

Evidence-based Practice Center Systematic Review Protocol

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

I. Background and Objectives for the Systematic Review

Asthma is a chronic respiratory disease characterized by airflow obstruction, bronchial hyper-responsiveness, and underlying airway inflammation. The interaction of these characteristics varies among susceptible individuals leading to differences in disease progression and symptoms over time. Symptoms can include shortness of breath, cough, wheezing, and chest pain or tightness.¹ When poorly controlled, asthma is associated with increased health care utilization, decreased quality of life, and significant activity limitations.^{2,3}

In the United States, an estimated 7.7 percent of people (22.2 million) had current asthma in 2007, affecting 9.4 percent (7.0 million) of children and 7.3 percent (16.4 million) of adults and accounting for nearly 3,500 deaths.⁴ Ethnic and racial disparities exist in asthma prevalence, with Puerto Ricans, African Americans, American Indians, and Alaska Natives having a higher prevalence than non-Hispanic whites. In addition, the prevalence of asthma is greatest among populations of low socioeconomic status.⁴ The morbidity associated with asthma adds tremendous costs to patients and health care organizations. In the United States, the annual cost (both direct and indirect) of asthma is estimated to be over \$20 billion.⁵

The aim of asthma management is to achieve and maintain control of the disease with as few adverse effects as possible. Current U.S. guidelines for the diagnosis and management of asthma recommend four components considered essential to effective asthma management: assessing and monitoring the disease, self-management education, controlling environmental and comorbid conditions, and adequate pharmacologic therapy (i.e., long-term control medications used to achieve and maintain control of persistent asthma and quick-relief medications used to treat acute symptoms and exacerbations).¹ Despite guidance surrounding asthma self-management education and medication use, many patients with asthma appear to adhere poorly to such recommendations.⁶ Studies have found that adults with asthma and 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.⁷⁻⁹

A variety of alternative therapies have been advocated for the complementary control of asthma including breathing exercises, herbal remedies, homeopathy, acupuncture, relaxation therapies, and manual therapy (e.g., chiropractic techniques, massage). Breathing exercises or retraining are among the most popular complementary and alternative modalities used by people with asthma.^{7,10-13} The original public nomination of this topic for systematic review by a certified Buteyko practitioner and physiotherapist requested a review focused specifically on the effectiveness of the Buteyko breathing method for reducing bronchodilator and inhaled steroid use and improving the health status of adults and children with asthma. The Buteyko technique, developed in Russia, is based on the theory that asthma is caused by hyperventilation and hypocapnia that can be controlled by training those with asthma to manage their ventilation.¹⁴ After receiving input from experts and consulting the literature, we expanded the topic to also address several other breathing retraining exercises, including pranayama techniques (derived from yoga), inspiratory muscle training, technology-assisted breathing retraining exercises, the

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Papworth method, and breathing physical therapy. Given the prevalence of asthma among children and adults and the growing interest in complementary treatment methods to manage asthma symptoms, a systematic review focusing on this topic should prove useful for clarifying the evidence regarding the effectiveness of various breathing therapies and the context in which they may be effective. Thus, the objective of this review is to synthesize the data on the effectiveness and comparative effectiveness of a variety of breathing techniques in the management of asthma.

II. The Key Questions

We initially developed three key questions (KQs) with five subquestions to guide the literature search, data abstraction, and synthesis for this topic. The proposed KQs were posted for public comment between August 16 and September 13, 2010, and reviewed by a Technical Expert Panel (TEP). KQs were modified to include additional subgroups based on the feedback received.

The final proposed KQs for this review are:

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?

*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.

- 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)?

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

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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)?

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?

- 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)?

PICOTS

Population	<ul style="list-style-type: none"> Adults and children 5 years of age and older with asthma of any type or severity
Interventions	<ul style="list-style-type: none"> Breathing exercises and/or retraining techniques Include: the Buteyko breathing technique; inspiratory or expiratory muscle training; breathing physical therapy including paced and pursed lip breathing exercises and diaphragmatic breathing techniques; the Papworth method; biofeedback- and technology-assisted breathing retraining; yoga breathing exercises; or others.
Comparators	<ul style="list-style-type: none"> Breathing techniques listed above, 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

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intervention group on another topic unrelated to breathing retraining)

- Wait-list controls (participants added to a waiting list in order to receive an intervention after the active treatment group does)
- No treatment offered (outside care is assumed)

Outcomes

Primary Health Outcomes:

