



# Effective Health Care Program

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Future Research Needs Paper  
Number 18

## **Future Research Needs for the Comparative Effectiveness of Breathing Exercises and/or Retraining Techniques in the Treatment of Asthma**



Agency for Healthcare Research and Quality  
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# **Future Research Needs for the Comparative Effectiveness of Breathing Exercises and/or Retraining Techniques in the Treatment of Asthma**

**Prepared for:**

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This report is based on research conducted by the Oregon Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2007-10057-I). The findings and conclusions in this document are those of the author(s), who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care researchers and funders of research make well-informed decisions in designing and funding research and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of scientific judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical research and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances.

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None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

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## Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

An important part of evidence reports is to not only synthesize the evidence, but also to identify the gaps in evidence that limited the ability to answer the systematic review questions. AHRQ supports EPCs to work with various stakeholders to identify and prioritize the future research that are needed by decisionmakers. This information is provided for researchers and funders of research in these Future Research Needs papers. These papers are made available for public comment and use and may be revised.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality. The evidence reports undergo public comment prior to their release as a final report.

We welcome comments on this Future Research Needs document. 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](mailto:epc@ahrq.hhs.gov).

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## Stakeholders

Although the target audience for a future research needs document is the research community and/or funders of research, other stakeholders have an important role in providing input into the future research agenda. Stakeholders include patients and caregivers, practicing clinicians, relevant professional and consumer organizations, researchers, purchasers of health care, and others with experience in making health care decisions. They are selected to provide broad expertise and perspectives specific to the topic, and input on types of information helpful in healthcare decision-making. The EPC solicits input from stakeholders when identifying high priority research gaps and needed new research. Stakeholders 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.

Stakeholders 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 stakeholders and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, and manage any potential conflicts of interest identified.

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# Executive Summary

## Background

An estimated 8.2 percent of the United States population has asthma including 9.6 percent of children and 7.7 percent of adults.<sup>1,2</sup> Alternative and complementary treatment methods such as breathing retraining techniques have been advocated for the control of asthma given the range of asthma severity and concerns about long-term medication use. Specific breathing retraining approaches include those related to hyperventilation reduction (e.g., the Buteyko and Papworth methods) or nonhyperventilation-targeted methods (e.g., yoga breathing techniques, other physical therapy methods, biofeedback, and inspiratory muscle training [IMT]). These methods are assumed to be adjunctive to guideline-based care, with the primary goals of improving asthma control and reducing the use of medication.

In 2010, the Agency for Healthcare Research and Quality commissioned the Oregon Evidence-based Practice Center to conduct a comparative effectiveness review (CER) on the effectiveness of breathing exercises and/or retraining in the treatment of asthma.<sup>3</sup> In this review, we addressed the following Key Questions:

1. 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?
2. 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?
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?

Our review sought to include studies that addressed the use of breathing techniques in adults and children 5 years of age and older with asthma and explored whether the effectiveness differed between different population subgroups (e.g., males/females; various types and severities of asthma; and/or different coexisting conditions). Additionally, we evaluated whether the effectiveness of these interventions varied by differences in intervention implementation or components.

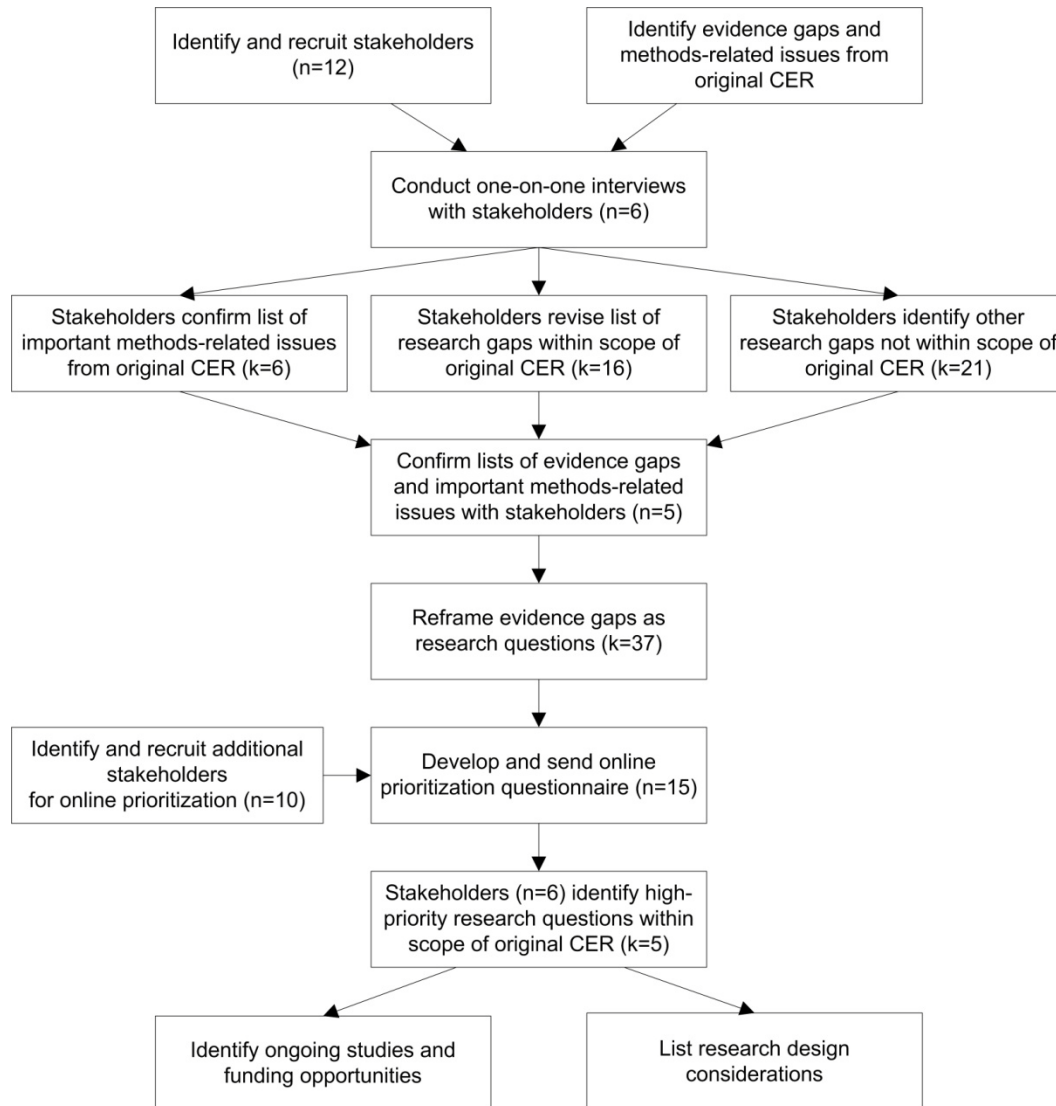
The review identified 22 studies published between 1990 and December 2011 that examined the effectiveness or comparative effectiveness of breathing techniques on intermediate and/or health outcomes.<sup>3</sup> In general, the evidence was low-to-moderate or insufficient to address the Key Questions adequately as it was based primarily on small, methodologically limited trials of heterogeneous populations with short followup and inconsistent outcome reporting.

The objective of this Future Research Needs project was to engage a diverse set of stakeholders to confirm, provide more detail, and prioritize the research needs that we identified in the CER. We also sought to provide information on ongoing studies of relevance to the prioritized list of research questions and study design considerations for the highly prioritized questions.

## Methods

To meet our objectives, we identified and recruited stakeholders, identified and revised the list of evidence needs articulated in the original CER, developed and administered a web-based prioritization questionnaire, and identified ongoing research, funding opportunities, and potential study designs for the high-priority future research needs (Figure A).

**Figure A. Future Research Needs process**



**Abbreviations:** CER: comparative effectiveness review

A total of 22 stakeholders were invited to participate in this project including patient advocates, researchers, research funders, providers/practitioners, and policymakers. We aimed to include individuals from both the respiratory and complementary and alternative medicine fields given the topic.

After developing a preliminary list of evidence gaps based on the CER and discussions with the lead author of the CER, we conducted one-on-one interviews with six stakeholders. We asked stakeholders to comment on whether or not they felt that the list of evidence needs was

comprehensive and if there were better ways to express any of the research topics. We also asked if there were specific questions or topics that seemed out of place or did not belong on the list in terms of their importance to the field. Based on input from the one-on-one interviews, we revised the original list of research needs, reframed them as research questions, and organized them according to the specific population, intervention, comparator, or outcome (PICO) they addressed. We also listed methodological issues that were identified in the original CER or through our discussions.

Once the stakeholders had an opportunity to review the revised list of research needs we developed a web-based prioritization questionnaire that listed 37 research questions organized according to the PICO element most relevant to the question. The 37 research questions reflected questions that were considered both within and not within the scope of the original CER. The questionnaire used a forced prioritization exercise where each stakeholder had a limited number of votes to assign amongst the 37 questions. Respondents were asked to consider the potential impact, information gap, variation in research or clinical care, and uncertainty related to each research question in casting their votes. Based on the distribution of votes, questions that received a total of six or more votes (out of a possible 30) were considered high priority, those with four to five votes were considered medium priority, and those with zero to three votes were considered low priority.

Next, we searched for ongoing studies and funding opportunities that were relevant to the high-priority needs. We replicated the original CER literature search in 16 databases and searched for current funding opportunities posted by the National Institutes of Health and organizations specific to the topic. Finally, we evaluated potential study designs to address each of the highest-ranked research questions.

## Results

We enlisted a total of eight stakeholders in the identification and/or prioritization of research needs related to the use of breathing techniques in the treatment of asthma. Four individuals took part in both the identification and prioritization of research questions, two individuals only participated in helping to identify and refine evidence needs, and two individuals only participated in the prioritization of research questions.

