s); VCR: videocassette recorder; w: week(s); y: year(s)

Evidence Table 1b. Description of intervention groups: hyperventilation reduction breathing techniques versus control

Study	Intervention group	Description	Intervention session	Homework	Additional components
Cooper 2003[52]	IG1 (BBT)	Eucapnic BBT taught by a certified Buteyko practitioner. Pts taught to reduce fx and depth of breathing, use the technique bid to relieve asthma sx (used 420 times over 6m) and use bronchodilator if BBT failed, nocturnal mouth-taping with Micropore hypoallergenic tape. F/U call provided 2w after training and open communication with trainer available. Avoid certain foods (e.g., highly processed food and additives), avoid stress, avoid oversleeping.	Five 2-hour sessions, over weekends or successive evenings. (10 hours total)	Home exercises with an audiotape or CD with technique reminders.	Also included dietary restrictions, stress management and instruction to avoid oversleeping.
	CG	Sham device with no valve and a leak ensured no resistance to breathing, use bid (420 times in 6m).	One session (Hours NR)	NR	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Grammatopoulou 2011[54]	IG (HRBT)	Phase 1: one 60min group session (5 pts/group) structured according to the health belief model. Pts educated in (1) normal breathing pattern and breathing pattern during exacerbations, (2) recognizing asthma sx, (3) comprehension of their ability to modify their breathing pattern targeting self-management of sx, (4) expressed their perceived asthma severity and the benefits and barriers of adapting a modified breathing pattern for 6m. 12 individual 60min sessions (3 times/w) comprised of asthma education and practice of: diaphragmatic breathing, nasal breathing, short hold of breath (2 to 3s), and adaptation of speech pattern (speaking, singing) in any position during physical activity and in asthma exacerbation. Taught by a physiotherapist. Phase 2: Development of specific action plan regarding duration (> 20 min) and frequency (2 to 3 times/d) of home training for 5m.	One 60-min group session, twelve 60-min individual sessions over 26w. (13 hours total)	Home training.	NR
	CG	Usual care, no additional treatment	NR	NR	NR
Holloway 2007[55,72]	IG (Papworth)	Papworth method training in addition to usual asthma care including medication and routine asthma education; integrate techniques in daily life activities. Breathing training to reduce dysfunctional breathing (e.g., hyperventilation, hyperinflation, education w/ emphasis on breathing and stress response, relaxation training). Pts taught by a respiratory physiotherapist.	Five 60-min sessions over 6m. (5 hours total)	Home exercises with an audiotape or CD with technique reminders.	Also included stress management.

Study	Intervention group	Description	Intervention session	Homework	Additional components
	CG	Received usual asthma care including medication and routine asthma education; usual care did not include advice about breathing exercises. Taught by practice nurse.	NR	NR	NR
McGowan 2003[56,99]	IG (BBT)	Buteyko Institute Method Program; introductory asthma education by the researcher in one 120-min session over 1w; followed by seven sessions over the next 3w comprising of information on normal physiology and pathophysiology of airways, use of medication and compliance, inhale technique, exercise "triggers", opportunistic infection and steroids.	Eight sessions over 4w. (Hours NR)	Home practice required.	NR
	CG1 (nurse education)	Introductory asthma education by the researcher in one 120min session over 1w; followed by seven sessions with a Practice Nurse over the next 3w.	Eight sessions over 4w. (Hours NR)	NR	NR
	CG2 (brief asthma education)	Introductory education course only.	One 120-min session over 1w. (2 hours total)	NR	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Opat 2000[57,77]	IG (BBT)	67min video including an explanation of the BBT theory and a 20min self-guided BBT session involving short periods of shallow breathing, interspersed breath holding; pts asked to watch a "portion of the video" daily. No mouth taping, no dietary change.	One 67-min video; 56 20-min sessions with video over 4w. (19.8 hours total)	Video viewed at home.	NR
	CG	60min video entitled "Nature Landscapes" watched for 20min bid for 4w.	56 20-min sessions over 4w. (18.6 hours total)	NR	NR
Thomas 2009[59,79-81]	IG (HRBT)	During group sessions, pts explained normal breathing and possible effects of dysfunctional breathing (e.g., mouth breathing, etc.). During individual sessions, pts taught regular diaphragmatic and nasal breathing techniques (similar to Papworth method) to improve hyperventilation reduction breathing. Pts taught by a physiotherapist.	One 60-min group session; two 30- to 45-min individual sessions w/ 2 to 4w between sessions. (2 to 2.5 hours total)	Encouraged to practice for at least 10min/d.	NR
	CG	Asthma education on the information on the nature of asthma followed by individual sessions presenting broad asthma and atopy concepts and explaining tx rationale w/out providing personalized asthma advice. Pts taught by a nurse.	One 60-min group session; two 30- to 45-min individual sessions w/ 2 to 4w between sessions. (2 to 2.5 hours total)	NR	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Thomas 2003[71,78,82]	IG (HRBT)	Diaphragm breathing retraining; pts practiced slow diaphragmatic breathing for short (e.g., 10min) periods qd using an established physiotherapy method as taught by a physiotherapist. Learned about effects of overbreathing (by abnormal breathing such as non-diaphragmatic breathing). Described as "identical" to above intervention in personal communication.	One 45-min group session, two 15-min individual sessions, over 2w. (1.25 hours total)	NR	NR
	CG	Asthma education provided by an asthma nurse; pts also invited to attend individual asthma review w/ nurse or doctor in which six (38%) participated.	One 60-min session.	NR	NR
Cooper 2009[51,75,89]	IG (mouth-taping)	Pts taped their mouth at night with 2.5cm wide micorporous tape (Micropore™) to facilitate nose breathing; options to practice during daytime to increase tolerance. Plus a meeting w/ study coordinator to describe mouth-taping.	One training session, mouth-taped for 28 nights for entire night for 4w. (Hours NA)	NR	NR
	CG	Usual breathing.	28 nights for entire night for 4w. (Hours NA)	NR	NR

Abbreviations: BBT: Buteyko breathing technique; bid: twice daily; CD: compact disc; CG: control group; cm: centimeters; d: day(s); F/U: followup; fx: frequency; HRBT: hyperventilation reduction breathing technique; IG: intervention group; m: month(s); min: minute(s); NA: not applicable; NR: not reported; qd: daily; pts: participants; s: second(s); sx: symptoms; w: week(s); w/: with.

Evidence Table 1c. Change in asthma symptoms: hyperventilation reduction breathing techniques versus control

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded lower= better)	Additional asthma symptom outcomes
Cooper 2003[52]	Mini-Juniper AQLQ, symptoms subscale (higher= better)	13w	IG1 (BBT)	30	26	5.0 (1.0)	0.42 (-0.17, 1.6)†	0.6 (for difference between all three groups)	Insufficient data to calculate	**Three groups differed across median daily symptom scores at 26w, p=0.003.*** NSD between groups in the number of exacerbations at 26w.
			CG	29	25	4.9 (0.9)	0.33 (-0.31, 0.58)†			
		26w	IG1	30	23	5.0 (1.0)	1.08 (0.08, 1.92)†	0.2 (for difference across all three groups)	Insufficient data to calculate	
			CG	29	22	4.9 (0.9)	0.33 (-0.19, 1.17)†			
Grammato-poulou 2011[54]	Asthma control test score (higher= better)	4w	IG (HRBT)	20	20	18.1 (2.59)	**4.1 (1.56)***	**0.007***	**-1.77 (-2.51, -1.03)***	Significant difference between groups at 4 and 12w for those with controlled asthma, NSD at 26w.
			CG	20	20	19.0 (3.52)	**0.7 (2.16)***			
		12w	IG	20	20	18.1 (2.59)	4.8 (1.56)	**0.001***	**-2.04 (-2.82, -1.26)***	
			CG	20	20	19.0 (3.52)	0.9 (2.14)			
		26w	IG	20	20	18.1 (2.59)	3.9 (2.02)	0.100	**-1.23 (-1.91, -0.55)***	
			CG	20	20	19.0 (3.52)	1.3 (2.12)			

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded lower= better)	Additional asthma symptom outcomes
Holloway 2007[55,72]	SGRQ symptoms subscale (lower= better)	26w	IG (Pap-worth)	39	33	42.9 (21.3)	-21.1 (12.8)	**0.001***	**-1.47** **(-1.98, -0.97)***	
			CG	46	45	35.1 (12.9)	-2.3 (12.5)			
		52w	IG	39	32	42.9 (21.3)	-18.0 (12.8)	**0.007***	**-1.46** **(-1.99, -0.94)***	
			CG	46	40	35.1 (12.9)	-1.6 (9.5)			
McGowan 2003[56,99]	Asthma symptoms score (lower= better)	26w	IG (BBT)	200	180	2.2 (0.4)	-1.46 (0.91)	NR	**CG1:** **-2.58** **(-2.86, -2.29)*** **CG2:** **-2.38** **(-2.66, -2.09)***	
			CG1 (nurse education)	200	165	2.2 (0.4)	0.3 (0.26)			
			CG2 (brief asthma education)	200	146	2.2 (0.4)	0.2 (0.25)			
Opat 2000[57,77]	Daytime symptoms score (lower= better)	4w	IG (BBT)	18	13	0.82 (0.58)	NR (NR) (-0.31 more in IG than CG)	0.10	Insufficient data to calculate	-0.21 greater change in IG than CG in nighttime symptom scores at 4w, p=0.24.
			CG	18	15	0.79 (0.56)	NR (NR)			

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded lower= better)	Additional asthma symptom outcomes
Thomas 2009[59,79-81]	ACQ, total score (lower= better)	4w	IG (HRBT)	94	73	1.4 (0.8)	-0.2 (0.5)	0.70	0.08 (-0.24, 0.40)	
			CG	89	79	1.5 (0.9)	-0.3 (0.7)			
		26w	IG	94	63	1.4 (0.8)	-0.3 (0.5)	0.12	-0.26 (-0.60, 0.09)	
			CG	89	66	1.5 (0.9)	-0.13 (0.6)			
Thomas 2003[71,78,82]	AQLQ-Juniper, symptoms, median (higher= better)	4w	IG (HRBT)	17	16	4.68 (1.06)	0.42 (0.11, 1.17)†	**0.042***	Insufficient data to calculate	
			CG	16	15	4.60 (1.35)	0.09 (-0.58, 0.50)†			
		26w	IG	17	16	4.68 (1.06)	0.33 (-0.13, 1.13)†	0.059	Insufficient data to calculate	
			CG	16	12	4.60 (1.35)	-0.17 (-0.73, 0.4))†			
Cooper 2009‡[51,75,89]	ACQ, total score	4w	IG (mouth-taping)	51	51	NR (NR)	2.41 (1.7)	0.92	Insufficient data to calculate	No differences between groups on nighttime wakening,

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded lower= better)	Additional asthma symptom outcomes
	(lower= better)		CG			NR (NR)	2.37 (1.3)			symptom diary scores, number experiencing exacerbations. Difference between treatment periods -0.03 (95% CI, -0.68 to 0.61) in ACQ.

*Statistically significant change from baseline or between groups (p<0.05)

†Median or median change from baseline (IQR)

‡Crossover study design, mouth-taping and control phases

Abbreviations: ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; BBT: Buteyko breathing technique; CG: control group; CI: confidence interval; HRBT: hyperventilation reduction breathing technique; IG: intervention group; IQR: inter-quartile range; NA: not applicable; NR: not reported; NSD: no significant difference; SD: standard deviation; SGRQ: St. George's Respiratory Questionnaire; w: week(s)

Evidence Table 1d. Change in asthma medication use: hyperventilation reduction breathing techniques versus control

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
Cooper 2003[52]	$Beta_2$-agonist use, median (puffs/d)	26w	IG1 (BBT)	30	23	2 (0, 4)†	-2 (-4, 0)†	**0.005 (for difference across all three groups)***	Insufficient data to calculate	NSD between all three groups in median number of days taking increased ICS dose or median number of prednisolone courses per subject at 26w, or median ICS reduction during extended followup phase.
			CG	30	22	2 (0, 3.8)†	0 (-2, 0)†			
Grammato-poulou 2011[54]	None	26w	IG (HRBT)	20	20	NA	NA	NA	NA	
			CG	20	20	NA	NA			
Holloway 2007[55]	None	52w	IG (Pap-worth)	39	32	NA	NA	NA	NA	
			CG	46	40	NA	NA			
McGowan 2003[56,99]	Bronchodilator use (puffs/w)	26w	IG (BBT)	200	180	18 (3)	-17.9 (2.66)	NR	**CG1: -7.67 (-8.19, -7.06)*** **CG2: -8.17**	IG group decreased use of preventer medication, oral reliever and oral prevent preparations by > 90 percent at 26w; no significant change in CG1 or CG2.
			CG1 (nurse education)	200	165	18 (3)	0 (1.90)	NR		
			CG2 (brief asthma education)	200	145	18 (3)	3 (2.41)	NR		