- 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, nocturnal control, missed school/work, daily activity tolerance and restrictions)
- Quick-relief medications (e.g., short-acting β_2 -agonists, anticholinergics)
- Long-term control medications (e.g., inhaled corticosteroids, long-acting immunomodulators, cromolyn sodium and nedocromil, methylxanthines, leukotriene modifiers, and long-acting β_2 -agonists)

Intermediate Outcomes:

- Pulmonary function tests: forced expiratory volume (FEV_1); forced vital capacity (FVC); peak expiratory flow (PEF); minute Volume (MV), exhaled nitric oxide (NO), methylcholine challenge and/or responsiveness, sputum eosinophil markers of inflammation, other measures of carbon dioxide (CO_2), other spirometry measures

Adverse Events:

- Increased asthma symptoms or acute asthma exacerbations
- Adverse reactions to therapies
- Reduction in/negative influences on quality of life

Timing

- Minimum of 4 weeks followup after baseline

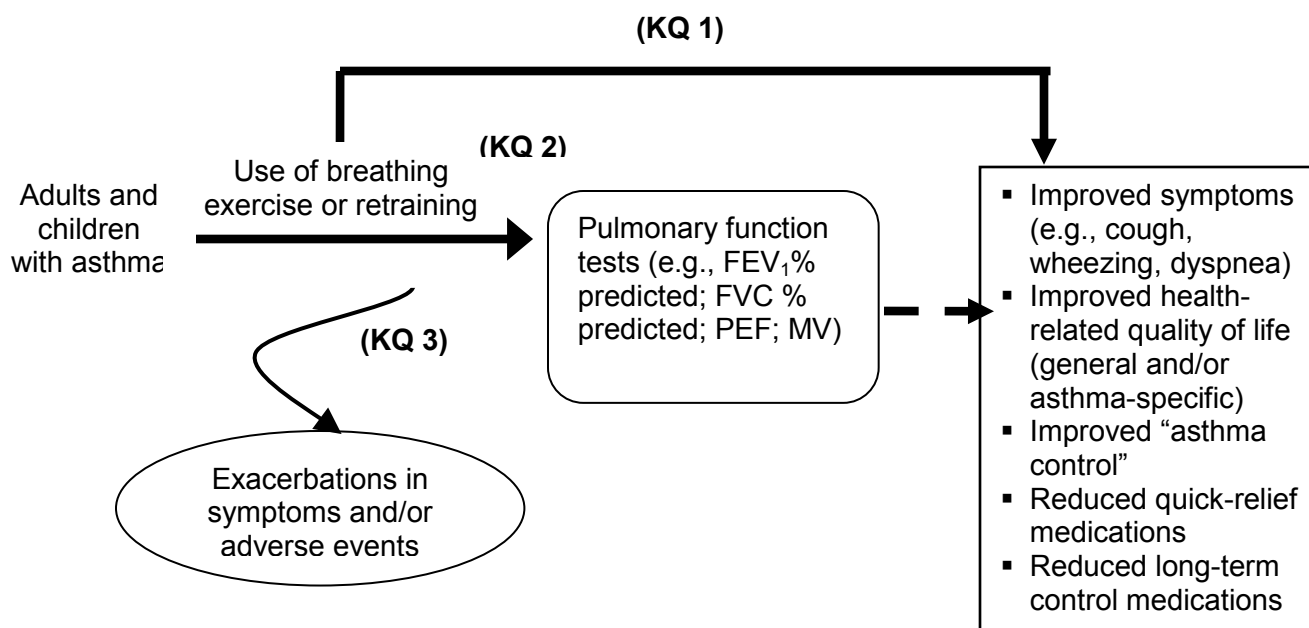
Settings

- All settings

III. Analytic Framework

Figure 1 provides an analytic framework to illustrate the population, interventions, and outcomes that will guide the literature search and synthesis. The figure depicts the KQs within the context of the PICOTS described in the previous section. In general, the figure illustrates how the use of breathing exercise or retraining may result in intermediate outcomes such as improved forced expiratory volume or peak expiratory flow, and/or ultimate health outcomes such as improved symptoms and quality of life. The figure also depicts the possibility of adverse events occurring at any time after treatment begins.

Figure 1. Provisional analytic framework for evaluating the comparative effectiveness of breathing exercise/retraining techniques for the treatment of asthma



Abbreviations: FEV₁% = forced expiratory volume 1 percent predicted; FVC = forced vital capacity; KQ = key question; MV = minute volume; PEF = peak expiratory flow; PFT = pulmonary function test.