A total of 37 specific research questions and six overarching methods-related research needs emerged after reviewing the original CER and consulting with the stakeholders. The six overarching issues were not included in the prioritization questionnaire, but were noted as extremely important issues in this area of research by all stakeholders. These issues were:

1. Trials of head-to-head comparisons of specific breathing techniques (matched for intensity), other lifestyle modifications, or medication regimens;
2. Studies with larger sample sizes, including multicenter trials;
3. Studies among specific population subgroups (e.g., non-White, children, older adults, individuals diagnosed with exercise-induced asthma) or heterogeneous trials with outcomes presented by subgroups;
4. Replication of or long-term followup of previous studies with positive effects or that use a standard breathing technique to further establish effectiveness;
5. Standardized intervention details reporting, including: specific breathing technique(s) practiced (e.g., shallow versus deep breathing, length of breath hold, nasal versus mouth breathing); and

6. Standardized outcomes reporting, including: asthma symptoms (e.g., wheezing, severity of asthma); pulmonary function (e.g., breathing rate, airway inflammation, daily PEF and PFV); cardiovascular outcomes (e.g., heart rate); quality of life (e.g., stress, anxiety); medication use; harms; psychosocial measures (e.g., self-efficacy)

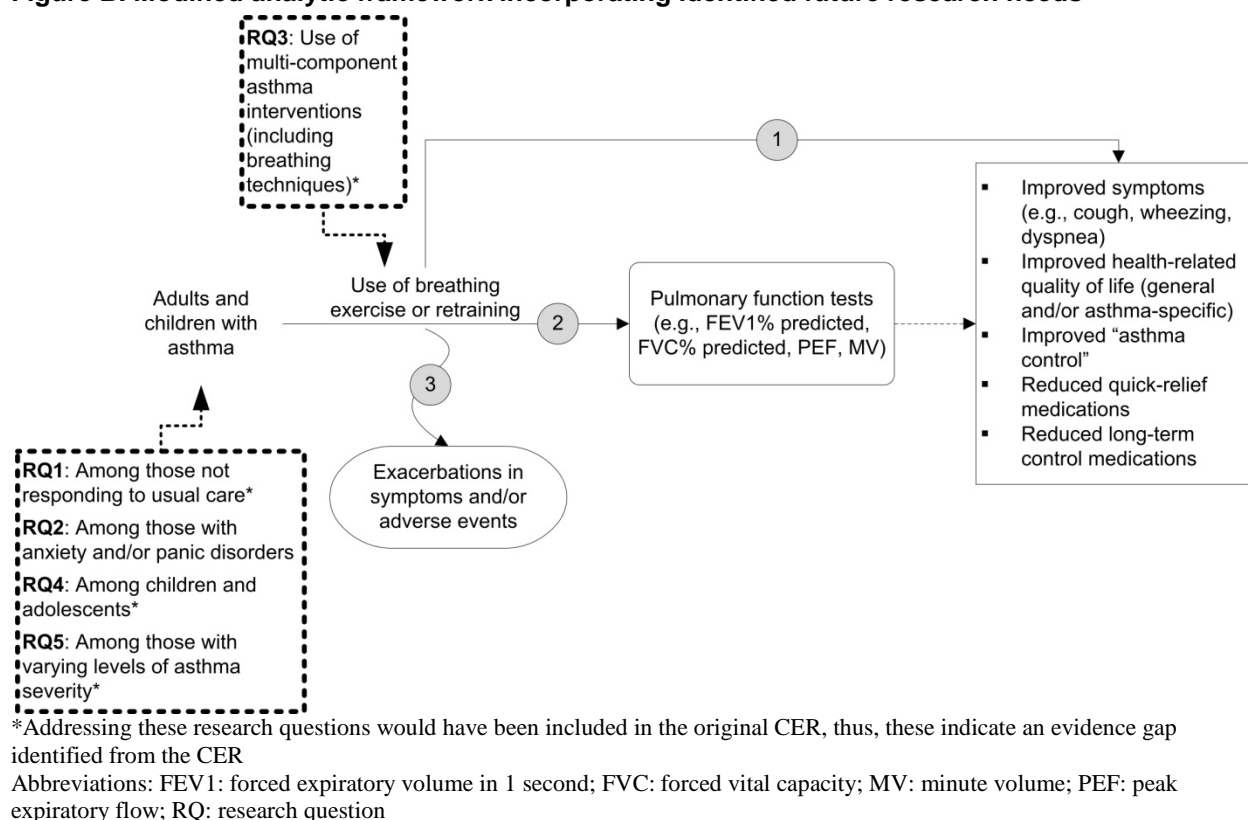
Of the 37 research questions, 16 were considered to be within the scope of the original CER while 21 were considered to be out-of-scope of the original CER. Based on the prioritization questionnaire, we organized all of the within-scope future research needs questions into three categories: high-priority research questions (n=5), medium-priority research questions (n=3), and low-priority research questions (n=8). Four out of the five highly prioritized questions also received a high-level of consensus among stakeholders (i.e., more than half of the stakeholders allocated at least one vote to these questions). These four questions are indicated with an asterisk (\*). Table A lists the final set of high-priority research questions and the number of total votes for each question.

**Table A. High-priority research questions**

Research Question	Number of Votes
1. Among individuals who are not responding to usual asthma care, what is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma?*	8
2. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with anxiety and/or panic disorders (with and without asthma)?*	8
3. What is the effectiveness of multicomponent asthma interventions (i.e., incorporating breathing techniques, relaxation techniques, and other lifestyle modifications) on asthma outcomes?*	8
4. What is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma among children and adolescents, and specifically adolescent females?	7
5. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with varying levels of asthma severity and which individuals (i.e., those with mild, moderate, or severe asthma) benefit the most from using breathing techniques to help manage their asthma?*	6

Using original CER analytic framework as starting point, we developed a modified framework linking the high-priority future research needs to specific elements of the population, intervention, outcomes, and overarching questions (Figure B).

**Figure B. Modified analytic framework incorporating identified future research needs**



Our literature search for relevant evidence yielded 126 unique citations. After title and abstract review, we identified 15 studies that could potentially address one or more of the research questions. We identified funding opportunities from 8 different organizations that are potentially relevant to one or more of the high-priority future research needs questions.

The appropriateness of a specific study design for a particular research topic depends on a number of factors, including how much is already known about the topic, the specific aims of the study, and other contextual factors regarding the populations, interventions, and outcomes of interest. As was previously mentioned, six overarching future research needs emerged from our original CER that the stakeholders confirmed to be perhaps the most important, and obvious, needs in this topic area. Many of these needs related to issues of study design (e.g., studies among specific population subgroups and replication of previous studies/interventions) and emerged as part of specific research questions in the high priority list. Targeting specific subpopulations such as those who are experiencing ongoing asthma symptoms despite usual care (RQ1), those with comorbid panic and/or anxiety conditions (RQ2), children and adolescents (RQ4), and those with varying levels of asthma severity (RQ5) should be considered in future research designs. Additionally, it was noted that all study designs should account for the need for larger sample sizes (allowing for stratification by important population subgroups), and to both collect and report standard intervention details and outcomes. Given the lack of trials in the original CER with direct comparisons of specific breathing techniques or other comparable interventions (e.g., other lifestyle modifications, asthma education, and changes to medication regimens), such designs are warranted. There is also a need to replicate the RCTs that test breathing technique interventions that most closely mirror “real world” interventions.

## Discussion

The purpose of this project was to engage a diverse set of stakeholders to identify and prioritize future research needs related to the use of breathing techniques in the management of asthma. Our findings suggested that future research in the area of the use of breathing techniques and retraining interventions for asthma management should focus on: the effectiveness of breathing retraining on asthma in specific subpopulations and the effectiveness of multicomponent interventions that include breathing techniques. Four out of the five high-priority questions related to understanding the effectiveness or comparative effectiveness of breathing techniques in specific groups including children and adolescents, those not responding to usual asthma care, those with asthma of varying severities, and those also experiencing panic or anxiety disorders.

Our process of engaging stakeholders and reviewing recent literature highlighted the fact that there continues to be limited research in this area in general. The most important research contributions in this field might relate to replicating the good quality studies included in our original CER and including standardized measurement and reporting, including details about the intervention itself. Well-designed randomized controlled trials would produce the most valid and generalizable results, if the studies' inclusion and exclusion criteria and setting reflect the context of real-world asthma care. However, such trials would need large sample sizes in order to account for presumably small-to-modest effect sizes. Prospective or retrospective cohort studies typically require fewer resources in terms of effort and funds to recruit a sufficient sample and execute the study. However, given that the exposure in question (breathing techniques with or without other intervention components) appears to be a relatively rare adjunctive strategy to usual asthma care, it is unclear how feasible such a design would be.

The list of prioritized research needs did not deviate considerably from the list of evidence gaps and future research needs articulated in our original CER. However, the engagement of diverse stakeholders helped to add more contextual details to these needs and helped articulate broader issues related to this topic area. The full list of 37 research questions and five highly-prioritized questions, lists of ongoing studies and potential funding opportunities, and research design considerations provide a basis for investigator-initiated research and related funding opportunities.

## References

1. American Lung Association - Epidemiology and Statistics Unit Research and Program Services Division. Trends in Asthma Morbidity and Mortality. Washington, DC: American Lung Association; 2009.
2. Zahran HS, Bailey C, Garbe P. Vital signs: asthma prevalence, disease characteristics, and self-management education - United States, 2001-2009. MMWR Morb Mortal Wkly Rep 2011;60(17):547-52.
3. O'Connor, E, Patnode, CO, Burda, BU, et al. Comparative effectiveness of breathing exercises and/or retraining techniques for the treatment of asthma. AHRQ Publication No. 12-EHC092-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2012.

# Background

## Context

An estimated 8.2 percent of the United States population has asthma including 9.6 percent of children and 7.7 percent of adults.<sup>1,2</sup> In general, long-term control and quick relief medications are used to control asthma by reducing airway inflammation and resolving acute exacerbations, respectively. These medications, although highly effective, are not without potential risks. Individuals with asthma are concerned about the use of asthma medications and are interested in alternative treatment methods to minimize symptoms related to their asthma and potentially reduce medication use.<sup>3,4</sup>

Alternative and complementary treatment methods such as breathing retraining techniques have been advocated for the control of asthma given the range of severity and causes in addition to the concerns about long-term medication use. Specific breathing retraining approaches include those related to hyperventilation reduction (e.g., the Buteyko and Papworth methods) or nonhyperventilation-targeted methods (e.g., yoga breathing techniques, other physical therapy methods, biofeedback, and inspiratory muscle training [IMT]). These methods are assumed to be adjunctive to guideline-based care, with the primary goals of improving asthma control and reducing the use of medication.