Study	Reliever medication outcome (unit)	Follow-up	Group	N randomized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
									(-8.84, -7.51)*	
Opat 2000[57,77]	Bronchodilator use (mcg/d)	4w	IG (BBT)	18	13	350 (342)	**-220 (206)***	NR	**-0.78**	NSD between groups in inhaled steroid use at 4w.
			CG	18	15	459 (478)	-10 (303)		**(-1.55, 0.00)***	
Thomas 2009[59,79-81]	Bronchodilator use (mcg)	4w	IG (HRBT)	94	73	NR (NR)	**"Reduced", data NR***	0.72	Insufficient data to calculate	Mean bronchodilator use difference between groups, -0.06 (95% CI, -0.36 to 0.25) at 4w. NSD between groups in ICS use.
			CG	89	79	NR (NR)	**"Reduced", data NR***			
Thomas 2003[71,78,82]	Bronchodilator use, canisters issued (number of canisters)	26w	IG (HRBT)	17	16	1 (0, 4) §	0 (NR)§	NR	NA	NSD in number of ICS canisters issued within each group at 26w.
			CG	16	12	0 (0, 10)§	1 (NR)§			
Cooper 2009‡[51,75,89]	Short-acting bronchodilator use, median (puffs/w)	4w	IG (mouth-taping)	51	51	10 (4.3,28)†	-0.5 (NR)†	0.12	Insufficient data to calculate	
			CG			10 (NR)†	-3.5 (NR)†			

*Statistical significant change from baseline or between groups (p<0.05)

†Median or median change from baseline (IQR)

‡Crossover study design, mouth-taping and control phases

§Median number of canisters issued (range)

Abbreviations: BBT: Buteyko breathing technique; CG: control group; CI: confidence interval; d: day(s); HRBT: hyperventilation reduction breathing technique; ICS: inhaled corticosteroids; IG: intervention group; IQR: inter-quartile range; mcg: microgram(s); NA: not applicable; NR: not reported; NSD: no significant difference; SD: standard deviation; w: week(s)

Evidence Table 1e. Change in quality of life: hyperventilation reduction breathing techniques versus control

Study	Quality of life outcomes	Follow-up	Group	N randomized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (coded higher= better)	Functioning or additional quality of life outcomes
Cooper 2003[52]	AQLQ-Juniper, total score (higher= better)	13w	IG1 (BBT)	30	26	5.1 (1.0)	0.45 (0.11, 1.47)†	0.4 (for difference across all three groups)	Insufficient data to calculate	**Groups differed in SF-36 role limitations due to physical problems at 13w.* Groups differed in SF-36 role limitations due to physical problems and social functioning at 26w.*** NSD between groups on other components of the SF-36 at 12 and 26w.
			CG	30	25	5.0 (0.8)	0.33 (-0.20, 0.75)†			
		26w	IG	30	23	5.1 (1.0)	1.03 (0.19, 1.69)†	0.2 (for difference across all three groups)	Insufficient data to calculate	
			CG	30	22	5.0 (0.8)	0.61 (-0.11, 0.95)†			
Grammato-poulou 2011[54]	None	4w, 12w, 26w	IG (HRBT)	20	20	NA	NA	NA	NA	Groups differed in SF-36 physical components at 4 and 12w, not 26w. NSD between groups in the SF-36 mental component at any time point.
			CG	20	20	NA	NA			

Study	Quality of life outcomes	Follow-up	Group	N randomized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (coded higher= better)	Functioning or additional quality of life outcomes
Holloway 2007[55,72]	SGRQ-total score (higher= worse)	26w	IG (Pap-worth)	39	32	25.2 (16.1)	-9.3 (9.7)	0.19	**0.68 (0.22. 1.15)**	No group differences on Impacts and Activities scales of SGRQ at 26 or 52w. **Groups differed in HADS anxiety and depression scores at 26 and 52w.***
			CG	46	40	19.7 (11.3)	-3.4 (7.5)			
		52w	IG (Pap-worth	39	32	25.2 (16.1)	-10.0 (9.9)	**0.05***	**0.81 (0.33, 1.23)**	
			CG	46	40	19.7 (11.3)	-3.0 (7.2)			
McGowan 2003[56,99]	None	26w	IG (BBT)	200	180	NA	NA	NA	NA	
			CG1 (nurse education)	200	165	NA	NA			
			CG2 (brief asthma education)	200	145	NA	NA			
Opat 2000[57,77]	AQLQ-Marks, total score	4w	IG (BBT)	18	16	2.72 (1.58)	NR (NR)	**0.043***	Insufficient data to	**Mean AQLQ difference**

Study	Quality of life outcomes	Follow-up	Group	N randomized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (coded higher= better)	Functioning or additional quality of life outcomes
	(lower= better)		CG	18	16	2.70 (1.61)	NR (NR)		calculate	**between groups -1.29 (95% CI, -2.53 to -0.05).***
Thomas 2009[59,79-81]	AQLQ-Juniper, total score (higher= better)	4w	IG (HRBT)	94	73	4.2 (1.0)	0.92 (1.11)	0.78	0.04 (-0.28, 0.36)	**Groups differed in HADS anxiety and depression scores at 26w.***
			CG	89	79	4.3 (0.9)	0.88 (1.00)			
		26w	IG	94	63	4.2 (1.0)	1.12 (0.81)	**0.01***	**0.43 (0.08, 0.78)***	
			CG	89	66	4.3 (0.9)	0.74 (0.95)			
		52w	IG	94	55	4.2 (1.0)	**1.52 (0.89)***	**0.002***	**0.46 (0.10, 0.82)***	
			CG	89	68	4.3 (0.9)	**1.04 (1.16)***			
Thomas 2003[71,78,82]	AQLQ-Juniper, total score, median (higher= better)	4w	IG (HRBT)	17	16	4.60 (1.01)	0.60 (0.05, 1.12)†	**0.018***	Insufficient data to calculate	
			CG	16	15	4.57 (1.27)	0.09 (-0.25, 0.26)†			
		26w	IG	17	16	4.60 (1.01)	0.79 (-0.09, 1.40)†	0.065	Insufficient data to calculate	

Study	Quality of life outcomes	Follow-up	Group	N randomized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (coded higher= better)	Functioning or additional quality of life outcomes
			CG	16	12	4.57 (1.27)	0.03 (-0.33, 0.47)†			
Cooper 2009§[51,75,89]	Mini-AQLQ, total score (higher= better)	4w	IG (mouth-taping)	51	51	NR (NR)	5.33 (1.19)‡	0.40	Insufficient data to calculate	
			CG			NR (NR)	5.43 (0.94)‡			

*Statistically significant change from baseline or between groups (p<0.05)

†Median or median change from baseline (IQR)

‡Mean (SD) at each time point

§Crossover study design, mouth-taping and control phases

Abbreviations: AQLQ: Asthma Quality of Life Questionnaire; BBT: Buteyko breathing technique; CG: control group; CI: confidence interval; HADS: Hospital Anxiety and Depression Scale; HRBT: hyperventilation reduction breathing technique; IG: intervention group; IQR: inter-quartile range; NA: not applicable; NR: not reported; NSD: no significant difference; SD: standard deviation; SF: social functioning (e.g., SF-36 Health Survey); SGRQ: St. George's Respiratory Questionnaire; w: week(s)

Evidence Table 1f. Change in pulmonary function: hyperventilation reduction breathing techniques versus control

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
Cooper 2003[52]	FEV_1 (L)	26w	IG1 (BBT)	30	23	2.58 (0.76)	0.06 (0.26)	0.4 (for difference across all three groups)	0.28 (-0.31, 0.86)	NSD between groups at 13 and 26w in provocative dose causing a fall of 20 percent in FEV_1.
			CG	30	22	2.71 (0.89)	0.001 (0.14)			
Grammato-poulou 2011[54]	FEV_1, predicted (%)	4w	IG (HRBT)	20	20	83.5 (7.74)	**1.85 (4.97)***	0.779	0.21 (-0.41, 0.83)	Significant differences between groups at 4, 12, and 26w in end-tidal CO_2 and respiratory rate.
			CG	20	20	83.9 (10.14)	0.6 (6.67)			
		12w	IG	20	20	83.5 (7.74)	3.15 (5.07)	0.510	0.40 (-0.23, 1.03)	
			CG	20	20	83.9 (10.14)	0.75 (6.59)			
		26w	IG	20	20	83.5 (7.74)	2.75 (5.06)	0.576	0.35 (-0.28, 0.98)	
			CG	20	20	83.9 (10.14)	0.65 (6.60)			
Holloway 2007[55,72]	FEV_1 (L)	26w	IG (Papworth)	39	32	2.7 (0.9)	0.2 (0.55)	0.974	0.35	NSD between

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
			CG	46	41	2.8 (0.9)	0 (0.57)		(-0.11, 0.82)	groups at 26 or 52w in end-tidal CO_2, FVC, PEF, vital capacity.
		52w	IG	39	30	2.7 (0.9)	0.1 (0.54)	0.583	0.36 (-0.12, 0.85)	
			CG	46	37	2.8 (0.9)	-0.1 (0.55)			
McGowan 2003[56,99]	FEV_1, predicted (%)	26w	IG (BBT)	200	180	80 (10.47)	1 (6.50)	NR	**CG1: 0.30 (0.09, 0.51)*** CG2: 0.15 (-0.07, 0.37)	
			CG1 (nurse education)	200	165	75 (11.31)	-1 (6.80)	NR		
			CG2 (brief asthma education)	200	145	75 (11.31)	0 (6.79)	NR		
Opat 2000[57,77]	None	4w	IG (BBT)	18	13	NA	NA	NA	NA	NSD between groups at 4w in PEF.
			CG	18	15	NA	NA			
Thomas 2009[59,79-81]	FEV_1 (L)	4w	IG (HRBT)	94	73	2.85 (0.83)	**0.1 (0.52)***	0.07	-0.10	NSD

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
			CG	89	79	2.82 (0.76)	**0.15 (0.48)***		(-0.42, 0.22)	between groups at 4w in F_{ENO}, sputum eosinophils, end-tidal CO_2, and minute volume.
Thomas 2003[71,78,82]	None	26w	IG (diaphragm breathing)	17	16	NA	NA	NA	NA	
			CG	16	12	NA	NA			
Cooper 2009†[51,75,89]	FEV_1 (L)	4w	IG (mouth-taping)	51	51	2.41 (0.80)	0.03 (0.51)	0.14	-0.37 (-0.77, 0.02)	NSD between groups at 4w in PEF (morning, evening, or amplitude percent mean).
			CG			2.41 (0.80)	0.27 (0.74)			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Crossover study design, mouth-taping and control phases

Abbreviations: BBT: Buteyko breathing technique; CG: control group; CI: confidence interval; CO_2: carbon dioxide; F_{ENO}: fraction of exhaled nitric oxide; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; HRBT: hyperventilation reduction breathing technique; IG: intervention group; L: liter(s); NA: not applicable; NSD: no significant difference; PEF: peak expiratory flow; SD: standard deviation; w: week(s)

Evidence Table 2a. Study characteristics: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
Bowler 1998[50,73,88]	Australia	IG1 (BBT)	19	45.5	43.6	892 mcg /d	1250 mcg /d	74	Aged 12 to 70y, reported a history of asthma (variable difficulty in breathing, wheeze or chest tightness w/ response to $beta_2$-agonist), taking substantial doses of asthma medication, using at least 1400mcg of SABA or equivalent doses of nebulised or LABA in the last week of run-in period.	Change in inhaled steroid dose or use of oral steroids within the 4w run-in period, other significant unstable medical conditions, undertaken BBT previously.
		IG2 (abdominal breathing)	20							
Cooper 2003[52]	UK	IG1 (BBT)	30	44	44.9	2 puffs /d*	657 mcg /d	80	Aged 18 to 70y, non-smoking volunteers with stable asthma, taking an inhaled SABA at least 2 times/w and regular ICS w/ no change in dose in previous 4w, pre-bronchodilator FEV_1 of at least 50 percent predicted and 10 percent increase following 400mcg inhaled salbutamol, a PD_{20} of methacholine causing a 20 percent fall in FEV_1 of 10.24 µmol or less, mean daily sx score of one or more during run-in.	No other important illnesses, taking tx other than sodium cromoglycate.
		IG2 (yoga breathing device	30							
Cowie 2008[53]	Canada	IG1 (BBT)	65	47.5	76.7	NR	840 mcg	81	Aged 18 to 50y, asthma (confirmed by physician's dx	Not suffered from an exacerbation of their disease

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
		IG2 (physiotherapy)	64				/d		and current use of asthma medications or by a current or previous demonstration of reversibility of their FEV_1 w/ $beta_2$-agonist of at least 12 percent and no less than 200mL.	requiring oral corticosteroids and/or a visit to an ED within 2m of their study entry, dx of another respiratory disease including COPD.
Slader 2006[58]	Australia	IG1 (BBT)	28	NR	56.1	3 puffs /d	NR	80	Aged 15 to 80y, as-needed reliever use ≥ 4 times/w use of ICS (≥ 200mcg/d for ≥ 3m w/ no dose change during previous 4w), current non-smoker, FEV_1 ≥ 50 percent, < 90 percent predicted or FEV_1/FVC < 70 percent, reversibility ≥ 200mL to bronchodilator w/in previous 6m, daily access to TV/VCR.	Current smoker, > 10 pack year smoking history, recently unstable asthma (defined as requiring urgent care or night waking more than 1 time/w), asthma exacerbation or respiratory infection in previous 4w, oral corticosteroids in previous 4w, current or planned pregnancy, substantial limitation of shoulders or thoracic spine, complete nasal obstruction, prior tuition in BBT, use of long-acting $beta_2$-agonists.
		IG2 (diaph-ragm breath-ing)	29							