IV. Methods

A. Criteria for Inclusion/Exclusion of Studies in the Review

We have developed a preliminary set of criteria for inclusion and exclusion of studies based on our understanding of the literature and discussions with key informants during the topic-refinement phase (Table 1).

Table 1. Inclusion/Exclusion criteria

Category	Criteria	
	Inclusion	Exclusion
Population	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Children < 5 years Individuals with comorbid chronic obstructive pulmonary disease (COPD), emphysema, chronic bronchitis or any other chronic disease that affects pulmonary function (e.g., heart disease, thyroid disease)
Interventions	<p>Interventions in which breathing retraining/exercises are a primary component. Such exercises include:</p> <ul style="list-style-type: none"> Buteyko breathing technique 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 	<ul style="list-style-type: none"> Interventions that do not focus primarily on asthma Interventions whereby breathing techniques are not a primary treatment
Comparator	<ul style="list-style-type: none"> Other breathing techniques alone or in combination with other intervention strategies Usual care as standard for the setting 	<ul style="list-style-type: none"> Other alternative or complementary methods that are potentially efficacious for asthma and are not focused on breathing retraining (e.g., relaxation)

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	<p>(e.g., asthma self-management education, control of environmental factors, pharmacologic therapy)</p> <ul style="list-style-type: none"> 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) 	<p>techniques, acupuncture, herbal therapies, chiropractic)</p> <ul style="list-style-type: none"> Physical activity or exercise
Outcomes	<p>KQ 1 and KQ 2:</p> <ul style="list-style-type: none"> 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) Quick-relief medication use (e.g., short-acting β_2-agonists, anticholinergics) Long-term control medications (e.g., inhaled corticosteroids, long-acting immunomodulators) Pulmonary function tests (FEV₁% predicted; FVC % predicted; PEF; MV, exhaled NO, methylcholine challenge and/or responsiveness, sputum eosinophil markers of inflammation, other measures of CO₂, other spirometry measures) <p>KQ 3:</p> <ul style="list-style-type: none"> Increased asthma symptoms or acute asthma exacerbations Adverse reactions to therapies Reduction in/negative influences on quality of life 	<ul style="list-style-type: none"> Costs

Time Period	1990–present	
Setting	All settings	
Study geography	Developed countries with a Human Development Index > 0.90 including: United States, Canada, United Kingdom, Europe, Australia, China, Japan, Hong Kong, Singapore, Israel, Greece, Korea, and New Zealand ¹⁵	All other countries
Publication language	English	All other languages
Study design	<p>KQ 1, KQ 2, and KQ 3:</p> <ul style="list-style-type: none"> 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 utilization with long-term (≥6 months) outcomes, with some validity of case ascertainment or in those with broadly representative samples <p>KQ1a and KQ2a:</p> <ul style="list-style-type: none"> 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 <p>KQ 1b and KQ 2b:</p> <ul style="list-style-type: none"> Randomized controlled trials Controlled clinical trials 	<p>KQ 1, KQ 2, and KQ 3:</p> <ul style="list-style-type: none"> 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 <p>KQ1a and KQ2a:</p> <ul style="list-style-type: none"> 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 <p>KQ 1b and KQ 2b:</p> <ul style="list-style-type: none"> Editorials, letters, nonsystematic literature reviews Observational studies
Intervention duration	All	

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Follow-up duration	≥ 4 weeks post intervention	< 4 weeks post intervention
Sample size	N ≥ 10	N < 10

B. Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies To Answer the Key Questions

The research librarian, in collaboration with the investigative team, will develop and implement search strategies designed to identify evidence relevant to each KQ. An example proposed search strategy is shown in Appendix A. Comprehensive searches in the following databases will be conducted:

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

The searches will be restricted to English-language literature and the time period 1990–present. In 1990, the conceptualization of asthma changed and the use of inhaled corticosteroids as first-line therapy in chronic asthma became the standard of care for asthma management.^{16,17} Comparisons of interventions prior to that date are not clinically relevant to current practice. Data are limited to English language because it is not possible to obtain and translate non-English literature and stay within the expected timeline of the project. However, we will retain the abstracts for non-English studies with English abstracts that appear to fit our inclusion criteria (aside from the language) for reporting purposes. Preliminary scans and examination of reference lists revealed no non-English trials published since 1990.