In 2010, the Agency for Healthcare Research and Quality (AHRQ) commissioned the Oregon Evidence-based Practice Center (EPC) to conduct a comparative effectiveness review (CER) on the effectiveness of breathing exercises and/or retraining in the treatment of asthma.<sup>5</sup>

The Key Questions addressed by the review were:

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?
  - 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?

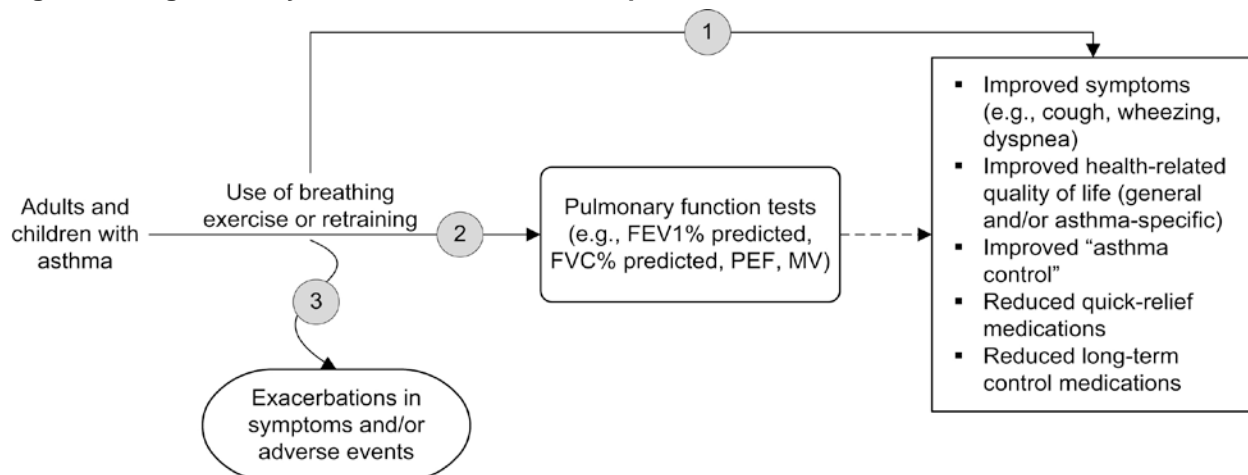
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\* For example: the Buteyko breathing technique; inspiratory muscle training; breathing physical therapy including paced and pursed lip breathing exercises; the Papworth method; biofeedback- and technology-assisted breathing retraining; and yoga breathing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

- a. Does the efficacy and/or effectiveness of breathing techniques for 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)?

The analytic framework (Figure 1), with Key Questions incorporated, guided the review and outlined the target populations, interventions and outcomes.

**Figure 1. Original analytic framework for the comparative effectiveness review<sup>5</sup>**



**Abbreviations:** FEV<sub>1</sub>: forced expiratory volume in 1 second; FVC: forced vital capacity; MV: minute volume; PEF: peak expiratory flow

## Findings of the CER

The review identified 22 studies published between 1990 and December 2011 that examined four different categories of breathing techniques: hyperventilation reduction breathing techniques (e.g., Buteyko breathing), yoga breathing techniques, inspiratory muscle training (IMT), and other nonhyperventilation reduction breathing techniques.<sup>5</sup> In general, the evidence was low-to-moderate or insufficient to address the Key Questions adequately as it was based primarily on small, methodologically limited trials of heterogeneous populations with short followup and inconsistent outcome reporting. There was moderate evidence that showed a reduction in asthma symptoms and reliever medication use with hyperventilation reduction breathing techniques interventions with five or more hours of direct instruction. There was also moderate evidence that hyperventilation reduction breathing techniques do not improve pulmonary function.<sup>5</sup>

The evidence was low or insufficient to show effects of hyperventilation reduction breathing techniques on medication use, quality of life, or functioning compared with controls. Compared to other breathing techniques, hyperventilation reduction was more likely to reduce reliever medication, but no more likely to improve asthma symptoms, medication use, quality of life, or pulmonary function, however, the evidence was low. Similarly, yoga breathing may improve asthma symptoms, quality of life and pulmonary function and quality of life but the strength of the evidence was low.<sup>5</sup>

There was insufficient evidence on the effect of yoga on asthma medication use and the effect of IMT and other nonhyperventilation reduction breathing techniques on asthma symptoms, medication use, quality of life or pulmonary function. There was no evidence of harms associated with the use of hyperventilation reduction breathing techniques, yoga breathing, IMT, and other nonhyperventilation reduction breathing techniques, although the evidence to support this was low. There was also insufficient evidence to determine whether individual patient characteristics (e.g., age, sex, etc.) or the provider's certification and/or training influenced the treatment effects or if the patient experienced any harms. Exploratory analyses suggested comprehensive approaches may be more likely to show a benefit than those that isolate a single aspect of breathing.<sup>5</sup>

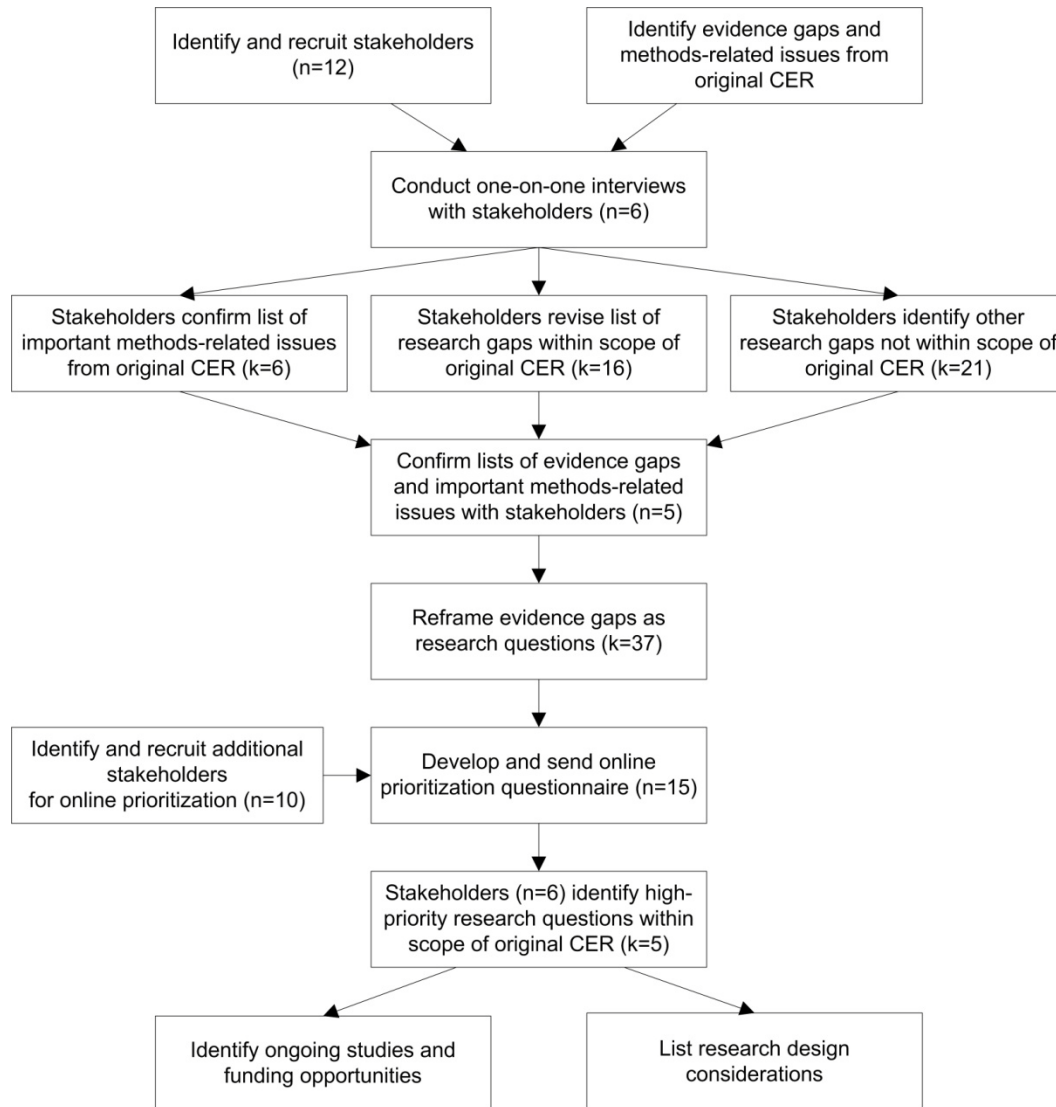
## **Objective**

The objective of this Future Research Needs (FRN) project was to engage a diverse set of stakeholders to confirm, provide more detail, and prioritize the research needs that were identified in the CER. We also sought to provide information on ongoing studies of relevance to the prioritized list of research questions and study design considerations for the highly prioritized questions.

# Methods

To meet our objectives, we identified and recruited stakeholders, identified and revised the list of evidence needs articulated in the original CER, developed and administered a web-based prioritization questionnaire (including identifying appropriate prioritization criteria), and identified study design considerations for the high-priority future research needs. Stakeholders were engaged at every step of the iterative process. The Kaiser Permanente Institutional Review Board (IRB) reviewed the proposal for this project and deemed that it did not require full IRB review. Figure 2 displays the full process and each step is described in detail below.