*Median puffs/d, typical dose per puff = 100 mcg

Abbreviations: BBT: Buteyko breathing technique; COPD: chronic obstructive pulmonary disease; d: day(s); dx: diagnosis; ED: emergency department; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; ICS: inhaled corticosteroids; IG: intervention group; LABA: long-acting $beta_2$-agonists; m: month(s); mcg: microgram(s); mL: milliliter(s); PD_{20}: provocative dose causing a decrease in FEV_1 of 20 percent; pred: predicted; SABA: short-acting $beta_2$-agonists; sx: symptoms; TV: television; tx: treatment; UK: United Kingdom; µmol: micromole(s); VCR: video cassette recorder; w: week(s); w/: with; y: year(s)

Evidence Table 2b. Description of intervention groups: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	Intervention group	Description	Intervention session	Homework	Additional components
Bowler 1998[50,73,88]	IG1 (BBT)	BBT training consisted of the teaching of a series of exercises in which subjects reduced the depth and frequency of respiration. Instructor (a representative of Buteyko Australia) provided F/U calls as necessary (mean 7, range 0 to 20). Pts experiencing difficulty w/ BBT given additional classes (7 subjects).	Seven or more 60 to 90-min session over 7 days, F/U calls as needed (range 0-20), duration NR. (7 to 10.5 or more hours face-to-face)	Encouraged to practice several times a day.	NR
	IG2 (abdominal breathing)	Given general asthma education and relaxation techniques; taught abdominal breathing exercises that did not involve hypoventilation. Instructor provided one F/U call to each pt.	Seven 60-90-min session over 7 days, one F/U call per person, duration NR. (7 to 10.5 hours face-to-face).	NR	NR
Cooper 2003[52]	IG1 (BBT)	Eucapnic BBT as taught by a certified Buteyko practitioner. Pts taught to reduce fx and depth of breathing, use the technique bid to relieve asthma sx (used 420 times over 6m) and use bronchodilator if BBT failed, nocturnal mouth-taping with Micropore hypoallergenic tape. F/U call provided 2w after training and open communication with trainer available. Avoid certain foods (e.g., highly processed food and additives), avoid stress, avoid oversleeping.	Five 2-hour sessions, over weekends or successive evenings. (10 hours total).	Home exercises with an audiotape or CD with technique reminders.	Also included dietary restrictions, stress management and instruction to avoid oversleeping.

Study	Intervention group	Description	Intervention session	Homework	Additional components
	IG2 (yoga breathing device)	Pink City Lung exerciser (yoga breathing device) imposed a 1:2 ratio on the duration of inspiration compared with expiration. Device set at largest aperture, pts asked to breathe at rate which they felt no resistance and could feel no check movement. Over time decrease aperture size to gradually reduce respiratory rate. Use $beta_2$-agonist only for sx relief. PCLE used bid (420 times over 6m).	One session, 6m practice. (Hours NR)	Use PCLE bid.	NR
Cowie 2008[53]	IG1 (BBT)	Received BBT instruction by an accredited Buteyko practitioner in the early evening for 5 consecutive days. Pts instructed in techniques designed to reduce (normalize) their ventilation including holding their breathing at FRC and avoid breathing through the mouth (e.g., mouth-taping at night).	Five sessions over 5 days. (Hours NR)	Encouraged to practice training repeatedly throughout the day.	NR
	IG2 (physiotherapy)	Received breathing instruction in early evening on 5 consecutive days from a registered physiotherapist. Pts instructed to developed slow, controlled exhalation, down into FRC toward their residual volume, pace breathing.	Five sessions over 5 days. (Hours NR)	NR	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Slader 2006[58]	IG1 (BBT)	BBT components: hypoventilation, breathing hold at functional residual capacity; accompanied by footage of scenery. Pts provided an instruction and daily exercises videos required to watch at least once daily while practicing breathing exercises bid. Unblinded researcher contacted pts biweekly to review essentials, answer questions and clarify concerns; offered in-person tuition. Practice shorter version as needed for relief, use reliever if sx persist.	420 13-min sessions, six F/U calls with study staff over 30w. (90 hours practice with video if fully compliant)	NR	NR
	IG2 (controlled breathing)	Components: shoulder rotations, forward curls, arm raises w/ controlled inspiratory-expiratory cycles; "control of breathing" through good posture and relaxation; route of breathing not specified w/ both mouth and nasal breathing demonstrated. Pts provided an instruction and daily exercises videos required to watch at least once daily while practicing breathing exercises bid. Unblinded researcher contacted pts biweekly to review essentials, answer questions and clarify concerns; offered in-person tuition. Practice "control of breathing" exercises (physical maneuvers optional) as needed for relief, use reliever if sx persist.	420 13-min sessions, six F/U calls with study staff over 30w. (90 hours practice with video if fully compliant)	NR	NR

Abbreviations: BBT: Buteyko breathing technique; bid: twice daily; CD: compact disc; FRC: functional residual capacity; F/U: followup; fx: frequency; min: minute(s); m: month(s); NR: not reported; PCLE: Pink City Lung exerciser; pt(s): patient(s); sx: symptoms; w/: with; w: weeks.

Evidence Table 2c. Change in asthma symptoms: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (coded lower=better)	Additional asthma symptom outcomes
Bowler 1998[50,73,88]	None	13w	IG1 (BBT)	19	18	NA	NA	NA	NA	NSD in number of participants in each group with exacerbations requiring hospitalization or short course of prednisone at 8m.
			IG2 (abdominal breathing)	20	19	NA	NA			
Cooper 2003[52]	Mini-Juniper AQLQ, symptoms subscale (higher=better)	13w	IG1 (BBT)	30	26	5.0 (1.0)	0.42 (-0.17,1.6)†	0.6 (for difference between all three groups)	Insufficient data to calculate	**Three groups differed across median daily symptom scores at 26w, p=0.003.*** NSD between groups in the number of exacerbations at 26w.
			IG2 (yoga breathing device)	30	25	5.0 (0.8)	0.50 (-0.38,1.21)†			
		26w	IG1	30	23	5.0 (1.0)	1.08 (0.08,1.92)†	0.2 (for difference across all three groups)	Insufficient data to calculate	
			IG2	30	24	5.0 (0.8)	0.58 (0, 1.21)†			
Cowie	Controlled	26w	IG1 (BBT)	65	56	26 (40%)‡	44 (68%)‡	0.40	NA	

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (coded lower=better)	Additional asthma symptom outcomes
2008[53]	asthma (number of participants)		IG2 (physio-therapy)	64	63	28 (64%)‡	45 (70%)‡			
Slader 2006[58]	ACQ, total score (lower=better)	12w	IG1 (BBT)	28	28	1.46 (0.61)	-0.12 (0.46)	0.23	0.33 (-0.24, 0.90)	Almost no group differences on daytime symptom intensity, nighttime symptom intensity, patient and clinician global rating of asthma control, and symptom free days at 12 and 28w. Both groups improved on ACQ and physician global assessment over time; IG2 improved over time on daytime and nighttime symptoms while IG1 did not.
			IG2 (controlled breathing)	29	29	1.37 (0.55)	**-0.28 (0.45)***			
		28w	IG1	28	23	1.46 (0.61)	**-0.38 (0.42)***	0.47	-0.14 (-0.71, 0.43)	
			IG2	29	25	1.37 (0.55)	**-0.32 (0.42)***			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Median or median change from baseline (IQR)

‡Number of participants (%) reporting controlled asthma at followup

Abbreviations: ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; BBT: Buteyko breathing technique; CG: control group; CI: confidence interval; IG: intervention group; IQR: inter-quartile range; m: month(s); NA: not applicable; NSD: no significant difference; SD: standard deviation; w: week(s)

Evidence Table 2d. Change in asthma medication use: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
Bowler 1998[50,73,88]	Daily adjusted $beta_2$-agonist dose, median (mcg)	13w	IG1 (BBT)	19	18	943 (NR)†	-904 (NR)†	**0.002***	Insufficient data to calculate	NSD between groups and little change in either group in absolute median daily inhaled steroid doses 13w; no group differences in prednisone use at 8m.
			IG2 (abdominal breathing)	20	19	843 (NR)†	-57 (NR)†			
Cooper 2003[52]	$Beta_2$-agonist use, median (puffs/d)	26w	IG1 (BBT)	30	23	2 (0, 4)†	-2 (-4, 0)†	**0.005 (for difference across all three groups)***	Insufficient data to calculate	NSD between all three groups and little change in any group in median number of days taking increased ICS dose or median number of prednisolone courses per subject at 26w. percent reduction in inhaled steroids (n=39).
			IG2 (yoga breathing device)	30	24	2 (0, 4)†	0 (-2, 0)†			
Cowie 2008[53]	None	26w	IG1 (BBT)	65	56	NA	NA	NA	NA	**IG1 showed greater reduction in ICS use (p=0.02), and greater likelihood of discontinuing LABA (p=0.005).***
			IG2 (physiotherapy)	64	63	NA	NA			

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
Slader 2006[58]	Reliever use (puffs/d)	12w	IG1 (BBT)	28	28	2.9 (2.2)	**-1.4 (1.3)***	0.17	0.36 (-0.16, 0.89)	Similar pattern of results for number of reliever free days and ICS use: both group improve, no group differences at 12 or 28w. ICS use reduced by 50 percent in both groups at 28w.
			IG2 (controlled breathing)	29	29	3.1 (2.3)	**-1.9 (1.4)***			
		28w	IG1	28	23	2.9 (2.2)	**-1.8 (1.3)***	0.99	-0.02 (-0.59, 0.55)	
			IG2	29	25	3.1 (2.3)	**-1.8 (1.5)***			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Median or median change from baseline (IQR)

‡Number of participants (%)

Abbreviations: BBT: Buteyko breathing technique; CG: control group; d: day(s); CI: confidence interval; ICS: inhaled corticosteroids; IG: intervention group; IQR: inter-quartile range; LABA: long-acting $beta_2$-agonist; m: month(s); mcg: microgram(s); NA: not applicable; NR: not reported; SD: standard deviation; w: week(s)

Evidence Table 2e. Change in quality of life: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	Quality of life outcomes	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (coded higher= better)	Functioning or additional quality of life outcomes
Bowler 1998[50,73,88]	AQLQ-Marks, median (lower= better)	13w	IG1 (BBT)	19	18	3.0 (NR)	-1.2 (NR)†	0.09	Insufficient data to calculate	
			IG2 (abdom. breathing)	20	19	3.0 (NR)	-0.4 (NR)†			
Cooper 2003[52]	AQLQ-Juniper, total score (higher= better)	13w	IG1 (BBT)	30	26	5.1 (1.0)	0.45 (0.11, 1.47)†	0.4 (for difference across all three groups)	Insufficient data to calculate	**BBT improved more in SF-36 role limitations due to physical problems at 13w.* BBT improved more in SF-36 role limitations due to physical problems and social functioning at 26w.*** NSD between groups on other components of the SF-36 at 13 and 26w.
			IG2 (yoga breathing device)	30	25	4.9 (0.8)	0.45 (-0.13, 1.11)†			
		26w	IG1	30	23	5.1 (1.0)	1.03 (0.19, 1.69)†	0.2 (for difference across all three groups)	Insufficient data to calculate	
			IG2	30	24	4.9 (0.8)	0.57 (0.07, 1.10)†			
Cowie 2008[53]	Mini-AQLQ, total score	26w	IG1 (BBT)	65	56	4.6 (NR)	**0.96 (1.04)***	1.0	Insufficient data to calculate	
			IG2 (physio-	64	63	4.7 (NR)	**0.95 (1.15)***			

	(higher= better)		therapy)							
Slader 2006[58]	AQLQ-Marks, total score (lower= better)	12w	IG1 (BBT)	28	25	0.77 (0.50)	0.03 (0.42)	0.29	-0.14 (-0.68, 0.41)	
			IG2 (controlled breathing)	29	27	0.54 (0.30)	-0.02 (0.30)			
		28w	IG1	28	23	0.77 (0.50)	-0.17 (0.32)	0.27	0.23 (-0.34, 0.80)	
			IG2	29	25	0.54 (0.30)	-0.1 (0.28)			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Median or median change from baseline (IQR)

Abbreviations: abdom: abdominal; AQLQ: Asthma Quality of Life Questionnaire; BBT: Buteyko breathing technique; CG: control group; CI: confidence interval; IG: intervention group; IQR: inter-quartile range; NR: not reported; NSD: no significant difference; SD: standard deviation; SF: social functioning (e.g., SF-36 Health Survey); w: week(s)

Evidence Table 2f. Change in pulmonary function: hyperventilation reduction breathing techniques versus nonhyperventilation reduction breathing techniques