In addition, the research librarian will perform grey literature searches for this comparative effectiveness review. For the purposes of this review, grey literature comprises any information that is not controlled by commercial publishing and includes 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 and WHO Clinical Trials), and conference abstracts (e.g., CSA's Conference Papers Index and Scopus conference papers). Upon receipt of the grey literature search results, we will review abstracts and/or full-text results according to the protocol described below and will match them to published studies, noting any discrepancies between sources. Additionally, we will request Scientific Information Packets (SIPs) from manufacturers of relevant devices or programs to supplement the literature search.

The reference lists of reviews and guidelines will also be examined to help identify potential studies for inclusion. Original studies identified in reference lists that meet the inclusion criteria for this review will be retrieved. If any studies are identified by reading the references of key primary studies, we will consult with the librarian conducting the search to examine why the original search strategy did not identify the article in question. We will also supplement our searches with suggestions from members of the TEP.

We will conduct bridge searches on an ongoing, monthly basis after the initial search is executed and will add relevant references as needed (including while the draft report is undergoing review). Additionally, we will incorporate references that are of particular relevance for background sections. Results from the literature searches will be entered into version 11.0.1 of Reference Manager[®] (Thomson Reuters, New York, NY), a bibliographic management database.

C. Data Abstraction and Data Management

A two-step process will be used for study selection. First, each title and abstract (if available) will be independently reviewed by at least two members of the research team to determine if an article may meet the broad inclusion/exclusion criteria for study design, population, and intervention (Table 1). Each article will be coded as: potentially included (I), excluded (E), or background (X). Next, we will retrieve full-text articles for all potentially included studies, including those that are questionable or unclear at the abstract stage. Two reviewers will independently assess each full-text article by using a standard form that details the predetermined inclusion and exclusion criteria. Disagreements will be resolved through discussion or third-party adjudication as needed. Next, articles will be assessed for methodological quality (see Section D below for details) and rated as “good,” “fair,” or “poor”.

Data from all included studies with a quality rating of “fair” or “good” will be abstracted into standard evidence tables by one abstractor and checked for accuracy and completeness by a second abstractor. The following information will be obtained from each study, where applicable: author identification, year of publication, source of study funding, study design, study setting, study population, intervention details (e.g., duration, intensity, description, including additional complementary techniques that might be included), comparator details, and participant baseline characteristics (e.g., sex, age, ethnicity, asthma severity). Outcomes will include: asthma symptom severity, health-related quality of life, asthma control, quick-relief medication use, long-term control medication use, and pulmonary function. The basic elements and design of the evidence table will be the same as multiple tables we have used for other systematic reviews. We will test the table on select studies and will revise it as necessary before data extraction is fully performed on all articles. Authors of included studies will be contacted if clarification of methods (e.g., randomization methods) or results (e.g., providing missing data or verifying the data) is needed.

We will code the reasons that articles, at the stage of full review, are not included in the review. Studies at the abstract and full-review stage will be managed by using Reference Manager, so that we can easily compile a list of included and excluded articles and the reasons for exclusion. Project staff will meet regularly to discuss the

results at each phase and review studies that are difficult to classify, and address any questions that the team may have.

D. Assessment of Methodological Quality of Individual Studies

To assess the methodological quality of included studies, we will use the criteria developed by the U.S. Preventive Services Task Force.¹⁸ Two independent reviewers will assign a quality rating of the internal validity for each study. Disagreements will be resolved by discussion and consensus or by consulting a third, independent reviewer. A rating of “good,” “fair,” or “poor” will be assigned by using the predefined criteria for each study design. Such criteria include: adequate randomization methods (for randomized controlled trials [RCTs]), consideration of potential confounders, maintenance of comparable groups, reliable and valid measurements, clear definition of interventions, and appropriate analyses (e.g., intention-to-treat analysis for RCTs). Generally, a good-quality study meets all criteria for that study design; a fair-quality study does not meet all criteria but is judged to have no fatal flaw that invalidates its results; and a poor-quality study contains a fatal flaw. In addition, the quality assessment of adverse effects and harms data will be informed by the AHRQ methods guidance for comparative effectiveness reviews.¹⁹ Quality ratings will be recorded in the evidence tables.

E. Data Synthesis

We anticipate that the data obtained from the literature review will be synthesized qualitatively, stratified by population (i.e., adults and children separately). In addition, we will examine subgroup analyses presented in the included trials that elucidate differences in effectiveness in pertinent subgroups (males/females; different races or ethnicities; smokers/nonsmokers; various types and severities of asthma; and/or different coexisting conditions). If we find a sufficient number of similar studies, we will consider quantitative analysis (meta-analysis) of data from those studies. If data are sufficient, we will further consider examining the effect of the patient characteristics listed above by using meta-regression.