**Figure 2. Future Research Needs process**



**Abbreviation:** CER=comparative effectiveness review

## Identification and Recruitment of Stakeholders

We considered several different categories of types of stakeholders who might be interested in future research in this area when identifying potential individuals/organizations to invite. Categories included patient advocates, researchers, research funders, providers/practitioners, and

policymakers; both federal and nonfederal representation was sought. We aimed to include individuals from both the respiratory and complementary and alternative medicine fields given the topic. Because the categories were not necessarily mutually exclusive, we aimed to identify individuals who had several roles and could represent multiple viewpoints. For instance, some practitioners were also members of professional societies and organizations who make guidelines for their field. Patient advocacy groups may not only represent the needs of patients, but might also advocate for and direct specific policy decisions.

In order to identify potential stakeholders, we started by identifying individuals who was considered for and/or participated as a Key Informant (KI) during topic refinement (n=11) or a Technical Expert Panel (TEP) member during the review process (n=15), and those who were invited or provided peer review (n=18) or public comments (n=3) on the draft CER (40 unique individuals). We identified an additional eight individuals in areas that we felt were underrepresented on the original list including individuals from federal agencies, professional societies, patient advocacy groups, and academic research institutions. Several of these individuals also served on the National Heart, Lung, and Blood Institute's National Asthma Education and Prevention Program Coordinating Committee. We also identified five investigators from the included studies in the CER that we felt might provide relevant insight into the current state of the research. Lastly, we asked the CER lead author for nominations and recommendations based on her experience working with the KIs, TEP members, and in addressing peer and public comment and we asked the stakeholders to refer colleagues where appropriate. We also identified seven individuals for back-up should specific stakeholders not be available. The resulting list included 60 potential stakeholders.

We narrowed the list of potential stakeholders based on our previous experience with individual stakeholders and in an attempt to ensure that an adequate mix of stakeholder categories was represented. In total, we invited 22 individuals to participate as stakeholders for this project. As described further, 12 individuals were invited to help identify and refine the research gaps and an additional 10 individuals were invited to help prioritize the final list of research questions. As part of the invitation, we provided potential stakeholders with a brief description of the project, including their role and the amount of time we expected them to participate, along with a copy of the original CER's executive summary. In the event that a potential stakeholder declined, we contacted an alternative stakeholder from our list or asked individuals to refer us to someone else from their organization and/or others working in the field that they thought would be a good fit. After agreeing to participate, each stakeholder was asked to complete a standard AHRQ Conflict of Interest (COI) disclosure form.

## **Identification of Evidence Gaps**

We developed a preliminary list of evidence gaps by reviewing the CER and discussing the evidence gaps and research needs with the lead author of the CER. We sought to identify areas with insufficient evidence or where future research was warranted. We organized the evidence gaps and research needs according to the most relevant element of the PICO (Population, Intervention, Comparators, and Outcomes) framework.

Upon organizing the evidence needs and receiving COI disclosure forms, we scheduled 30 to 45 minute one-on-one interviews with the stakeholders. We sent them a copy of the preliminary list of evidence gaps and used a semi-structured interview guide (Appendix A) to facilitate the discussions. Stakeholders were asked to comment on whether or not they felt that the list of evidence needs was comprehensive and if there were better ways to express any of the research

topics. We also asked if there were specific questions or topics that seemed out of place or did not belong on the list in terms of their importance to the field. Among stakeholders who specifically conducted research in this area, we asked them to describe, in general, what study they would conduct next if given funding to initiate a large study.

Based on input from the one-on-one interviews, the project team revised the original list of research needs, reframed them as research questions, and organized them according to the specific PICO they addressed. We also listed any methodological issues that were identified in the original CER or through our discussions for consideration in the final report. To ensure that we had adequately addressed all of the stakeholders' comments, we sent a follow-up e-mail with the revised list of research needs to all of the stakeholders who participated in a one-on-one interview and asked them to let us know if any of the questions were not clear or did not adequately represent our conversation with them. We also welcomed them to add additional research questions if they felt we had missed something.

## **Prioritization of Evidence Gaps**

Once the stakeholders had an opportunity to review and edit the revised list of research needs we developed a web-based questionnaire using prioritization software developed by the Research Triangle Institute International and University of North Carolina EPC (Appendix B). The questionnaire listed 37 research questions organized according to the PICO element most relevant to the question (non-rank ordered within group). Of the 37 research questions, 16 were considered to be within the scope of the original CER while 21 were considered to be out-of-scope of the original CER. We asked stakeholders to prioritize among all of the research questions as to not diminish the questions that they felt were important yet not within the specific scope of this topic. The questionnaire used a forced prioritization exercise where we assigned each stakeholder a total of 20 "stars" or votes to assign amongst the 37 questions. Individual stakeholders could assign a maximum of five stars to any one research question. Respondents were asked to consider the following criteria when prioritizing the questions. These criteria were adapted from AHRQ's Effective Health Care Program and our recent experience in identifying and prioritizing CER questions within our organization.<sup>6</sup>

1. Impact: New research related to this question could potentially lead to improved health care quality, efficiency, or equity (i.e., better health outcomes, reduced variation in quality of care, cost improvement, or reduced health disparities).
2. Information Gap: More research on this topic is needed since it is not adequately answered by existing research.
3. Variation: Addressing this issue would contribute to solving important variation in research or clinical care, or controversy in what constitutes optimal care.
4. Uncertainty: Addressing the issue would contribute to solving important uncertainty for decision makers.

Data from the surveys were imported into Microsoft Excel<sup>®</sup> (Microsoft, Seattle, WA) for analysis. In order to determine the most highly prioritized research questions, we examined the total number of votes assigned to each research question considered within the scope of the original CER. We also evaluated the level of consensus for each question (i.e., the number of participants who assigned at least one star to each question). Based on the distribution of votes, research questions that received a total of six or more stars (out of a possible 30 stars) were considered high priority, those with four to five stars were considered medium priority, and those

with zero to three stars were considered low priority. Questions were considered to have a high level of consensus if more than half of the respondents (i.e., four or more) assigned at least one star to it.

## **Identification and Selection of Ongoing Studies and Funding Opportunities**

After identifying the highly prioritized research questions we searched for ongoing studies and funding opportunities that were relevant to these needs.<sup>7</sup> To identify ongoing or recently published research, we searched MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, Physiotherapy Evidence Database, Cochrane Central Register of Controlled Trials, AltHealthWatch, and Indian Medical Journals. In addition, we conducted searches of regulatory documents (e.g., the Authorized Medicine for the European Union and the U.S. Food and Drug Administration Medical and Statistical Reviews), clinical trial registries (e.g., National Institute of Health Research Portfolio Online Reporting Tools, ClinicalTrials.gov, the World Health Organization's International Clinical Trials Registry Platform, and International Standard Randomized Controlled Trial Number registry [also known as Current Controlled Trials]), and conference abstracts (e.g., CSA's Conference Paper Index, Scopus conference papers, ProceedingsFirst and PapersFirst). We searched these sources for relevant literature from the last search date of the CER (December 8, 2011) to June 25, 2012. The literature searches were not restricted to the English language. We replicated the original CER search in 16 databases (Appendix C). We reviewed titles and abstracts to identify relevant studies; only those that were not already included in the CER are included in this report.

To identify relevant funding opportunities, we searched for current funding opportunities posted by the National Institutes of Health (e.g., grants.gov) and organizations specific to the topic (e.g., American Lung Association and the Breathing Center [formerly Buteyko Center U.S.A.]) using keywords "asthma" and "breathing" where applicable. We also examined the funding sources of the included studies from the CER to identify additional organizations that may provide additional funding opportunities. Of 22 included studies, nine potential funding sources were identified: National Heart Lung and Blood Institute, Australian Association of Asthma Foundations, British Lung Foundation, National Asthma Campaign, Medical Capital Corporation, Centers for Disease Control and Prevention, Asthma UK, Royal College of General Practitioners, and the Central Council for Research in Yoga and Naturopathy. We searched for funding opportunities in June 2012 and we reviewed announcement details determine if the relevance of the funding to the highly prioritized research questions.

## **Approach to Research Design Considerations**

We evaluated potential study designs to address each of the highest-ranked research questions considering several factors presented in an AHRQ methods paper.<sup>8</sup> We considered factors such as advantages of the study design to produce a valid result; resource use, size, and duration; potential social, legal, and ethical issues; and availability of data or ability to recruit participants. It is clear that more than one study design may be appropriate to address a given research question. Likewise, specific study designs and study details are likely to apply to more than one research question. We imagine that the study design chosen is dependent on the study setting, administrative feasibility, and funding availability. Thus, this discussion is meant to

provide considerations to potential researchers and funders for future research in this area, rather than being prescriptive or definitive.

# Results

## Stakeholder Engagement

We enlisted a total of eight stakeholders in the identification and/or prioritization of research needs related to the use of breathing techniques in the treatment of asthma. Four individuals took part in both the identification and prioritization of research questions, two individuals only participated in helping to identify and refine evidence needs, and two individuals only participated in the prioritization of research questions.

Figure 3 details the flow of stakeholders through the process. Of the twelve stakeholders invited to participate in one-on-one interviews to help identify evidence gaps; six agreed to participate. They included two academic researchers whose primary research studies were included in the CER, one federal employee working on asthma-related programs, one practicing pediatric allergist and immunologist, a licensed Naturopathic physician, and a registered respiratory therapist-neonatal pediatric specialist who also serves on the board of directors for a national asthma patient advocacy organization.

None of the identified stakeholders had a conflict judged to preclude participation in the process. Disclosed conflicts included serving as a consultant to several medical technology and pharmaceutical companies, involvement with professional organizations focused on respiratory care, funded research from the National Heart, Lung, and Blood Institute, and being a curator at a college of natural medicine and being involved with two organizations focused on the Buteyko Breathing method.

Three individuals declined our invitation to participate in one-on-one interviews. One felt she was not familiar enough with the topic to be of assistance (Professor of Medicine in a Division of Pulmonary and Critical Care Medicine). Another individual who worked for a large nonprofit organization that focused on asthma patient advocacy felt that she was not an appropriate fit for this project. After further discussion, she felt it was not appropriate for someone who was not a scientist to participate. Lastly, a representative from one of the institutes of the National Institutes of Health (NIH) said that her Division was reluctant to participate in projects which would be making research recommendations to agencies such as the NIH; as if they would be advising themselves. We did not receive a response from the remaining three stakeholders despite more than one invitation sent.