Study	FEV_1 outcome (unit)	Follow-up	Group	N randomized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
Bowler 1998[50,73,88]	FEV_1, predicted (%)	13w	IG1 (BBT)	19	18	75 (17)	-3 (13.21)	0.40	-0.16 (-0.80, 0.49)	**Groups differed in minute volume at 13w, p=0.004**.* NSD between groups at 13w in end-tidal CO_2 and pre-bronchodilator PEF (morning).
			IG2 (abdominal breathing)	20	19	73 (19)	-1 (11.4)			
Cooper 2003[52]	FEV_1 (L)	26w	IG1 (BBT)	30	25	2.58 (0.76)	0.06 (0.26)	0.4 (for difference across all three groups)	0.29 (-0.28, 0.87)	NSD between group at 12 and 26w in provocative dose causing a fall of 20 percent in FEV_1.
			IG2 (yoga breathing device)	30	24	2.64 (0.94)	-0.002 (0.14)			
Cowie 2008[53]	FEV_1, predicted (%)	26w	IG1 (BBT)	65	56	83 (19.2)	-0.05 (0.47)	0.60	-0.09 (-0.45, 0.27)	
			IG2 (physiotherapy)	64	63	79 (21.6)	-0.01 (0.37)			
Slader 2006[58]	FEV_1, predicted (%)	12w	IG1 (BBT)	28	28	80.8 (16.1)	-1.1 (10.5)	0.30	0.17 (-0.35, 0.69)	NSD between groups at 12 or 28w in predicted FVC, end-tidal CO_2,
			IG2 (controlled breathing)	29	29	78.9 (17.0)	**-3.0 (11.8)***			

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
		28w	IG1	28	23	80.8 (16.1)	-2.0 (10.6)	0.23	0.11 (-0.46, 0.67)	and mannitol responsiveness.
			IG2	29	25	78.9 (17.0)	-3.2 (10.9)			

*Statistically significant change from baseline or between groups ($p<0.05$)

Abbreviations: BBT: Buteyko breathing technique; CI: confidence interval; CO_2: carbon dioxide; FEV_1: forced expiratory volume in 1 second; FVC forced vital capacity; IG: intervention group; L: liter(s); NSD: no significant difference; PEF: peak expiratory flow; SD: standard deviation; w: week(s)

Evidence Table 3a. Study characteristics: yoga breathing technique versus control

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
Khare 1991[60]	India	IG (yoga breath-ing)	17	38.9	0	NR	NR*	NR	Aged 25 to 50y, male asthmatics not suffering from other disease (e.g., coronary heart disease, valvular disease, chronic bronchitis and emphysema). Pts on vegetarian diet only.	Cigarette smokers
		CG	17							
Kligler 2011[61]	United States	IG (yoga)	77	44.6	81.2	NR	79%‡	NR	Aged 18 to 80y, Class II through IV asthma sufferers (mild, moderate and severe persistent asthma); ability to read/write at 5th grade level; willingness to comply with study instructions; English speakers.	Pregnant or lactating; concurrent serious or life-threatening illness as determined by clinical judgment; psychiatric disorder as determined by clinical judgment; inability to understand and following direction associated with the clinical study as determined by clinical judgment; fish allergy; history of adverse reaction to vitamin C or fish oil as determined by clinical history.
		CG	77							
Sabina 2005[62]	United States	IG (yoga breath-ing)	29	51	74.2	1 puffs /d	NR	NR	Aged ≥ 18y, dx of mild to moderate asthma for ≥ 6m (ATS spirometry criteria: FEV_1/FVC below lower limit of normal, response to bronchodilator [≥ 12 percent increase and ≥ 200mL	Smoked currently (within past 12m), smoking history > 5 pack years, lung disease, only EIA, practices yoga in past 3y, pregnancy, chronic medical condition that

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
		CG	33						absolute increase in FEV_1 15min after two puffs of short-acting $beta_2$-agonist]), taking ≥ one of the following: inhaled corticosteriods, inhaled $beta_2$-agonists, methylxanthines, anticholinergics, leukotriene inhibitors, receptor antagonists, or mast cell-stabilizing agents > 6m, stable medication dosing for ≥ 1m.	required tx w/ oral corticosteroids within 1m, medical condition that contraindicated exercise, or another unstable medical condition.
Saxena 2009[63]	India	IG (yoga breath-ing)	25	29.25	50	NR	NR	72	Bronchial asthma pts with diagnostic confirmation: sx of asthma, FEV_1 < 85 percent, reversibility (increase in FEV_1) > 12 percent after 20min of two salbutamol puffs. Study cases has FEV_1 > 70 percent, interest in yoga and a 6m minimum experience in performing yogic practices.	Pts with sx suggestive of disease other than bronchial asthma like ischemic heart disease, bronchitis, and anemia; history of smoking.
		CG	25							
Vempati 2009[64,74,83-87]	India	IG (yoga breath-ing)	30	33.45	42.1	2.1 puffs/d (plus 11 non-users)	339 mcg/d (plus 25 non-users)	66	Aged ≥ 18y; had an established diagnosis of mild-to-moderate asthma for at least 6m (meeting the ATS spirometry criteria for mild-to-moderate asthma, which requires either FEV_1/FVC < the lower limit of normal w/a significant response to a	Smoked currently (or in the past year) or had a smoking history of > 5 pack years; had a concomitant lung disease; were taking leukotriene inhibitors or receptor antagonists, or mast cell-stabilizing agents for at least

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
		CG	30						bronchodilator [a ≥ 12 increase and a ≥ 200mL absolute increase in FEV_1 15min after the administration of two puffs of a SABA] or PEFR variability > 20%); taking at least one of the following: inhaled $beta_2$-agonists, methylxanthines, anticholinergics, ICS; and stable medication dosing for the past 1m.	6m; practiced yoga or any other similar discipline during 6m prior to the study; pregnant; had a chronic medical condition that required treatment with oral or systemic corticosteroids in the past 1m; had a medical condition that contraindicated exercise; or had an unstable medical condition.

*19/34 (56%) "disturbed sleep and dyspnea on daily routine work which was relieved by oral drugs"; 8/34 (24%) "asthma required injection frequently to control dyspnea or admission in the hospital"

†Median puffs/d, typical dose per puff = 100 mcg

‡Percent using corticosteroid or other asthma medication

Abbreviations: ATS: American Thoracic Society; CG: control group; d: day(s); dx: diagnosis; EIA: exercise-induced asthma; FEV_1: forced expiratory flow in 1 second; FVC: forced vital capacity; ICS: inhaled corticosteroids; IG: intervention group; m: month(s); min: minute(s); mL: milliliter(s); NR: not reported; PD_{20}: provocative dose causing a decrease in FEV_1 of 20 percent; PEFR: pulmonary expiratory flow rate; pts: participants; pred: predicted; SABA: short-acting $beta_2$-agonists; sx: symptoms; tx: treatment; µmol: micromole(s); US: United States; y: year(s)

Evidence Table 3b. Description of intervention groups: yoga breathing techniques versus control

Study	Intervention group	Description	Intervention session	Homework	Additional components
Khare 1991[60]	IG (yoga breathing)	Pts underwent yoga asana training (once) taught by a yogasana instructor. Practices included Surya Namaskar (2min), Sarvang asana (3min), Halasana (3min), Matsyasana (3min), Bhujang asana (2min), Shalabasana (2min), Dhanurasana Vajrasana (5min), Meditation (15min), Pranayama (15min), Shavasana (20min). Practices performed daily from to 7 AM. Any error in learning were rectified; weekly followup of most pts possible. All pts hospitalized initially to facilitate training.	180 70-min sessions over 6m. (210 hours total of yoga practice)	Perform daily at home.	NR
	CG	Pts received only bronchodilators, antibiotics and expectorants as indicated. Pts did not perform yoga.	NR	NR	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Kligler 2011[61]	IG (yoga)	Pts attended two yoga and prayanama breathing classes with a certified yoga instructor. Yoga included (1) brief centering focused on breath and body awareness, (2) diaphragmatic abdominal breathing while lying on back, (3) mountain brook pose followed by gentle yoga stretch pulling the knees towards the chest while lying supine to release tension in the lower back, (4) legs up the wall (modified inversion) followed by modified fish pose (counterpose for inversion), (5) guided deep relaxation with imagery (20min). During second yoga session, deerga swasaam breathing replaced diaphragmatic breathing. Pts also attended two sessions on healthy eating with a nutritionist, focused on eliminating inflammation-promoting foods and common causes of food sensitivity (e.g., eggs, dairy, soy, wheat, corn, citrus, nuts, shellfish, pork, chocolate) (2-4w) followed by a testing phase in which each excluded food group is singly introduced and eat regularly for 3-5d with close monitoring for asthma sx. Food groups that provoke asthma are removed from the diet during the study period. Pts also took fish oil (2800mg/d containing EPA 860mg/DHA 580mg), vitamin C supplements (100 mg/d) and on a standardized hops extract with natural anti-inflammatory products and pts provided w/ 6m supply. Pts also attended one guided journaling session (facilitated by a social worker) to write about the most traumatic or stressful experience to date (30min). Pts also attended one information session to ask questions regarding their asthma or specific treatments delivered during the study.	Six 60 to 90-min sessions over 6w. (9 hours maximum of direct instruction)	Perform at home, frequency NR.	Also include dietary modification and restrictions, supplement use and stress management

Study	Intervention group	Description	Intervention session	Homework	Additional components
	CG	Usual care	NR	NR	NR
Sabina 2005[62]	IG (yoga breathing)	The principles of Iyengar yoga including 15 asana (postures), pranayma (breathing), and dhyana (meditation) were taught to pts in 90min classes two times/w. The experience Iyengar yoga instructor individually tailored advice to improve each pt's technique. Classes concluded with relaxation and meditation. Pts provided handouts and cassettes to practice at home. At end of 4w, pts asked to continue home practice for 20min/d, 3 times/w for additional 3m.	Eight 90-min sessions with instructor over 4w, then 36 20-min sessions at home sessions over 12w. (12 hours direct instruction)	Encouraged to practice at home during 4w instruction period, 2m homework-only phase.	NR
	CG	Sham intervention of basic muscle stretching exercises during a 1hr class, two times/w. Classes taught by a certified exercise physiologist or graduate studies in exercise physiology. Instruction based on ACSM published guidelines. Pts provided handouts and cassettes to practice at home. At end of 4w, pts asked to continue home practice for 20min/d, 3 times/w for additional 3m.	Eight 90-min sessions with instructor over 4w, then 36 20-min sessions at home sessions over 12w. (12 hours direct instruction)	Encouraged to practice at home during 4w instruction period, 2m homework-only phase.	NR
Saxena 2009[63]	IG (yoga breathing)	Pts practiced yoga breathing exercises/pranyama for 20min bid for 12w. Breathing exercises included: (1) deep breathing (sit in sukhasana, breathing through nostrils), (2) sasankasana breathing, (3) Anumloma viloma (alternate nostrils), (4) Bhramari chanting (breathing through nostrils, hum like a bee), and (5) Omkara (modified, exhalation exercise). First three exercises normalize breathing, last two are expiratory muscles.	168 20-min sessions over 12w (unclear how many supervised versus at home). (56 hours of practice)	168 20-min sessions over 12w (unclear how many supervised versus at home).	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
	CG	Pts practiced meditation (closed eyes, sitting posture) for 20min bid for 12w. Pts advised to confirm the side of nostril from wherein the air is coming maximum, then to concentrate on the same nostril, to appreciate the sound of the air along the inward/outward movement of outer wall of nostril.	168 20-min sessions over 12w (unclear how many supervised versus at home). (56 hours of practice)	168 20-min sessions over 12w (unclear how many supervised versus at home).	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Vempati 2009[64,74,83-87]	IG (yoga breathing)	Conventional care in addition to yoga (raja-based) as taught by a qualified yoga instructor. Yoga-based lifestyle modification and stress management program for 4hrs/d for 2w. Sessions conducted btwn 8 AM and noon. Program consisted of lectures (on yoga, stress management, nutrition, health education), practice session on asanas (postures), pranayama (breathing techniques), kriyas (cleansing techniques), meditation and shavasna (relaxation). Session included 1hr of asanas/pranayama, breakfast and group support (30min), lecture/discussion (2hrs); meditation (30min). Pts received at least one individualized counseling session by physicians with special interest in yoga. Yoga practice sessions about 1.5hrs during 2w training period, followed by 6w home practice (1hr asana/pranayama, 10min relaxation, 20min meditation). Pts provided audiocassettes and printed materials to reference; telephonic support as provided. Predominantly vegetarian diet (unrefined cereals and pulses, moderate amounts of judiciously chosen fats, mild, milk products, spices; vegetables/fruits 500g/d predominantly leafy greens/raw). Predominantly vegetarian diet (unrefined cereals and pulses, moderate amounts of judiciously chosen fats, mild, milk products, spices; vegetables/fruits 500g/d predominantly leafy greens/raw).	14 240-min program sessions over 2w; 30 90-min home practice sessions (5 times/w to be compliant) over 6w. (56 hours direct instruction)	Practice at home for additional 6w at least five times/w to be compliant.	Also included dietary advice, instruction on cleansing techniques, meditation, and relaxation.
	CG	Conventional care, a session on health education relevant to their illness. At end of 8w study period, pts offered the intervention based on yoga (wait-list).	One session.	NR	NR

Abbreviations: ACSM: American College of Sports Medicine; addtl: additional; bid: twice daily; btwn: between; d: day; g: grams; hr(s): hour(s); IG: intervention group; m: month(s); mg: milligram; min: minute(s); NR: not reported; pts: participants; sx: symptoms; w: weeks; w/: with.