We have proposed to examine a large number of outcomes, largely based on feedback from Key Informants and TEP members. For KQ 1, we have chosen summary measures of asthma control as the primary outcome, which appears to be one of the most consistently reported outcomes based on our preliminary examination of existing trials and, thus, is least subject to reporting bias. The other consistently reported outcome was use of β_2 -agonists, but TEP members had concerns about the quality of this outcome. For KQ 2, we will select either FEV₁ or PEF as the primary outcome, depending on which is most consistently reported.

F. Grading the Evidence for Each Key Question

We will grade the strength of evidence for primary outcomes using the standard process of the Evidence-based Practice Centers as outlined in the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.^{20,21} The grade will be based on

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four major domains: risk of bias, consistency, directness, and precision of the evidence. We will classify the bodies of evidence pertaining to each primary outcome into four basic grades: high, moderate, low, and insufficient (Table 2).²¹ As advised, the number of studies that form that basis of given findings or conclusions will also be recorded.²¹ Additional domains—such as dose-response association, plausible confounding, strength of association, and publication bias—will be assessed and reported as appropriate.

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 either is unavailable or does not permit a conclusion.

G. Assessing Applicability

Judgments of applicability for each outcome (including harms) will be performed separately from assessments of the other domains of strength of evidence as recommended.^{21,22} We will identify and abstract factors in individual studies that might affect applicability, particularly including factors related to the populations—for example, how highly select they were (what portion of those recruited were randomized), how they were recruited (whether the participant contacted the study staff in order to be included vs. individual outreach to potentially eligible participants by the study staff, etc.), and the intervention they received (whether there were multiple interventionists, level/degree of training among interventionists, whether there was a clearly defined protocol, etc.). Based on these characteristics, we will note any potential limitations to applicability on the interpretation of each individual study and will conclude with an evaluation of the applicability of the total body of evidence. In addition to describing these characteristics of the included trials, where data are sufficient we will examine these features to see if they appear to affect effect size. If appropriate, we will summarize important applicability issues in table format.

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VI. Definition of Terms

Attention Control: Control participants given intervention with similar intensity and format, but with different content

Wait-list Control: Control participants are offered the intervention after a delay, during which the intervention group receives the intervention.

VII. Summary of Protocol Amendments

Date	Section	Protocol Deviation	Rationale
Feb 19, 2011	IV. Methods/ Section A/ Table 1	Updated from previous Human Development Index (HDI) methodology to 2010 methodology, limiting to trials rated as having “Very High” level of development.	Believe this represents most current methods in rating the level of human development.
April 20, 2011	IV. Methods/ Section A/ Table 1	Inclusion of studies in all geographic locations, not just developed countries with a Human Development Index rated as “Very High”.	We identified four trials conducted in countries that were not rated as having a “Very High” level of development that met quality standards. Some areas have been studied more extensively in non-highly developed countries (particularly yoga in India), so evidence on efficacy of some techniques would be incomplete if there trials were excluded, so decided not to exclude trials on the basis of country.

VIII. Review of Key Questions

For all EPC reviews, key questions were reviewed and refined as needed by the EPC with input from Key Informants and the Technical Expert Panel (TEP) to assure that the questions are specific and explicit about what information is being reviewed. In addition, for Comparative Effectiveness reviews, the key questions were posted for public comment and finalized by the EPC after review of the comments.

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IX. 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 systematic review or when identifying high priority research gaps and needed new research. 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 peer or 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 TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts

Technical Experts comprise a multi-disciplinary group of clinical, content, and methodologic experts who provide input in defining populations, interventions, comparisons, or outcomes as well as identifying particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicted opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore study questions, design and/or methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor contribute to the writing of the report and have not reviewed the report, except as given the opportunity to do so through the public comment mechanism.

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

XI. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodologic expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments are documented and will, for CERs and Technical briefs, be published three months after the publication of the Evidence report.

Potential Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

Appendix A: Example Draft MEDLINE Search Strategy

- 1 asthma/ or asthma, exercise-induced/
- 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 ((breath\$ or respirat\$) adj5 (physiotherap\$ or physical therap\$)).ti,ab.
- 13 ((breath\$ or respirat\$) adj5 (paced or pursed or biofeedback)).ti,ab.
- 14 ((breath\$ or respirat\$) adj5 (exercise\$ or training or retraining or pattern\$ or technique\$)).ti,ab.
- 15 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
- 16 3 and 15
- 17 limit 16 to english language
- 18 limit 17 to yr="1990 - Current"