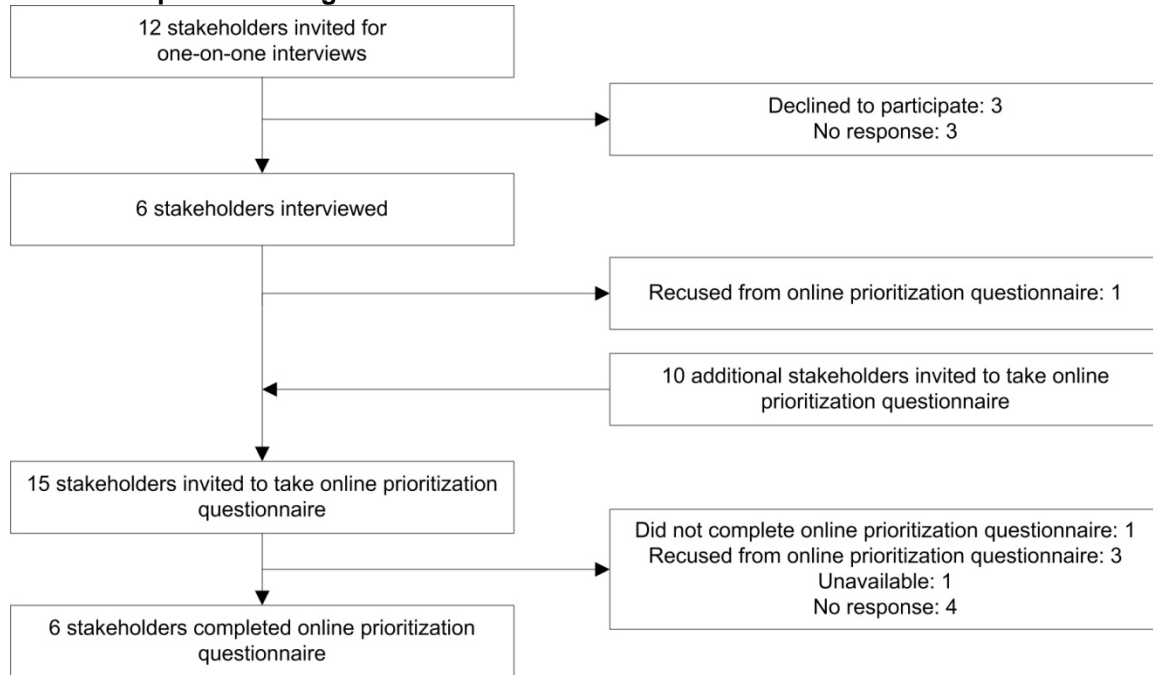
After conducting the one-on-one interviews, revising and adding evidence needs, and reframing the needs as research questions, we sent the revised list via e-mail to five of the six stakeholders for their feedback on the revisions. One stakeholder who participated in a one-on-one interview felt she would not be appropriate to continue working with us to prioritize the research questions given her limited knowledge of the field. We received e-mail responses from two of the five stakeholders; both stated that they felt the list was complete.

In addition to these five stakeholders, we invited another 10 individuals to prioritize the list of research questions. Individuals were identified and invited on a rolling basis. We attempted to maximize engagement by sending additional invitations as particular stakeholders either declined to participate or we received no response after multiple attempts. Ultimately, six stakeholders completed the online prioritization questionnaire (four original stakeholders and two new stakeholders).

On average, the stakeholders completed the online prioritization questionnaire in 17 minutes (range: 7 to 49 minutes). One stakeholder started the questionnaire but never submitted his responses despite several e-mail requests. The six stakeholders who completed the questionnaire

included two academic researchers, three practitioners (naturopathic medicine, allergist/immunologist, and respiratory therapist) and a director of patient advocacy for a state-based asthma control program. Of the additional eight stakeholders we invited to participate in the prioritization exercise, three individuals responded that they were not experts in the area and did not feel comfortable participating (despite being referred by colleagues), one individual was too busy to participate, and four individuals were not responsive after multiple email invitations.

**Figure 3. Participant flow diagram**



## Research Needs

The original CER identified a number of research gaps that provided a starting point for the development and prioritization of research questions for future studies. Below is a summary of these research gaps categorized by the most relevant element of the PICO framework (Table 1).

**Table 1. Future research needs identified by review of the comparative effectiveness review**

Category	Research Needs
Population	<ul style="list-style-type: none"> <li>• Studies with large sample sizes</li> <li>• Studies in population subgroups (e.g., non-White, children, older adults)</li> <li>• Studies in populations applicable to the U.S. healthcare system</li> <li>• Determination of the optimal candidates for treatment with breathing techniques (e.g., those without well-controlled asthma)</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>• Determination of optimal intensity and duration of treatment</li> <li>• Studies on expiratory muscle training and how this intervention differs from IMT</li> <li>• Studies on breathing physical therapy</li> <li>• Studies of other emerging breathing techniques and technologies</li> <li>• Studies of strategies to optimize benefits and minimize harms, such as additional lifestyle modifications and treatment components</li> <li>• Studies of breathing techniques with a component targeting autonomic arousal (e.g., relaxation)</li> <li>• Studies of breathing techniques with a component requiring the delay of reliever use medication</li> <li>• Replication of previous studies to establish effectiveness</li> <li>• Studies to determine theoretical basis of breathing techniques (i.e., nonhyperventilation reduction breathing techniques)</li> <li>• Standardized asthma and asthma-related terms to characterize interventions and explore effectiveness of specific elements of the intervention</li> <li>• Standardized interventions and level of detail reported (e.g., route, region, timing, etc.)</li> <li>• Interventions consistent with the standard of care in the United States by including asthma treatment with medications and education</li> </ul>
Comparator	<ul style="list-style-type: none"> <li>• Head-to-head comparison trials (i.e., comparative effectiveness research such as IMT versus Buteyko breathing)</li> <li>• Intensity-matched control groups</li> </ul>
Outcome	<ul style="list-style-type: none"> <li>• Standardized asthma outcome reporting including the requirement of reporting asthma symptoms</li> <li>• Additional evaluation of breathing techniques to determine their safety</li> <li>• Long-term evaluation of outcomes, including conducting an extended followup evaluation of previous studies</li> </ul>

**Abbreviation:** IMT: inspiratory muscle training

## Additional Future Research Needs Identified Through Interviews

During the individual interviews, six stakeholders reviewed and commented on the list of preliminary FRN (Table 1) identified from the original CER. One stakeholder also provided detailed written comments. A number of additional themes and specific evidence needs emerged in this stage. Based on these discussions, the project team revised the list of research needs, including reframing them all as research questions. In total, 37 future research questions were identified (Appendices D and E). The majority (k=21) of the additional research gaps related to issues considered to be out-of-scope of the original CER (e.g., understanding the mechanisms by which specific breathing techniques might affect asthma outcomes [including autonomic responses]; Appendix E). The remaining 16 research questions were considered to be within the scope of the original CER (Appendix D). Most of these questions related to the need for more studies that targeted specific subgroups such as children and adolescents, those who are not adherent to usual asthma treatment, and those with varying levels of asthma severity and studies that evaluated specific breathing techniques or multicomponent interventions.

## Methods-Related Research Needs

Six methods-related issues and overarching questions were detailed in the original CER and were confirmed as important considerations throughout the one-on-one interviews. These issues were not included in the prioritization questionnaire, but were noted as extremely important issues in this area of research by all stakeholders. These issues were:

1. Trials of head-to-head comparisons of specific breathing techniques (matched for intensity), other lifestyle modifications, or medication regimens;
2. Studies with larger sample sizes, including multicenter trials;
3. Studies among specific population subgroups (e.g., non-White, children, older adults, individuals diagnosed with exercise-induced asthma) or heterogeneous trials with outcomes presented by subgroups;
4. Replication of or long-term followup of previous studies with positive effects or that use a standard breathing technique to further establish effectiveness;
5. Standardized intervention details reporting, including: specific breathing technique(s) practiced (e.g., shallow versus deep breathing, length of breath hold, nasal versus mouth breathing); and
6. Standardized outcomes reporting, including: asthma symptoms (e.g., wheezing, severity of asthma); pulmonary function (e.g., breathing rate, airway inflammation, daily PEF and PFV); cardiovascular outcomes (e.g., heart rate); quality of life (e.g., stress, anxiety); medication use; harms; psychosocial measures (e.g., self-efficacy)

## Prioritization of Future Research Needs

Based on the methods described above, we organized the future research needs questions that were considered to be within the scope of the original CER into three categories: high-priority research questions (n=5), medium-priority research questions (n=3), and low-priority research questions (n=8). Four out of the five highly prioritized questions also received a high-level of consensus among stakeholders (i.e., more than half of the stakeholders allocated at least one vote to these questions). These four questions are indicated with an asterisk (\*) below.

## High-Priority Research Questions and Study Design Considerations

The following is the final set of high-priority research questions. Only the research questions considered to be within the scope of the original CER that received six or more votes are included in this discussion. Although the research questions are listed from 1 to 5; research questions 1 to 3 had identical levels of ranking (i.e., eight stars total), research question 4 had seven stars, and research question 5 had six stars total. Research questions noted with an asterisk (\*) after them indicate a high level of consensus among stakeholders (i.e., four or more stakeholders assigned at least one vote to this question).

1. Among individuals who are not responding to usual asthma care, what is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma?\*
2. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with anxiety and/or panic disorders (with and without asthma)?\*
3. What is the effectiveness of multicomponent asthma interventions (i.e., incorporating breathing techniques, relaxation techniques, and other lifestyle modifications) on asthma outcomes?\*

4. What is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma among children and adolescents, and specifically adolescent females?
5. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with varying levels of asthma severity and which individuals (i.e., those with mild, moderate, or severe asthma) benefit the most from using breathing techniques to help manage their asthma?\*

## **Literature Search Results**

Our literature searches yielded 126 unique citations. After title and abstract review, we identified 15 studies that could potentially address one or more of the five high-priority research questions. All ongoing and recently published studies that were deemed to be relevant to one or more five high-priority research questions are provided in Appendix F. Funding opportunities that are potentially relevant to one or more high-priority future research needs questions are presented in Appendix G.