Evidence Table 3c. Change in asthma symptoms: yoga breathing techniques versus control

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded lower=better)	Additional asthma symptom outcomes
Khare 1991[60]	Severity score, mild (number of participants)	26w	IG (yoga breathing)	17	17	3 (17.6%)†	9 (52.9%)†	NR	Insufficient data to calculate	**More improved symptoms in IG (47%) than CG (12%); more symptom deterioration in CG (41%) than IG (18%), p-value NR but likely statistically significant.***
			CG	17	17	4 (23.5%)†	5 (29.4%)†			
	Severity score, moderate (number of participants)	26w	IG	17	17	9 (52.9%)†	6 (35.3%)†	NR	Insufficient data to calculate	
			CG	17	17	10 (58.8%)†	8 (47.1%)†			
	Severity score, severe (number of participants)	26w	IG	17	17	5 (29.4%)†	2 (11.7%)†	NR	Insufficient data to calculate	
			CG	17	17	3 (17.6%)†	4 (23.5%)†			
Kliger 2011[61]	AQLQ-Juniper symptoms subscale (higher=better)	6w	IG (yoga)	77	NR	4.28 (1.41)	**0.94 (0.85)***	NR	**-0.51**	
			CG	77	NR	4.38 (1.24)	0.52 (0.79)		**(-0.86, -0.16)***	
		12w	IG	77	66	4.28 (1.41)	**1.16 (0.85)***	NR	**-0.75**	
			CG	77	60	4.38 (1.24)	0.54 (0.79)		**(-1.11, -0.39)***	
		26w	IG	77	67	4.28 (1.41)	**1.23 (0.85)***	**0.02***	**-0.53**	

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded lower=better)	Additional asthma symptom outcomes
			CG	77	62	4.38 (1.24)	0.80 (0.75)		**(-0.88, -0.18)***	
Sabina 2005[62]	Asthma symptom score, morning	4w	IG (yoga breathing)	29	23	1.90 (1.08)	**NR (NR)***	NSD	Insufficient data to calculate	NSD between groups in evening asthma symptom score at 4 and 16w.
			CG	33	22	0.40 (0.63)	**NR (NR)***			
		16w	IG	29	23	1.90 (1.08)	**NR (NR)***	NSD	Insufficient data to calculate	
			CG	33	22	0.40 (0.63)	**NR (NR)***			
Saxena 2009[63]	Overall symptoms, severity score (% with symptoms)	12w	IG (yoga breathing)	25	NR	74%	10%	**<0.01***	Insufficient data to calculate	**Groups differed across cough, dyspnea and wheezing symptom severity scores at 12w, p<0.01.***
			CG	25	NR	78%	72%			
Vempati 2009[64,74,83-87]	AQLQ-Juniper, symptoms subscale	2w	IG (yoga breathing)	30	28	3.77 (1.3)	**1.3 (0.87)***	NR	**-1.00** **(-1.55, -0.45)***	
			CG	30	29	3.62 (1.42)	0.34 (1.02)			
		4w	IG	30	28	3.77 (1.3)	**1.61 (0.8)***	NR	**-0.92**	

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded lower=better)	Additional asthma symptom outcomes
	(higher=better)		CG	30	29	3.62 (1.42)	**0.8 (0.93)***		**(-1.47, -0.37)***	
		8w	IG	30	28	3.77 (1.3)	**1.65 (0.81)***	0.033	**-0.61**	
			CG	30	29	3.62 (1.42)	**1.08 (1.02)***		**(-1.14, -0.08)***	

*Statistically significant change from baseline or between groups (p<0.05)

†Number of participants (%) reporting severity score

‡Median or median change from baseline (IQR)

Abbreviations: AQLQ: Asthma Quality of Life Questionnaire; CG: control group; CI: confidence interval; IG: intervention group; IQR: inter-quartile range; NA: not applicable; NR: not reported; NSD: no significant difference; SD: standard deviation; w: week(s)

Evidence Table 3d. Change in asthma medication use: yoga breathing techniques versus control

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
Khare 1991[60]	None	26w	IG (yoga breathing)	17	17	NA	NA	NA	Insufficient data to calculate	**More in IG than CG reduced drug dose by 50% or more at 26w. More IG (53%) than CG (18%) reduced medication use at 26w p-value NR but likely <0.05.***
			CG	17	17	NA	NA			
Kliger 2011[61]	None	26w	IG (yoga)	77	67	NA	NA	NA	NA	
			CG	77	62	NA	NA			
Sabina 2005[62]	Rescue inhaler use (times/d)	4w	IG (yoga breathing)	29	23	1.13 (2.15)	-0.06 (0.77)	NR	0.28 (-0.31, 0.86)	
			CG	33	22	0.79 (1.15)	-0.47 (1.92)			
		16w	IG	29	23	1.13 (2.15)	-0.31 (1.92)	NR	-0.48 (-1.08, 0.11)	
			CG	33	22	0.79 (1.15)	0.45 (1.03)			
Saxena 2009[63]	None	12w	IG (yoga breathing)	25	NR	NA	NA	NA	NA	
			CG	25	NR	NA	NA			
Vempati	Rescue	2w	IG (yoga	30	28	2.27 (1.5)	-1.14 (0.92)	**<0.05***	**-1.14**	

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
2009[64,74,83-87]	medication use (puffs/d)		breathing)						**(-1.71, -0.58)***	
			CG	30	29	1.98 (2.09)	0.21 (1.36)			
		4w	IG	30	28	2.27 (1.5)	-1.64 (0.96)	**<0.01***	**-1.36**	
			CG	30	29	1.98 (2.09)	-0.04 (1.33)		**(-1.94, -0.78)***	
		6w	IG	30	28	2.27 (1.5)	-1.39 (0.90)	NR	**-0.78**	
			CG	30	29	1.98 (2.09)	-0.48 (1.36)		**(-1.32, -0.24)***	
		8w	IG	30	28	2.27 (1.5)	**-1.46 (0.90)***	NR	**-0.84**	
			CG	30	29	1.98 (2.09)	**-0.48 (1.36)***		**(-1.38, -0.29)***	

*Statistically significant change from baseline or between groups (p<0.05)

†Median or median change from baseline (IQR)

Abbreviations: CG: control group; CI: confidence interval; d: day(s); ICS: inhaled corticosteroids; IG: intervention group; IQR: inter-quartile range; NA: not applicable; NR: not reported; NSD: no significant difference; SD: standard deviation; w: week(s)

Evidence Table 3e. Change in quality of life: yoga breathing techniques versus control

Study	Quality of life outcomes	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded higher= better)	Functioning or additional quality of life outcomes
Khare 1991[60]	None	26w	IG (yoga breathing)	17	17	NA	NA	NA	NA	
			CG	17	17	NA	NA			
Kligler 2011[61]	AQLQ-Juniper, total score (higher= better)	6w	IG (yoga)	77	NR	4.21 (1.29)	**0.98 (0.78)***	NR	**0.66** **(0.30, 1.02)***	**Groups differed on the activities (p<0.001) and emotions (p<0.001) subscale of the AQLQ at 26w.* Groups differed on the SF-12 on all domains except pain, general health, vitality and emotional role limitation.***
			CG	77	NR	4.43 (1.21)	0.47 (0.76)			
		12w	IG	77	66	4.21 (1.29)	**1.14 (0.80)***	NR	**0.83** **(0.47, 1.20)***	
			CG	77	60	4.43 (1.21)	0.49 (0.75)			
		26w	IG	77	67	4.21 (1.29)	**1.15 (0.78)***	<0.001	**0.70** **(0.34, 1.06)***	
			CG	77	62	4.43 (1.21)	0.61 (0.75)			
Sabina 2005[62]	Mini-AQLQ, total score (higher= better)	4w	IG (yoga breathing)	29	23	4.82 (1.02)	0.17 (0.67)	NR	-0.22 (-0.80, 0.37)	
			CG	33	22	4.80 (0.8)	0.36 (1.03)			
		16w	IG	29	23	4.82 (1.02)	0.57 (1.77)	NR	0.16 (-0.43, 0.74)	
			CG	33	22	4.80 (0.8)	**0.35 (0.75)***			

Study	Quality of life outcomes	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI) (all coded higher= better)	Functioning or additional quality of life outcomes
Saxena 2009[63]	None	12w	IG (yoga breathing)	25	NR	NA	NA	NA	NA	
			CG	25	NR	NA	NA			
Vempati 2009[64,74,83-87]	AQLQ-Juniper, total score (higher= better)	2w	IG (yoga breathing)	30	28	3.72 (1.17)	**1.21 (0.79)***	NR	**1.11** **(0.54, 1.67)***	**Groups differed on the activities (p=0.033) and emotions (p=0.006) subscale of the AQLQ at 8w.***
			CG	30	29	3.64 (1.14)	0.26 (0.9)			
		4w	IG	30	28	3.72 (1.17)	**1.56 (0.7)***	NR	**1.31** **(0.74, 1.89)***	
			CG	30	29	3.64 (1.14)	**0.53 (0.84)***			
		8w	IG	30	28	3.72 (1.17)	**1.74 (0.72)***	**0.013***	**1.06** **(0.51, 1.62)***	
			CG	30	29	3.64 (1.14)	**0.86 (0.9)***			

*Statistically significant change from baseline or between groups (p<0.05)

†Median or median change from baseline (IQR)

Abbreviations: AQLQ: Asthma Quality of Life Questionnaire; CG: control group; CI: confidence interval; IG: intervention group; IQR: inter-quartile range; NR: not reported; NSD: no significant difference; SD: standard deviation; SF: social functioning (e.g., SF-36 Health Survey); w: week(s)

Evidence Table 3f. Change in pulmonary function: yoga breathing techniques versus control

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
Khare 1991[60]	FEV_1 (L)	26w	IG (yoga breathing)	17	17	2.16 (0.37)	**0.4 (0.23)***	NR	**1.05 (0.33, 1.77)***	Larger changes observed in IG at 26w in end-tidal volume, inspiratory reserve volume, inspiratory capacity, maximal voluntary ventilation, FVC, PEFR, and FEV_1/VC ratio.
			CG	17	17	1.73 (0.32)	0.16 (0.21)			
Kligler 2011[61]	FEV_1 (NR)	26w	IG (yoga)	77	67	NR	NR	0.46	Insufficient data to calculate	NSD between groups in FVC (data NR). PFTs did not show a significant change over time in either group (FVC, FEV_1, FEF_{25-75}, MEF).
			CG	77	62	NR	NR			
Sabina 2005[62]	FEV_1 (NR)	4w	IG (yoga breathing)	29	23	2.05 (0.65)	NR (NR)	NR	Insufficient data to calculate	Follow-up data NR. NSD between groups at 4 and 16w in FEV_1. FEV_{25-75}, FVC, PEFR (evening and morning), and FEV_1/FVC ratio.
			CG	33	22	2.69 (0.92)	NR (NR)			
		16w	IG	29	23	2.05 (0.65)	NR (NR)	NR	Insufficient data to calculate	
			CG	33	22	2.69 (0.92)	NR (NR)			
Saxena 2009[63]	FEV_1, predicted (%)	12w	IG (yoga breathing)	25	NR	72 (1.7)	12 (1.38)	**<0.001***	**6.73 (5.25, 8.21)***	**Groups differed in PEFR at 12w, p<0.001.***
			CG	25	NR	73 (2.07)	2 (1.54)			

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
Vempati 2009[64,74,83-87]	FEV_1, predicted (%)	2w	IG (yoga breathing)	30	28	70.2 (17.4)	3.7 (11.89)	NR	0.25 (-0.27, 0.77)	**At 8w, groups differed in PEFR (p<0.001), predicted FEV_1/FVC ratio (p=0.011), and FEF_{25-75} (p=0.035).*** NSD between groups at 8w in serum ECP level, EIB, and predicted FVC.
			CG	30	29	62.5 (19.2)	0.6 (12.61)			
		4w	IG	30	28	70.2 (17.4)	5.9 (12.13)	NR	**0.62 (0.09, 1.15)***	
			CG	30	29	62.5 (19.2)	-2 (13.1)			
		8w	IG	30	28	70.2 (17.4)	**7.7 (10.94)***	**0.009***	**0.88 (0.34, 1.43)***	
			CG	30	29	62.5 (19.2)	-2.6 (12.11)			

*Statistically significant change from baseline or between groups (p<0.05)

Abbreviations: CG: control group; CI: confidence interval; ECP: eosinophilic cationic protein; EIB: exercise-induced bronchoconstriction; ECP: eosinophilic cationic protein; FEF: forced expiratory flow; FEV_1: forced expiratory volume in 1 second; FEV_{25-75}: forced expiratory volume between 25 and 75 percent; FVC: forced vital capacity; IG: intervention group; L: liter(s); MEF: maximum expiratory flow; NR: not reported; NSD: no significant difference; PEF: peak expiratory flow; PEFR: peak expiratory flow rate; PFT: pulmonary function test; SD: standard deviation; VC: vital capacity; w: week(s)

Evidence Table 4a. Study characteristics: inspiratory muscle training versus control