## **Research Design Considerations**

The appropriateness of a specific study design for a particular research topic depends on a number of factors, including how much is already known about the topic, the specific aims of the study, and other contextual factors regarding the populations, interventions, and outcomes of interest. Research areas with limited evidence bases and those considered to be at the hypothesis generating stage may be suitable for exploratory studies, including qualitative and observational designs, whereas areas with established theories and/or application may be more appropriate for experimental designs.

As was previously mentioned, six overarching future research needs emerged from our original CER that the stakeholders confirmed to be perhaps the most important, and obvious, needs in this topic area. Many of these needs related to issues of study design (e.g., studies among specific population subgroups and replication of previous studies/interventions) and emerged as part of specific research questions in the high priority list. Targeting specific subpopulations such as those who are experiencing ongoing asthma symptoms despite usual care (RQ1), those with comorbid panic and/or anxiety conditions (RQ2), children and adolescents (RQ4), and those with varying levels of asthma severity (RQ5) should be considered in future research designs. Additionally, it was noted that all study designs should account for the need for larger sample sizes (allowing for stratification by important population subgroups), and to both collect and report standard intervention details and outcomes.

Given the lack of trials in the original CER with direct comparisons of specific breathing techniques or other comparable interventions (e.g., other lifestyle modifications, asthma education, and changes to medication regimens), such designs are warranted. There is also a need to replicate the RCTs that test breathing technique interventions that most closely mirror “real world” interventions, for example the comparative effectiveness trial by Cowie and colleagues that evaluated the effects of the Buteyko breathing technique versus breathing physical therapy on asthma symptoms, controller medication use, quality of life, and pulmonary function.<sup>9</sup>

All of the highly-prioritized future research questions would ideally be addressed by conducting good-quality comparative effectiveness or effectiveness RCTs. Randomized controlled trials (RCTs), however, are often not the most practical option given the complexities involved and the resources required. In particular, many of the research questions may require

large samples because of the small treatment effects expected for several outcomes. The feasibility of conducting RCTs may be also an issue, specifically in finding a sufficiently large population of individuals with specific characteristics (e.g., patients not responding to usual care [RQ1] or adolescent females [RQ4]) willing to comply with the intervention components for the duration of the intervention. Additionally, several of the breathing retraining interventions and other lifestyle interventions encourage patients to reduce or delay long-acting and quick-relief medications; future studies will require adequate justification and procedures for ensuring appropriate management of asthma symptoms.

For all of the high-priority research questions it is nearly impossible to have double-blind trials (i.e., where both participants and investigators are blind to the allocated treatment group) given that the intervention(s) being evaluated involve physical/lifestyle changes except for the case of sham interventions or direct comparisons of one breathing technique versus another. In this case, it is difficult to tell whether subjective outcomes such as self-reported quality of life or asthma symptoms are due to the actual interventions, to the extra attention participants receive, or merely to their belief that the intervention will help (a noted limitation in the original CER).

At least one of the research questions (RQ3) could be addressed within a two-by-two factorial design, in which participants are first randomized to an intervention focusing on one specific breathing technique, and then within each treatment group there is further randomization to evaluate a second question such as the effect of relaxation techniques. The principle advantage of a factorial design is the ability to answer two or more questions in a single trial for only a marginal increase in resources. The use of a two-by-two factorial design allows for the assessment of an interaction; typically testing a less mature hypothesis together with a more mature question with more reliable evidence. While the fact that a possible interaction might affect the magnitude of the effect might be seen as a limitation, in this case it could be seen as a strength when we are trying to understand if such an interaction exists. However, disadvantages of this design include the potential for poor compliance or losses to followup given the additional intervention and more complicated trial operations in general.

In lieu of experimental designs or systematic reviews, prospective cohort studies could be considered. Given that the exposure in question (breathing techniques with or without other intervention components), appears to be a relatively rare adjunctive strategy to usual asthma care, however, it is unclear how feasible such a design would be. In addition, one of the issues expressed by several stakeholders and alluded to in the CER is that there is really no “standard” breathing technique intervention or therapy. Even within one specific category of breathing techniques (e.g., hyperventilation reduction), the specific interventions themselves (e.g., Buteyko vs. Papworth) and the components vary widely. Ideally, a prospective study with participant recruitment, data collection and analysis would be designed and carried out that is specifically intended to address the question(s) of interest. Limitations of prospective cohort studies, however, include the strong potential for confounding and again, the feasibility of finding a sufficient number of individuals practicing or willing to practice breathing retraining as an adjunctive treatment to manage their asthma for an ongoing period of time, and the risk of selection bias.

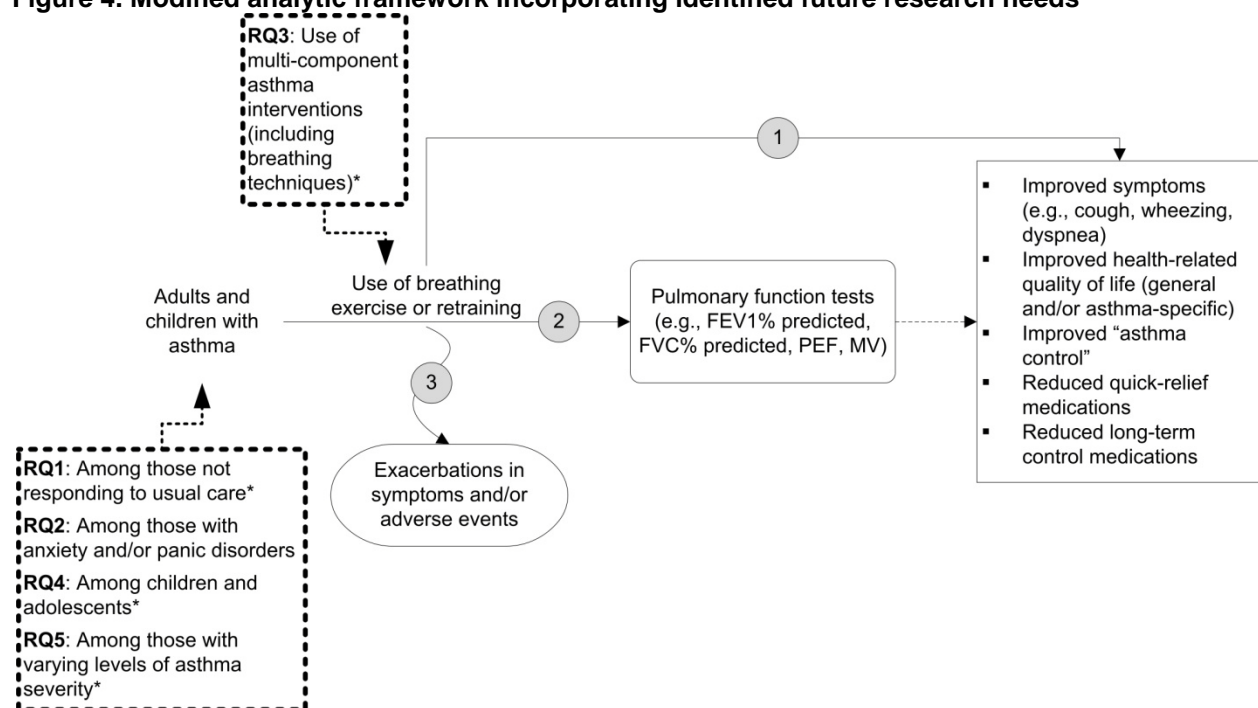
As more guidance becomes available regarding the minimal or standard components that should be included in the specific breathing interventions such as the Buteyko breathing technique, observational designs may become more appropriate. In fact, under the auspices of the Buteyko Breathing Educators Association, such standardization is underway. Establishing a registry of participants and/or conducting a prospective study designed to track patients receiving

this standardized intervention (matched with equivalent controls) could allow for robust analysis of patient subgroups and multiple outcomes over time. While a retrospective cohort study would be appropriate for a number of the high-priority research questions, we feel that it is highly unlikely that there is any existing observational data available that captures the exposures of interest (e.g., the use of breathing techniques or other related interventions), outcomes of interest (e.g., asthma symptoms, quality-of-life), for the specific populations of interest (e.g., children, those with panic/anxiety disorders).

## Modified Analytic Framework

Using Figure 1 from our original CER as starting point, we developed a modified framework linking the identified future research needs to specific elements of the population, intervention, outcomes, and overarching questions (Figure 4).

**Figure 4. Modified analytic framework incorporating identified future research needs**



\*Addressing these research questions would have been included in the original CER, thus, these indicate an evidence gap identified from the CER

**Abbreviations:** FEV<sub>1</sub>: forced expiratory volume in 1 second; FVC: forced vital capacity; MV: minute volume; PEF: peak expiratory flow; RQ: research question

## Discussion

The purpose of this project was to engage a diverse set of stakeholders to identify and prioritize future research needs related to the use of breathing techniques in the management of asthma. Our recent CER included an initial list of evidence gaps and future research needs from which this process drew from.<sup>5</sup> We also aimed to provide relevant information regarding ongoing studies and research design considerations for the highly-prioritized topics. Our findings suggested that future research in the area of the use of breathing techniques and retraining interventions for asthma management should focus on the effectiveness of breathing retraining on asthma in specific subpopulations and the effectiveness of multicomponent interventions that include breathing techniques. Four out of the five high-priority questions related understanding the effectiveness or comparative effectiveness of breathing techniques in specific groups including children and adolescents, those not responding to usual asthma care, those with asthma of varying severities, and those also experiencing panic or anxiety disorders.

Our process of engaging stakeholders and reviewing recent literature highlighted the fact that there continues to be limited research in this area in general. The most important research contributions in this field might relate to replicating the good quality studies included in our original CER and including standardized measurement and reporting, including details about the intervention itself. The list of prioritized research needs did not deviate considerably from the list of evidence gaps and future research needs articulated in our original CER. The engagement of diverse stakeholders, however, helped to add more contextual details to these needs and helped articulate broader issues related to this topic area.

Although not within the scope of our original review, a common theme throughout the stakeholder discussions and in several of the future research needs related to the mechanisms or pathophysiology by which breathing techniques might affect asthma outcomes. Several stakeholders expressed the need for more research related to the effects of breathing techniques on the autonomic system, including needing a better understanding of the role that general relaxation and reduced anxiety played in affecting asthma symptoms.

For questions that were out-of-scope for the original CER (e.g., cost-effectiveness of breathing technique interventions or questions that address the effectiveness of breathing techniques on other outcomes such as sleep apnea) it may be appropriate to consider a systematic review to identify if trials or observational studies have already been conducted to answer these questions. We suspect, however, that there is minimal data of fair or good quality that address many of these other areas given the paucity of data we found related to the Key Questions from the original CER. Given a sufficient number and quality of existing research, however, some questions may be addressable through narrative review or meta-analysis. If we were to broaden the inclusion/exclusion criteria from the original CER, we may find relevant data to abstract that pertains specifically to the future research needs identified here. For instance, we did not include any studies that were limited to individuals with anxiety or panic disorder without asthma (RQ2) in the original CER. Expanding our search strategy and inclusion criteria to include these studies might allow for more data to include in a systematic review.

There are a number of limitations to this future research needs project worth noting. First, this area of research – the use of breathing techniques and even complementary and alternative therapies more broadly, in asthma management—is relatively small and specialized. There is a paucity of research in this area, as seen in our CER, which included only 22 studies of low applicability to health care in the United States addressing four types of breathing techniques: hyperventilation reduction, yoga breathing, IMT and other nonhyperventilation reduction

methods. Also, throughout the original CER and FRN processes, we discovered that there are a very small number of individuals and organizations conducting research in this area. While there are likely thousands of practitioners—respiratory therapists, physical therapists/physiotherapists, and Buteyko educators—with practical expertise in this area, identifying such individuals with a keen knowledge of the research needs was difficult. While several of the potential stakeholders we identified were considered experts in the area of asthma management or complementary and alternative medicine, most of them declined from participating given their lack of knowledge regarding the use of breathing techniques specifically. Half of the stakeholders who agreed to participate were the principal investigator or a co-investigator of studies included in our CER. While their involvement provided rich detail and highly applicable considerations, their participation may have biased the development of the research gaps and the final prioritized list in favor of *their* future research plans. The involvement of other stakeholders, however, should have reduced this bias. Likewise, we identified very few funding opportunities specific to research in breathing techniques; most opportunities broadly addressed asthma in general which may limit the possibility of addressing the high-priority research questions identified in this FRN project.

Second, we did not search for or provide a list of ongoing studies for the full list of research questions *before* we provided the stakeholders the opportunity to review and prioritize the questions, as is recommended.<sup>7</sup> Providing this information to the stakeholders while they were prioritizing questions may have resulted in a different set of priorities if they felt that the topic was already being covered in current research or alternatively, if a lack of research on one particular subject was identified. In our review of the ongoing and recently completed research, however, we only identified 15 studies that may apply to one or more of the high-priority questions. We suspect that the yield would have been similar for all 37 questions and expect that the stakeholders' awareness of these studies would have not changed the results if presented to them before to the prioritization activity.

Finally, we did not engage the stakeholders in qualitative discussions specifically about the high-priority research questions. Our original interviews helped shape the final list of questions listed on the prioritization questionnaire, yet, did not provide specific detail on any particular question. Such discussions may have yielded more depth regarding the specific populations, interventions, comparators, outcomes and even the ideal study designs that should be used when answering the research questions.

Despite these limitations, we successfully identified and engaged a diverse group of stakeholders to help further elucidate research needs in this specialized field. The full list of 37 research questions and five highly-prioritized questions within the scope of the original CER, lists of ongoing studies and potential funding opportunities, and research design considerations provide a basis for investigator-initiated research and related funding requests.

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## **Abbreviations and Acronyms**

AHRQ	Agency for Healthcare Research and Quality
CER	comparative effectiveness review
COI	conflict of interest
EPC	Evidence-based Practice Center
FRN	future research needs
IMT	inspiratory muscle training
IRB	Institutional Review Board
KI	Key Informant
NIH	National Institutes of Health
PICO	Populations, Interventions, Comparators, Outcomes
RCT	randomized controlled trial
RQ	research question
TEP	Technical Expert Panel

# Appendix A. Interview Script

## Introduction:

- Thank you for agreeing to help us with this project.
- The interview should take 30 to 45 minutes.
- Did you receive the list of evidence gaps that we e-mailed?
- Let me tell you a little bit about this project: Although we identified 22 studies to include in our review, we identified multiple areas where insufficient evidence existed to answer our Key Questions and general evidence gaps related to this topic. The list that we provided you summarizes the broad future research needs that were identified throughout the review process. However, we understand that this list might not be exhaustive and there may be other research needs in this area that are important to clinicians, other practitioners, researchers, and patients. The purpose of this project is to develop and prioritize a future research agenda to close evidence gaps identified from this systematic review.
- We are aiming to recruit another 10 individuals to help us with this project who represent clinicians and practitioners, federal agencies who fund such research, representatives from asthma patient advocacy groups, and asthma researchers.
- We know that there are a lot of research needs and questions related to asthma management in children and adults. However, for this project, we want to stay focused on the research agenda related to the use of breathing techniques and exercises and other complementary and alternative therapies in the management of asthma. If our conversation starts to drift into a broader discussion of asthma management, I might try to steer us back to this.
- Before we jump into specific research questions, can you tell me a little bit about yourself and any research you have been involved with on this topic or the level of familiarity you have with this topic.

## Interview Questions:

1. After looking at the full list we provided, do you feel that this list is comprehensive?
2. If not, what other research questions do you think are important to consider?
3. Are there better ways to express any of these research topics? What suggestions do you have to improve the clarity of the wording?
4. Are there specific questions or topics on this list that seem like they are out of place or do not belong on this list in terms of their importance to the field?
5. Thinking specifically about different populations, interventions, and outcomes...
  - a. Are there particular populations where more research is required?
  - b. What types of interventions do you believe are most important to study?
  - c. What outcomes do you believe are most important to include?
6. Are there any emerging areas of research or practice in the area of complementary and alternative strategies for managing asthma that are not reflected in this list?
7. *Specifically for patient advocates:*
  - a. Are there any other questions that you have heard expressed by patients or other people in this field that might be good candidates for research in this area?
8. *Specifically for trialists:*

- a. If you were given funding to conduct a large research study in this area, what would that study look like? (We do not need to get into specific study methods or design issues, but rather what populations, intervention, and outcomes you would be interested in.)

**Conclusions and wrap-up:**

- Before we wrap things up and talk about next steps, are there any last comments you have regarding this area of research?
- As I mentioned earlier, we are planning to speak with up to 10 individuals conducting research or practicing in this area. Once this list is finalized, we will send you an e-mail with a link to an online questionnaire in which we will ask you to rank the research questions according to the level of priority you believe they each have. Our goal in the end is to have a list of important research questions to pursue and considerations for research designs to answer these questions. AHRQ will distribute this list widely and a full report will be posted on their website.
- Thank you for your participation. We look forward to getting your feedback on the survey. You should look for that in your inbox sometime in March. And, please do not hesitate to call or e-mail should you think of additional areas that we should include or if you have any questions.

# Appendix B. Online Prioritization Software

## Breathing Techniques Research Priorities

For the survey, we would like you to prioritize the research questions that were identified by experts and from a comparative effectiveness review. This list includes 37 questions in no particular order.

Please prioritize the list by adding stars to the questions listed below. The more stars you add by any question, the higher you rank that question compared to other questions on the list. We have provided you with **20** total stars. You may use up to five stars on any one research question. To add stars to a selection, position your mouse over the dots in the right-hand column. To remove stars, click on the outlined star on the left next to the yellow stars.

Please consider the following criteria in prioritizing the questions:

**IMPACT:** New research related to this question could potentially lead to improved health care quality, efficiency, or equity (i.e., better health outcomes, reduced variation in quality of care, cost improvement, or reduced health disparities).

**INFORMATION GAP:** More research on this topic is needed since it is not adequately answered by existing research.

**VARIATION:** Addressing this issue would contribute to solving important variation in research or clinical care, or controversy in what constitutes optimal care.

**UNCERTAINTY:** Addressing the issue would contribute to solving important uncertainty for decision makers.

Remaining stars: (20 of 20)



General Asthma/Breathing Techniques Research Questions	
1. What is the prevalence of asthma misdiagnosis in the primary care population?	☆ ● ● ● ● ●
2. What is the prevalence of hyperventilation in the primary care population?	☆ ● ● ● ● ●
3. What are the breathing characteristics (e.g., respiratory rate, etc.) of primary care subgroups (e.g., females, older adults, etc.)?	☆ ● ● ● ● ●
4. What is the etiology of hyperventilation?	☆ ● ● ● ● ●
5. What is the cost-effectiveness of breathing technique interventions compared to usual asthma care?	☆ ● ● ● ● ●
Population-specific Research Questions	
6. What is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma among children and adolescents, and specifically adolescent females?	☆ ● ● ● ● ●
7. Among individuals who are not responding to usual asthma care, what is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma?	☆ ● ● ● ● ●
8. Among individuals who are not adherent to usual care, what is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma?	☆ ● ● ● ● ●
9. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with varying levels of asthma severity and which individuals (i.e., those with mild, moderate, or severe asthma) benefit the most from using breathing techniques to help manage their asthma?	☆ ● ● ● ● ●
10. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with anxiety and/or panic disorders (with and without asthma)?	☆ ● ● ● ● ●
11. What is the effectiveness or comparative effectiveness of breathing techniques among individuals who experience high levels of stress (with and without asthma)?	☆ ● ● ● ● ●
12. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with vocal cord dysfunction (with and without asthma)?	☆ ● ● ● ● ●
13. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with sleep apnea (with and without asthma)?	☆ ● ● ● ● ●
14. What is the effectiveness or comparative effectiveness of breathing techniques among individuals with comorbid conditions (e.g., depression, heart disease) (with and without asthma)?	☆ ● ● ● ● ●
15. What are the characteristics of individuals with asthma who benefit the most from breathing technique interventions?	☆ ● ● ● ● ●