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
Lima 2008[65]	Brazil	IG (IMT)	25	9.68	68	NR	NR	NR	Asthmatic children aged 8 to 12y having received no previous tx for asthma and presenting with uncontrolled asthma.	NR
		CG	25							
Shaw 2011[66,91]	South Africa	IG (abdom. strength-ening)	22	21.9	NR	NR	NR	NR	Caucasian pts with moderate-persistent asthma (based on NIH guidelines), inactive, weight stable for 6m prior to commencement of study, non-smokers, exhibited daily and nocturnal asthmatic sx more than 1 night/w, peak flow variability > 30 percent.	Influenza-like or respiratory infections 2 to 3w prior to the evaluations, contraindications for exercise, not free from asthma exacerbations for at least 7d prior to study inception, unable to abstain from asthma medication 12 hours prior to each evaluation .
		CG	22							
Weiner 1992[67]	Israel	IG (IMT)	15	40.5	40	6 puffs /d	NR	59	Pts w/ moderate to severe asthma, satisfied criteria of the ATS.	NR
		CG	15							
Weiner 2000[69]	Israel	IG (IMT)	12	34.0	34.8	2.7 puffs /d	NR	91	Pts w/ mild, stable asthma (FEV_1 > 80 percent predicted normal value on at least two visits), satisfied ATS definition of asthma (sx of episodic wheezing, cough and shortness of breath responding to bronchodilators and reversible airflow function study), stable clinical condition. Subjects who were high consumers (> 1 puff/d) of $beta_2$-agonists randomized.	Pts recorded PEFR < 80 percent predicted of their best value during run-in period.
		CG	11							

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
Weiner 2002[68]	Israel	IG (IMT)	11	36.2	100	3.2 puffs /d	NR	83	Pts w/ mild persistent-to-moderate asthma (FEV_1 > 60 percent predicted normal values), satisfied ATS definition of asthma w/ sx of episodic wheezing, cough and shortness of breath responding to bronchodilators and reversible airflow obstruction documented in at least one previous pulmonary function study.	NR
		CG	11							

Abbreviations: abdom: abdominal; ATS: American Thoracic Society; CG: control group; CI: confidence interval; d: day(s); FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroids; IG: intervention group; IMT: inspiratory muscle training; NIH: National Institute of Health; NR: not reported; PEFR: pulmonary expiratory flow rate; pred: predicted; pts: participants; SABA: short-acting $beta_2$-agonists; sx: symptoms; tx: treatment; y: year(s)

Evidence Table 4b. Description of intervention groups: inspiratory muscle training versus control

Study	Intervention group	Description	Intervention session	Homework	Additional components
Lima 2008[65]	IG (IMT)	Inspiratory muscle training and breathing exercises, two 50min sessions/w for 7w. First 25min, breathing exercises in supine and sitting positions to provide respiratory reeducation/awareness. Breathing training included diaphragmatic breathing, fractionated breathing, pursed-lip breathing; each performed as a series of 10 repetitions. Last 25min, IMT using Threshold IMT (Respironics): 20min IMT used in 10 series of 60s each, separated by rest of 60s to develop muscle strength; final 5min IMT used uninterrupted to develop endurance. IMT pressure threshold load was 40 percent of maximal inspiratory pressure. In addition to monthly medical visits and educational program (one 60min session/m) about asthma, signs and signals of exacerbation, asthma triggers, environmental control, rescue medication, and preventive medication.	Three 60-min asthma education classes; three medical visits over 13w (minutes NR); 14 50-min IMT sessions over 7w. (14.6 hours, not including medical visits)	Home exercises with an audiotape or CD with technique reminders.	Environmental modification and awareness of asthma triggers.
	CG	Monthly medical visits and educational program (one 60min session/m) about asthma, signs and signals of exacerbation, asthma triggers, environmental control, rescue medication, and preventive medication.	Three 60-min sessions (asthma education classes / medical visits) over 13 weeks. (3 hours)	NR	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Shaw 2011[66,91]	IG (abdominal strengthen-ing)	Diaphragmatic breathing combined with inspiratory resistive breathing in the semi-recumbent position. Pts inspired and expired through a 10cm x 1cm tube principally using abdominal motion while reducing upper rib cage motion. One hand of pts stabilized a 2.5kg (weeks 1 to 4) or a 5kg (weeks 5 to 8) onto the abdominal cavity. Pts completed three sets of 5 to 10 repetitions using 1s of inspiration and 2s of expiration (1:2 ratio), three sets of 10 to 15 repetitions of 2:4 inspiration-expiration ratio and three sets of 15 to 20 repetitions at 3:6 inspiration-expiration ratio.	NR, training over 8 weeks. (Hours NR)	NR	NR
	CG	No structured exercise program.	NR	NR	NR
Weiner 1992[67]	IG (IMT)	Inspiratory muscle training with resistance equal to 15 percent of PI_{max} taught by a physiotherapist. Resistance incrementally increased to 60 percent of PI_{max} within 1m; adjusted q2m according to PI_{max} achieved. During last 2m, resistance equality to 80 percent of PI_{max}.	120 30-min sessions over 6m. (60 hours total)	None	NR
	CG	Sham-training with a threshold inspiratory muscle trainer with no resistance; taught by a physiotherapist.	120 30-min sessions over 6m. (60 hours total)	NR	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
Weiner 2000[69]	IG (IMT)	Specific inspiratory muscle training with a threshold inspiratory muscle trainer (Threshold® Inspiratory Muscle Trainer, Health Scan). Baseline resistance level equal to 15 percent of PI_{max} for 1w; increased incrementally 5 to 10 percent each session to reach 60 percent of their PI_{max} at end of 1m; continued and adjusted q1w to the new PI_{max} achieved.	72 30-min sessions over 3m. (36 hours total)	Trained 6 times/w.	NR
	CG	Sham-training, no resistance.	72 30-min sessions over 3m. (36 hours total)	NR	NR
Weiner 2002[68]	IG (IMT)	Inspiratory muscle training with a threshold inspiratory muscle trainer (Threshold® IMT, Respironics); end-point when the mean inspiratory muscle strength of women equaled to that of the male subjects (not randomized).	120 30-min sessions over 20w. (60 hours total)	NR	NR
	CG	Sham muscle training with same device, no resistance.	120 30-min sessions over 20w. (60 hours total)	NR	NR

Abbreviations: CG: control group; CI: confidence interval; cm: centimeter; d: day; IG: intervention group; IMT: inspiratory muscle training; kg: kilogram; m: month(s); min: minute(s); NR: not reported; PI_{max}: maximal inspiratory mouth pressure; q1w: every one week; q2m; every 2 months; s: seconds; SIMT: specific inspiratory muscle training; w: week(s).

Evidence Table 4c. Change in asthma symptoms: inspiratory muscle training versus control

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional asthma symptom outcomes
Lima 2008[65]	Daytime symptoms (number of participants)	13w	IG (IMT)	25	25	NA	0 (0%)†	**<0.0001***	NA	**Groups differed in number of participants with frequent asthma attack, p<0.0001.***
			CG	25	25	NA	25 (100%)†			
	Nighttime symptoms (number of participants)	13w	IG	25	25	NA	3 (12%)†	**<0.0001***	NA	
			CG	25	25	NA	25 (100%)†			
Shaw 2011[66,91]	None	8w	IG (abdom. strength-ening)	22	22	NA	NA	NA	NA	
			CG	22	22	NA	NA			
Weiner 1992[67]	Chest tightness, morning (diary score)	26w	IG (IMT)	15	15	NR (NR)	**NR (NR)***	NR	Insufficient data to calculate	
			CG	15	15	NR (NR)	NR (NR)			
	Cough (diary score)	26w	IG	15	15	1.4 (NR)	**-1.1 (NR)***	NR	Insufficient data to calculate	
			CG	15	15	2.4 (NR)	0.1 (NR)			
	Daytime asthma (diary score)	26w	IG	15	15	1.7 (NR)	**-1.1 (NR)***	NR	Insufficient data to calculate	
			CG	15	15	2.0 (NR)	-0.2 (NR)			

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional asthma symptom outcomes
	Night-time asthma (diary score)	26w	IG	15	15	2.2 (NR)	**-1.5 (NR)***	NR	Insufficient data to calculate	
			CG	15	15	2.4 (NR)	0.1 (NR)			
Weiner 2000[69]	None	13w	IG (IMT)	12	11	NA	NA	NA	NA	
			CG	11	11	NA	NA			
Weiner 2002[68]	None	4, 8, 12, 16, 20w	IG (IMT)	11	10	NA	NA	NA	NA	
			CG	11	9	NA	NA			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Number of participants (%) experiencing symptoms at followup

Abbreviations: abdom: abdominal; CG: control group; CI: confidence interval; IG: intervention group; IMT: inspiratory muscle training; NA: not applicable; NR: not reported; SD: standard deviation; w: week(s)

Evidence Table 4d. Change in asthma medication use: inspiratory muscle training versus control

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
Lima 2008[65]	Rescue bronchodilator use (number of participants)	13w	IG (IMT)	25	25	NA	4 (16%)†	**<0.0001***	Insufficient data to calculate	
			CG	25	25	NA	21 (84%)†			
Shaw 2011[66,91]	None	8w	IG (abdom. strength-ening)	22	22	NA	NA	NA	NA	
			CG	22	22	NA	NA			
Weiner 1992[67]	$Beta_2$-agonist use (puffs/d)	26w	IG (IMT)	15	15	5.5 (NR)	**-4.3 (NR)***	NR	Insufficient data to calculate	**More participants able to stop oral steroid use in IG than CG at 26w.***
			CG	15	15	6.5 (NR)	-0.5 (NR)			
Weiner 2000[69]	$Beta_2$-agonist use (puff/d)	13w	IG (IMT)	12	11	2.6 (1.33)	**-1 (0.84)***	NR	-0.76 (-1.63, 0.11)	
			CG	11	11	2.8 (2.65)	0.1 (1.78)			
Weiner 2002[68]	$Beta_2$-agonist use (puffs/d)	4w	IG (IMT)	11	10	3.4 (1.99)	-0.4 (NR)	NR	Insufficient data to calculate	
			CG	11	9	3.0 (1.66)	0.2 (NR)			
		8w	IG	11	10	3.4 (1.99)	-0.6 (NR)	NR	Insufficient data to calculate	
			CG	11	9	3.0 (1.66)	-0.1 (NR)			

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
		12w	IG	11	10	3.4 (1.99)	-0.9 (NR)	NR	Insufficient data to calculate	
			CG	11	9	3.0 (1.66)	0.2 (NR)			
		16w	IG	11	10	3.4 (1.99)	-1 (NR)	NR	Insufficient data to calculate	
			CG	11	9	3.0 (1.66)	0.3 (NR)			
		20w	IG	11	10	3.4 (1.99)	**-1.3 (1.2)***	NR	Insufficient data to calculate	
			CG	11	9	3.0 (1.66)	0 (NR)			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Number of participants (%) using bronchodilator at followup

Abbreviations: abdom: abdominal; CG: control group; CI: confidence interval; d: day(s); IG: intervention group; IMT: inspiratory muscle training; NA: not applicable; NR: not reported; SD: standard deviation; w: week(s)

Evidence Table 4e. Change in quality of life: inspiratory muscle training versus control

Study	Quality of life outcomes	Followup	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Functioning or additional quality of life outcomes
Lima 2008[65]	None	13w	IG (IMT)	25	25	NR	NR	**<0.0001***	NA	0 percent with impaired ability to perform activities of daily living in IG vs 100 percent in CG at followup, all impaired at baseline.
			CG	25	25	NR	NR			
Shaw 2011[66,91]	None	8w	IG (abdom. strength-ening)	22	22	NR	NR	NA	NA	
			CG	22	22	NR	NR			
Weiner 1992[67]	None	26w	IG (IMT)	15	15	NR	NR	NR	Insufficient data to calculate	Absences from work/school in past 3m reduced by 1.7 days in IG, increased by 0.2 in CG.
			CG	15	15	NR	NR			
Weiner 2000[69]	None	4w	IG (IMT)	13	11	NA	NA	NA	NA	
			CG	11	11	NA	NA			
Weiner 2002[68]	None	4,8,12,16,20w	IG (IMT)	11	10	NA	NA	NA	NA	
			CG	11	9	NA	NA			

*Statistically significant change from baseline or between groups (p<0.05)

Abbreviations: CG: control group; CI: confidence interval; d: day(s); IG: intervention group; m: month(s); IMT: inspiratory muscle training; NA: not applicable; NR: not reported;

SD: standard deviation; w: week(s)

Evidence Table 4f. Change in pulmonary function: inspiratory muscle training versus control

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
Lima 2008[65]	None	7w, 13w	IG (IMT)	25	25	NA	NA	NA	NA	**Significant difference between groups at 7 and 13w in PEF, p-value NR.***
			CG	25	25	NA	NA			
Shaw 2011[66,91]	FEV_1 (L)	8w	IG (abdom. strength-ening)	22	22	2.85 (0.57	**0.37 (0.38)***	**0.006***	**0.80** **(0.18, 1.42)***	**Significant change from baseline in FVC, PEF, inspiratory vital capacity in IG only (p<0.05).*** NSD from baseline in maximal voluntary ventilation in either group.
			CG	22	22	2.62 (0.53)	0.08 (0.33)			
Weiner 1992[67]	FEV_1, predicted (%)	26w	IG (IMT)	15	15	57.3 (12.47)	**7.9 (7.48)***	NR	**1.31** **(0.51, 2.11)***	**Significant change from baseline in FVC (p<0.005) in IG only.***
			CG	15	15	62.5 (10.07)	-1.7 (6.37)			
Weiner 2000[69]	None	13w	IG (IMT)	12	11	NA	NA	NA	NA	
			CG	11	11	NA	NA			
Weiner	FEV_1, predicted	20w	IG (IMT)	11	10	NR (NR)	NR (NR)	NSD	Insufficient	

Study	FEV_1 outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
2002[68]	(%)		CG	11	9	NR (NR)	NR (NR)		data to calculate	

*Statistically significant change from baseline or between groups (p<0.05)

Abbreviations: abdom: abdominal; CG: control group; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; IG: intervention group; IMT: inspiratory muscle training; NA: not applicable; NR: not reported; NSD: no significant difference; PEF: peak expiratory flow; SD: standard deviation; w: week(s)

Evidence Table 5a. Study characteristics: nonhyperventilation reduction breathing techniques versus control

Study	Country	Group	N random-ized	Age (mean)	% Female	SABA use	ICS use	FEV_1 % pred.	Inclusion criteria	Exclusion criteria
Cooper 2003[52]	UK	IG2 (yoga breathing device)	30	44	44.9	2 puffs /d†	657 mcg /d	80	Aged 18 to 70y, non-smoking volunteers with stable asthma, taking an inhaled SABA at least 2 times/w and regular ICS w/ no change in dose in previous 4w, pre-bronchodilator FEV_1 of at least 50 percent predicted and 10 percent increase following 400mcg inhaled salbutamol, a PD_{20} of methacholine causing a 20 percent fall in FEV_1 of 10.24 µmol or less, mean daily sx score of one or more during run-in.	No other important illnesses, taking tx other than sodium cromoglycate.
		CG	30							
Lehrer 2004[70,76,90]	US	IG (abdominal breathing w/ biofeedback)	23	37.3	68.1	NR	NR	NR*	Aged 18 to 65y, history of asthma sx, positive bronchodilator test results (postbronchodilator FEV_1 increase of ≥ 12%) within past 1y, positive methacholine inhalation challenge test result, or documented recent history (i.e., within past 1y) of clinical improvement and FEV_1 increase ≥ 12 percent following instigation of inhaled steroid therapy among individuals with a protracted history of asthma.	Disorder that would impede performing the biofeedback procedures (e.g., abnormal cardiac rhythm), a negative methacholine challenge test result, an abnormal diffusing capacity (testing among all subjects aged > 55y or w/ > 20 pack years of smoking), current practice of any relaxation, biofeedback or breathing technique.
		CG1 (biofeedback)	22							
		CG2 (placebo)	24							
		CG3 (waitlist)	25							
		CG	16							

*Most patients rated as having moderate-persistent asthma according to the NAEPP guideline

Abbreviations: CG: control group; d: day(s); FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroids; IG: intervention group; m: month(s), mcg: microgram(s); NR: not reported; pred: predicted; SABA: short-acting $beta_2$-agonists; sx: symptom(s); tx: treatment(s); UK: United Kingdom; µmol: micromole(s); US: United States; w: week(s); y:

year(s)

Evidence Table 5b. Description of intervention groups: nonhyperventilation reduction breathing techniques versus control

Study	Intervention group	Description	Intervention session	Homework	Additional components
Cooper 2003[52]	IG2 (yoga breathing device)	PCLE (yoga breathing device) imposed a 1:2 ratio on the duration of inspiration compared with expiration. Device set at largest aperture, pts asked to breathe at rate which they felt no resistance and could feel no check movement. Over time decrease aperture size to gradually reduce respiratory rate. Use $beta_2$-agonist only for sx relief. PCLE used bid (420 times over 6m).	One session, 6m practice. (Hours NR)	Use PCLE bid.	NR
	CG	Sham device with no valve and a leak ensured no resistance to breathing, use bid (420 times in 6m).	One session.	Use device bid.	NR
Lehrer 2004[70,76,90]	IG (abdominal breathing w/ biofeedback)	Pursed-lips abdominal breathing w/ prolonged exhalation biofeedback targeting respiratory resistance, respiratory reactance, and HRV. Pts asked to practice a home for 20min bid using a home trainer unit (KC-3, Biosvyaz).	10 sessions over 10w. (Hours NR)	Asked to practice at home for 20min bid.	NR
	CG1 (biofeedback)	HRV biofeedback only. Pts asked to practice a home for 20min bid using a home trainer unit (KC-3®, Biosvyaz).	10 sessions over 10w. (Hours NR)	Asked to practice at home for 20min bid.	NR

Study	Intervention group	Description	Intervention session	Homework	Additional components
	CG2 (placebo)	Placebo biofeedback procedure involving bogus subliminal suggestions designed to help asthma (with no further details provided and no actual suggestions given) and biofeedback training to alternately increase and decrease frontal EEG alpha-rhythms. Maintain a state of relaxed alertness during home practice using mental strategies developing during the sessions, given tape recording w/ classical music and supposed subliminal suggestions to improve asthma.	10 sessions over 10w. (Hours NR)	Asked to practice at home for 20min bid.	Practice (but no instruction) maintaining state of relaxed alertness, classical music tapes.
	CG3 (waitlist)	Waitlist control	Waited for 30w.	NA	NR

Abbreviations: bid: twice daily; CG: control group; EEG: electroencephalography; HRV: heart rate variability; IG: intervention group; m: month(s); min: minute(s); NR: not reported; PCLE: Pink City Lung exerciser; pts: patients; sx: symptoms; w: week(s).

Evidence Table 5c. Change in asthma symptoms: nonhyperventilation reduction breathing techniques versus control

Study	Symptom outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional asthma symptom outcomes
Cooper 2003[52]	Mini-AQLQ, symptoms subscale (higher= better)	13w	IG2 (yoga breathing device)	30	25	5.0 (0.8)	0.50 (-0.38, 1.21)†	0.6 (for difference between all three groups)	Insufficient data to calculate	**Three groups differed across median daily symptom scores at 26w, p=0.003.*** NSD between groups in the number of exacerbations at 26w.
			CG	30	24	4.9 (0.9)	0.33 (-0.31, 0.58)†			
		26w	IG2	30	24	5.0 (0.8)	0.58 (0, 1.21)†			
			CG	30	22	4.9 (0.9)	0.33 (-0.19, 1.17)†	0.2 (for difference across all three groups)	Insufficient data to calculate	
Lehrer 2004[70,76,90]	Asthma symptoms (diary score) (lower= better)	12w	IG (abdominal breathing with biofeedback)	23	17	0.81 (NR)	**-0.48 (NR)***	**<0.0001***	Insufficient data to calculate	More exacerbations occurred in CG2 and CG3 than IG and CG1.
			CG1 (biofeedback)	22	17	0.95 (NR)	**-0.47 (NR)***			
			CG2 (placebo)	24	19	0.71 (NR)	**-0.33 (NR)***			
			CG3 (waitlist)	25	23	1.15 (NR)	-0.2 (NR)			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Median or median change from baseline (IQR)

Abbreviations: AQLQ: Asthma Quality of Life Questionnaire; CG: control group; CI: confidence interval; IG: intervention group; NR: not reported; NSD: no significant difference; SD: standard deviation; w: week(s)

Evidence Table 5d. Change in asthma medication use: nonhyperventilation reduction breathing techniques versus control

Study	Reliever medication outcome (unit)	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Controller and additional medication outcomes
Cooper 2003[52]	$Beta_2$-agonist use, median (puffs/d)	26w	IG2 (yoga breathing device)	30	24	2 (0, 4)†	0 (-2, 0)†	NR	Insufficient data to calculate	NSD between all three groups in median number of days taking increased ICS dose or median number of prednisolone courses per subject at 26w.
			CG	30	22	2 (0, 3.8)†	0 (-2, 0)†			
Lehrer 2004[70,76,90]	None	12w	IG (abdominal breathing with biofeedback)	23	17	NA	NA	NA	NA	Fewer IG and CG1 participants increased use of controlled medication from baseline than CG2 and CG3 (after run-in to achieve lowest ICS use that stabilizes symptoms).
			CG1 (biofeedback)	22	17	NA	NA			
			CG2 (placebo)	24	19	NA	NA			
			CG3 (waitlist)	25	23	NA	NA			

*Statistically significant change from baseline or between groups ($p<0.05$)

†Median or median change from baseline (IQR)

Abbreviations: CG: control group; CI: confidence interval; ICS: inhaled corticosteroids; IG: intervention group; IQR: inter-quartile range; NA: not applicable; NR: not reported; NSD: no significant difference; SD: standard deviation; w: week(s)

Evidence Table 5e. Change in quality of life: nonhyperventilation breathing techniques versus control

Study	Quality of life outcomes	Follow-up	Group	N random-ized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Functioning or additional quality of life outcomes
Cooper 2003[52]	AQLQ-Juniper, total score (higher= better)	13w	IG2 (yoga breathing device)	30	25	4.9 (0.8)	0.45 (-0.13, 1.11)†	0.4 (for difference across all three groups)	Insufficient data to calculate	**Groups differed in SF-36 role limitations due to physical problems at 13w.* Groups differed in SF-36 role limitations due to physical problems and social functioning at 26w.*** NSD between groups on other components of the SF-36 at 13 and 26w.
			CG	30	24	5.0 (0.8)	0.33 (-0.22, 0.75)†			
		26w	IG2	30	24	4.9 (0.8)	0.57 (0.07, 1.10)†	0.2 (for difference across all three groups)	Insufficient data to calculate	
			CG	30	22	5.0 (0.8)	0.61 (-0.11, 0.95)†			
Lehrer 2004[70,76,90]	None	12w	IG (abdominal breathing with biofeedback)	23	17	NA	NA	NA	NA	
			CG1 (biofeedback)	22	17	NA	NA			
			CG2 (placebo)	24	19	NA	NA			
			CG3 (waitlist)	25	23	NA	NA			

*Statistically significant change from baseline or between groups (p<0.05)

†Median or median change from baseline (IQR)

Abbreviations: AQLQ: Asthma Quality of Life Questionnaire; CG: control group; CI: confidence interval; IG: intervention group; IQR: inter-quartile range; NA: not applicable; NSD: no significant difference; SD: standard deviation; SF: social functioning (e.g., SF-36 Health Survey); w: week(s)

Evidence Table 5f. Change in pulmonary function: nonhyperventilation reduction breathing techniques versus control

Study	FEV_1 outcome (unit)	Follow-up	Group	N randomized	Follow-up N	Baseline mean (SD)	Mean change (SD) from baseline	p-value for difference between groups at followup	Standardized Effect Size Hedges' d (95% CI)	Additional pulmonary function outcomes
Cooper 2003[52]	FEV_1 (L)	26w	IG2 (yoga breathing device)	30	24	2.64 (0.94)	-0.002 (0.14)	0.4 (for difference across all three groups)	-0.02 (-0.60, 0.56)	NSD between groups at 13 and 26w in provocative dose causing a fall of 20 percent in FEV_1.
			CG	30	22	2.71 (0.89)	0.001 (0.14)			
Lehrer 2004[70,76,90]	"Spirometry", specific measures NR	12w	IG (abdominal breathing with biofeedback)	23	17	NR	NR	NSD	NR	NSD from baseline within each group at 12w.
			CG1 (biofeedback)	22	17	NR	NR			
			CG2 (placebo)	24	19	NR	NR			
			CG3 (waitlist)	25	23	NR	NR			

Abbreviations: CG: control group; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; IG: intervention group; NA: not applicable; NR: not reported; NSD: no significant difference; SD: standard deviation; w: week(s)

Appendix E. List of Excluded Studies

1. Abramson M, Borg B, Doran C, et al. A randomised controlled trial of the Buteyko method for asthma. Int J Immunorehabil 2004;6(2):244. PMID: 11059522. **Abstract only, insufficient data to evaluate inclusion.**

2. Agent P. Breathing training improves subjective health status but not pathophysiology in asthmatic adults. J Physiother 2010;56(1):60. PMID: 20500141. **Synopsis of a potentially relevant study.**

3. Anokhin MI, Sergeev VN, Domanskii VL. Biological feedback correction of respiration during treatment of bronchial asthma. Biomed Eng (NY) 1996;30(1):26-29. **Other quality issues.**

4. Anonymous. Breathing exercises help cut asthma symptoms. Practice Nurse 2007 Jul 13;34(1):8. **Synopsis of a potentially relevant study.**

5. Anonymous. Breathing training leads to improved asthma-specific health status. AJP 2010;91(1076):62-63. **Unable to obtain, unlikely a trial.**

6. Anonymous. Inconclusive study of yoga as an adjunct therapy for asthma. 5th Annual Symposium Complementary Health Care; Exeter. 1998. p. 164. **Synopsis of a potentially relevant study.**

7. Anonymous. Randomised controlled trial of treating dysfunctional breathing to reduce breathlessness in severe asthma. Curr Control Trials. 2011. **Ongoing trial, no outcomes at time of review.**

8. Asher MI, Douglas C, Airy M, et al. Effects of chest physical therapy on lung function in children recovering from acute severe asthma. Pediatr Pulmonol 1990;9(3):146-51. PMID: 2277735. **Management of serious acute exacerbations.**

9. Austin G, Brown C, Watson T, et al. Buteyko breathing technique improves exercise capacity and control of breathing in uncontrolled asthma. European Respiratory Society Annual Congress; Vienna, Austria. 2009. p. E4306. **Not a study of breathing techniques.**

10. Austin G, Brown C, Watson T, et al. Buteyko breathing technique reduces hyperventilation-induced hypocaponea and dyspnoea after exercise in asthma. American Thoracic Society International Conference; San Diego, CA. 2009. p. A3409. **Not a study of breathing techniques.**

11. Beth Israel Medical Center. Integrative medicine approach to the management of asthma in adults. clinicaltrials gov 2011;NCT00843544. **Ongoing trial, no outcomes at time of review.**

12. Bhikshapathi DVRN, Jayanthi C, Kishan V, et al. Influence of yogasanas on the physiology, therapy and theophylline pharmacokinetics in bronchial asthma patients. Acta Pharm Sci 2007;49(2):187-94. **Not a study of breathing techniques.**

13. Bingol Karakoc G, Yilmaz M, Sur S, et al. The effects of daily pulmonary rehabilitation program at home on childhood asthma. Allergol Immunopathol (Madr) 2000 Jan;28(1):12-14. PMID: 10757852. **Other quality issues.**

14. Birch M. Asthma and the Buteyko breathing method. Aust Nurs J 2001 Mar;8(8):35. PMID: 11894574. **Synopsis of a potentially relevant study.**

15. Birkel DA, Edgren L. Hatha yoga: improved vital capacity of college students. Altern Ther Health Med 2000 Nov;6(6):55-63. PMID: 11076447. **Not one of specified study designs.**

16. Bowler SD, Green A, Mitchell CA. Positive evidence of the effectiveness of Buteyko breathing techniques in asthma. Focus Alt Comp Ther 1999;4:207-08. **Synopsis of a potentially relevant study.**

17. Brown JV, Demi AD, Wilson SR, et al. A home-based asthma education program for low-income families and their young asthmatic children. Am J Respir Crit Care Med 2000;161(Suppl 3):A902. **Not a study of breathing techniques.**

18. Brown JV, Demi AS, Celano MP, et al. A home visiting asthma education program: challenges to program implementation. Health Educ Behav 2005 Feb;32(1):42-56. PMID: 15642753. **Not a study of breathing techniques.**

19. Brown JV, Bakeman R, Celano MP, et al. Home-based asthma education of young low-income children and their families. J Pediatr Psychol 2002 Dec;27(8):677-88. PMID: 12403858. **Not a study of breathing techniques.**

20. Bruton A. Breathing and relaxation training improves respiratory symptoms and quality of life in asthmatic adults. Aust J Physiother 2008;54(1):76. PMID: 18298365. **Synopsis of a potentially relevant study.**

21. Carvalho LC, Albuquerque HF, Pontes C, et al. Computerized Biofeedback Tool: Application in Electromyogram-Biofeedback. A New Beginning for Human Health. Annual International Conference of the IEEE Engineering in Medicine and Biology; 2003 Sep 17; Cancun, Mexico. 2003. p. 1609-12. **Not one of specified study designs.**

22. Ceugniet F, Cauchefer F, Gallego J. Do voluntary changes in inspiratory-expiratory ratio prevent exercise-induced asthma? Biofeedback Self Regul 1994 Jun;19(2):181-88. PMID: 7918755. **Not a study of breathing techniques.**

23. Ceugniet F, Cauchefer F, Gallego J. Voluntary decrease in breathing frequency in exercising asthmatic subjects. Eur Respir J 1996 Nov;9(11):2273-79. PMID: 8947071. **Not one of specified interventions.**

24. Chiang LC, Ma WF, Huang JL, et al. Effect of relaxation-breathing training on anxiety and asthma signs/symptoms of children with moderate-to-severe asthma: a randomized controlled trial. Int J Nurs Stud 2009 Aug;46(8):1061-70. PMID: 19246041. **Not a study of breathing techniques.**

25. Cooper SE, Oborne J, Newton S, et al. The effect of two breathing exercises (Buteyko and Pranayama) on the ability to reduce inhaled corticosteroids in asthma: a randomised controlled trial. American Thoracic Society 99th International Conference 2003:B023. **Unable to obtain, likely from another reviwed study.**

26. Cowie RL, Conley DP, Underwood MF, et al. A randomized controlled trial of buteyko technique for asthma management. Proceedings of the American Thoracic Society. American Thoracic Society International Conference; 2006 May 19; San Diego, CA. 2006. p. A530. **Unable to obtain, likely from another reviwed study.**

27. Dahl J, Gustafsson D, Melin L. Effects of a behavioral treatment program on children with asthma. J Asthma 1990;27(1):41-46. PMID: 1968453. **Not one of specified interventions.**

28. Foglio K, Bianchi L, Bruletti G, et al. Long-term effectiveness of pulmonary rehabilitation in patients with chronic airway obstruction. Eur Respir J 1999 Jan;13(1):125-32. PMID: 10836336. **Not a study of breathing techniques.**

29. Girodo M, Ekstrand KA, Metivier GJ. Deep diaphragmatic breathing: rehabilitation exercises for the asthmatic patient. Arch Phys Med Rehabil 1992 Aug;73(8):717-20. PMID: 1642520. **High or differential attrition.**

30. Gomieiro LT, Nascimento A, Tanno LK, et al. Respiratory exercise program for elderly individuals with asthma. Clinics (Sao Paulo, Brazil) 2011;66(7):1163-69. PMID: 21876968. **Not one of specified study designs.**

31. Goncalves RC, Nunes MPT, Cukier A, et al. Comparison between breathing exercises and aerobic conditioning on symptoms, quality of life and exhaled nitric oxide in asthmatic adults. Eur Respir J 2006;28:370s. **Not one of specified comparators.**

32. Huntley AL, Marks GB. Sahaja yoga has limited effects in the management of asthma. Focus Alt Comp Ther 2002 Sep;7(3):275-76. **Only comparator includes relaxation training.**

33. Janson-Bjerklie S, Clarke E. The effects of biofeedback training on bronchial diameter in asthma. Heart Lung 1982;11(3):200-07. PMID: 6918383. **Published prior to 1990.**

34. Kuiper D. Dysfunctional breathing and asthma. Trial shows benefits of Buteyko breathing techniques. BMJ 2001 Sep 15;323(7313):631-32. PMID: 11575317. **Synopsis of a potentially relevant study.**

35. Lehrer P, Hochron S, Carr R, et al. Biofeedback for increasing respiratory sinus arrhythmia as a treatment for asthma. 30th Annual Convention of the Association for the Advancement of Behavior Therapy; 1996 Nov 21; New York. New York: Association for the Advancement of Behavior Therapy; 1996. **Not a study of breathing techniques.**

36. Lehrer P, Carr RE, Smetankine A, et al. Respiratory sinus arrhythmia versus neck/trapezius EMG and incentive inspirometry biofeedback for asthma: a pilot study. Applied Psychophysiol Biofeedback 1997 Jun;22(2):95-109. PMID: 9341966. **Other quality issues.**

37. Lewis S, Cruft S, Egbagbe E, et al. A controlled trial of the effect of a breathing exercise device in asthma. Eur Respir J Suppl 1996;9:337s. **Synopsis of a potentially relevant study.**

38. Lima EVN, Oliveira AN, Vieira RAF, et al. Inspiratory muscle training in children with asthma effect on muscle strength and pulmonary function. Eur Respir J 2006;28:478s. **Duplicate report of included study.**

39. Manocha R, Marks GB, Kenchington P, et al. Sahaja yoga in the management of moderate to severe asthma: a randomised controlled trial. Thorax 2002 Feb;57(2):110-15. PMID: 11828038. **Not one of specified interventions.**

40. McConnell AK, Caine MP, et a. Inspiratory muscle training improves lung function and reduces exertional dyspnoea in mild/moderate asthmatics. Clin Sci 1998;95 Suppl 39:4P. **Followup less than 4 weeks.**

41. McHugh P, Aitcheson F, Duncan B, et al. Buteyko Breathing Technique for asthma: an effective intervention. N Z Med J 2003 Dec 12;116(1187):U710. PMID: 14752538. **Only comparator includes relaxation training.**

42. Meuret AE, Ritz T, Wilhelm FH, et al. Pco2 Biofeedback-Assisted Breathing Training for Panic Disorder and Asthma: Rationale and Empirical Findings. 64th Annual Scientific Conference of the American Psychosomatic Society; 2006 Mar 1; Denver. American Psychosomatic Society; 2008. **Other quality issues.**

43. Meuret AE, Ritz T, Wilhelm FH, et al. Targeting pCO(2) in asthma: pilot evaluation of a capnometry-assisted breathing training. Appl Psychophysiol Biofeedback 2007 Jun;32(2):99-109. PMID: 17564826. **Other quality issues.**

44. Mussell MJ, Hartley JP. Trachea-noise biofeedback in asthma: a comparison of the effect of trachea-noise biofeedback, a bronchodilator, and no treatment on the rate of recovery from exercise- and eucapnic hyperventilation-induced asthma. Biofeedback Self Regul 1988 Sep;13(3):219-34. PMID: 3228551. **Published prior to 1990.**

45. Nagarathna R, Nagendra HR. Yoga for bronchial asthma: a controlled study. Br Med J (Clin Res Ed) 1985 Oct 19;291(6502):1077-79. PMID: 3931802. **Published prior to 1990.**

46. Nagendra HR, Nagarathna R. Integrated approach of yoga therapy for seasonal and perennial bronchial asthma. IEEE/Engineering in Medicine and Biology Society Annual Conference; 1986. p. 1759-62. **Not one of specified study designs.**

47. Neffen HE, Baena-Cagnani CE, Yanez A. Breathing Exercises for Asthmatic Children: Asthma Music and the Asthma Symphony. 16th World Congress of Asthma; Buenos Aires, Argentina. 1999. p. 83-88. **Unable to obtain, unlikely a trial.**

48. Perrin JM, MacLean WE, Jr., Gortmaker SL, et al. Improving the psychological status of children with asthma: a randomized controlled trial. J Dev Behav Pediatr 1992 Aug;13(4):241-47. PMID: 1506461. **Not a study of breathing techniques.**

49. Reuther I, Aldridge D. Qigong Yangsheng as a complementary therapy in the management of asthma: a single-case appraisal. J Altern Complement Med 1998;4(2):173-83. PMID: 9628207. **Not one of specified study designs.**

50. Ritz T, Meuret AE, Wilhelm FH, et al. Changes in pCO2, symptoms, and lung function of asthma patients during capnometry-assisted breathing training. Appl Psychophysiol Biofeedback 2009 Mar;34(1):1-6. PMID: 19048369. **Other quality issues.**

51. Sato K, Kawamura T, Abo T. "Senobi" stretch ameliorates asthma symptoms by restoring autonomic nervous system balance. J Investig Med 2010 Dec;58(8):968-70. PMID: 20930645. **Not one of specified interventions.**

52. Singh V, Wisniewski A, Britton J, et al. Effect of yoga breathing exercises (pranayama) on airway reactivity in subjects with asthma. Lancet 1990 Jun 9;335(8702):1381-83. PMID: 1971670. **Followup less than 4 weeks.**

53. Slader CA, Reddel HK, Spencer LM, et al. Impact of breathing exercises on asthma symptoms and control. American Thoracic Society International Conference; San Diego, CA. 2005. p. D97. **Duplicate report of included study.**

54. Sodhi C, Singh S, Dandona PK. A study of the effect of yoga training on pulmonary functions in patients with bronchial asthma. Indian J Physiol Pharmacol 2009 Apr;53(2):169-74. PMID: 20112821. **Other quality issues.**

55. Stanton AE, Vaughn P, Carter R, et al. An observational investigation of dysfunctional breathing and breathing control therapy in a problem asthma clinic. J Asthma 2008;45(9):758-65. PMID: 18972291. **Not one of specified study designs.**

56. Stepans MB. Biofeedback and relaxation therapy: symptom control in individuals with lung disease. Communicating Nursing Research. 33rd Annual Communicating Nursing Research Conference/14th Annual WIN Assembly; Denver, CO. 2000. p. 192. **Patients with other respiratory diseases.**

57. Thomas M. Are breathing exercises an effective strategy for people with asthma? Nurs Times 2009 Mar 17;105(10):22-27. PMID: 19400340. **Duplicate report of included study.**

58. Thomas M. Study of the effectiveness of breathing training exercises taught by a physiotherapist by either instructional videos/DVDs/internet download or by face-to-face sessions in the management of asthma in adults. Curr Control Trials. 2011. **Ongoing trial, no outcomes at time of review.**

59. Thomas M, McKinley RK, Prodger P, et al. Breathing retraining improves quality of life in asthmatic patients with dysfunctional breathing. Eur Respir J 2001;18:330s. **Duplicate report of included study.**

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61. Vedanthan PK, Kesavalu LN, Murthy KC, et al. Clinical study of yoga techniques in university students with asthma: a controlled study. Allergy Asthma Proc 1998 Jan;19(1):3-9. PMID: 9532318. **Other quality issues.**

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