Intervention-specific Research Questions	
16. What are the mechanism(s) by which breathing techniques interventions affect asthma outcomes?	☆ ● ● ● ● ● ●
17. Does anxiety mediate the relationship between breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
18. What effects do breathing techniques have on the autonomic nervous system? Do effects on the autonomic nervous system mediate the relationship between breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
19. To what extent does increased baroreflex gain mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
20. To what extent does stress management mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
21. To what extent does mechanical dilation of airways mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
22. To what extent does anti-inflammatory effects mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
23. To what extent does increased gas exchange mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
24. To what extent does decreased hyperventilation mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
25. To what extent does endorphin effect mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
26. To what extent does improved pulmonary function mediate or modify the relationship between specific breathing techniques and asthma outcomes?	☆ ● ● ● ● ● ●
27. What is the effectiveness or comparative effectiveness of the standard Buteyko breathing intervention (as set forth by the Buteyko Breathing Educators Association) on asthma outcomes compared with usual asthma care or other breathing techniques?	☆ ● ● ● ● ● ●
28. What is the effectiveness of multicomponent asthma interventions (i.e., incorporating breathing techniques, relaxation techniques, and other lifestyle modifications) on asthma outcomes?	☆ ● ● ● ● ● ●
29. What is the comparative effectiveness of breathing techniques plus dietary modifications versus dietary modifications alone in the treatment of asthma?	☆ ● ● ● ● ● ●
30. What is the effectiveness of acupuncture in the treatment of acute asthma symptoms?	☆ ● ● ● ● ● ●
31. What is the effectiveness or comparative effectiveness of the POWERbreathe® inspiratory muscle trainer on asthma outcomes?	☆ ● ● ● ● ● ●
32. What is the independent effect of the specific breathing techniques used in school-based asthma education programs (e.g., Open Airways, Power Breathing) on children/adolescent asthma outcomes?	☆ ● ● ● ● ● ●
33. What specific evidence-based breathing techniques should school-based asthma education programs (e.g., Open Airways, Power Breathing) incorporate?	☆ ● ● ● ● ● ●
34. What is the optimal intensity and duration of breathing techniques interventions?	☆ ● ● ● ● ● ●
Outcome-specific Research Questions	
35. What is the effectiveness of specific breathing techniques (e.g., the Buteyko breathing method) on other health outcomes (beyond asthma) including sleep apnea, anxiety, panic attacks, rhinitis, sinusitis, allergies, or headaches/migraines?	☆ ● ● ● ● ● ●
36. Does the exact respiration rate or depth of respiration matter in producing improvements in pulmonary function?	☆ ● ● ● ● ● ●
37. What is the effectiveness of specific breathing techniques on end-tidal carbon dioxide?	☆ ● ● ● ● ● ●

Remaining stars: (20 of 20)



Save and Continue

## Breathing Techniques Research Priorities

Are there any other areas of research related to this topic that are not included in this questionnaire (please list)?

What additional criteria did you use when casting your votes?

What perspective(s) are you representing (please list all that apply): consumer advocate, clinician, policy maker, researcher, funder of research, other (list)?

[If you would like to return to the activity please click here](#)

[To submit your response please click here](#)

## Appendix C. Literature Search Strategies

Database: **AltHealthWatch**

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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: **CINAHL**

---

S27 S3 and S25 Limiters - Published Date from: 19900101-20120625

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 2012

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 2012 June 25>

---

- 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/
- 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: 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

**For all other databases (e.g., CSA Proceedings, etc.):**

asthma AND (buteyko OR pranayama OR papworth OR yoga OR yogic OR biofeedback OR paced OR pursed OR "muscle training" OR "physical therapy" OR physiotherapy OR "breathing exercise" OR "breathing exercises" OR "breathing training" OR "breathing retraining" OR "diaphragmatic breathing" OR "breathing technique" OR "breathing techniques")

## Appendix D. Prioritized Research Questions Within Scope of Original CER

Priority level	Research question	Total number of stars
High	Among individuals who are not responding to usual asthma care, what is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma?	8
	What is the effectiveness or comparative effectiveness of breathing techniques among individuals with anxiety and/or panic disorders (with and without asthma)?	8
	What is the effectiveness of multicomponent asthma interventions (i.e., incorporating breathing techniques, relaxation techniques, and other lifestyle modifications) on asthma outcomes?	8
	What is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma among children and adolescents, and specifically adolescent females?	7
	What is the effectiveness or comparative effectiveness of breathing techniques among individuals with varying levels of asthma severity and which individuals (i.e., those with mild, moderate, or severe asthma) benefit the most from using breathing techniques to help manage their asthma?	6
Medium	What is the effectiveness or comparative effectiveness of breathing techniques among individuals with sleep apnea (with and without asthma)?	5
	What are the characteristics of individuals with asthma who benefit the most from breathing technique interventions?	5
	What is the effectiveness or comparative effectiveness of the standard Buteyko breathing intervention (as set forth by the Buteyko Breathing Educators Association) on asthma outcomes compared with usual asthma care or other breathing techniques?	5
Low	Among individuals who are not adherent to usual care, what is the effectiveness or comparative effectiveness of breathing techniques in the treatment of asthma?	3
	What is the optimal intensity and duration of breathing techniques interventions?	3
	What is the effectiveness or comparative effectiveness of breathing techniques among individuals who experience high levels of stress (with and without asthma)?	2
	What is the effectiveness or comparative effectiveness of breathing techniques among individuals with vocal cord dysfunction (with and without asthma)?	2
	What is the comparative effectiveness of breathing techniques plus dietary modifications versus dietary modifications alone in the treatment of asthma?	2
	What is the effectiveness of specific breathing techniques on end-tidal carbon dioxide?	1
	What is the effectiveness or comparative effectiveness of the POWERbreathe® inspiratory muscle trainer on asthma outcomes?	0
	What is the independent effect of the specific breathing techniques used in school-based asthma education programs (e.g., Open Airways, Power Breathing) on children/adolescent asthma outcomes?	0

## Appendix E. Prioritized Research Questions Not Within Scope of Original CER

Priority level	Research question	Total number of stars
High	What is the cost-effectiveness of breathing technique interventions compared to usual asthma care?	8
	What is the effectiveness of specific breathing techniques (e.g., the Buteyko breathing method) on other health outcomes (beyond asthma) including sleep apnea, anxiety, panic attacks, rhinitis, sinusitis, allergies, or headaches/migraines?	7
Medium	What is the prevalence of hyperventilation in the primary care population?	5
	What are the mechanism(s) by which breathing techniques interventions affect asthma outcomes?	5
	To what extent does decreased hyperventilation mediate or modify the relationship between specific breathing techniques and asthma outcomes?	5
	What is the prevalence of asthma misdiagnosis in the primary care population?	4
	Does anxiety mediate the relationship between breathing techniques and asthma outcomes?	4
Low	To what extent does anti-inflammatory effects mediate or modify the relationship between specific breathing techniques and asthma outcomes?	3
	What effects do breathing techniques have on the autonomic nervous system? Do effects on the autonomic nervous system mediate the relationship between breathing techniques and asthma outcomes?	2
	To what extent does stress management mediate or modify the relationship between specific breathing techniques and asthma outcomes?	2
	To what extent does improved pulmonary function mediate or modify the relationship between specific breathing techniques and asthma outcomes?	2
	Does the exact respiration rate or depth of respiration matter in producing improvements in pulmonary function?	2
	What is the etiology of hyperventilation?	1
	What is the effectiveness or comparative effectiveness of breathing techniques among individuals with comorbid conditions (e.g., depression, heart disease) (with and without asthma)?	1
	To what extent does increased baroreflex gain mediate or modify the relationship between specific breathing techniques and asthma outcomes?	1
	To what extent does endorphin effect mediate or modify the relationship between specific breathing techniques and asthma outcomes?	1
	What is the effectiveness of acupuncture in the treatment of acute asthma symptoms?	1
	What specific evidence-based breathing techniques should school-based asthma education programs (e.g., Open Airways, Power Breathing) incorporate?	1
	What are the breathing characteristics (e.g., respiratory rate, etc.) of primary care subgroups (e.g., females, older adults, etc.)?	0
	To what extent does mechanical dilation of airways mediate or modify the relationship between specific breathing techniques and asthma outcomes?	0
	To what extent does increased gas exchange mediate or modify the relationship between specific breathing techniques and asthma outcomes?	0

## Appendix F. Recently Published and Ongoing Studies of Relevance

1. Randomized trial of the effect of an integrative medicine approach to the management of asthma in adults on disease-related quality of life and pulmonary function. *J Aust Tradit Med Soc.* 2011;17:165-7.
2. LUCAR - Latinos Using Counseling for Help With Asthma and Anxiety Reduction. New York, NY: Yeshiva University; 2012. <http://clinicaltrials.gov/ct2/show/NCT01583296>. Accessed June 7, 2012.
3. The effectiveness of a comprehensive lifestyle modification programme for asthma patients (ETHICO study): a randomized controlled trial. Hradec Kralove Charles University; 2012. [www.drks.de/DRKS00003535](http://www.drks.de/DRKS00003535). Accessed June 7, 2012.
4. Ahmad R. Breathing and mild physical exercise therapy for asthma. Kuwait: Dasman Diabetes Institute; 2012. <http://clinicaltrials.gov/ct2/show/NCT01509443>. Accessed June 7, 2012.
5. Ashfaq K, Bhat MR. A clinical study on effect of breathing exercises on bronchial asthma: a controlled trial. *Biomedicine* 2012;32(1):96-100.
6. Balk J. Yoga and peak flow rates in pregnant asthmatics. Pittsburgh, PA: Magee Women's Institute and Foundation; 2002. [http://projectreporter.nih.gov/project\\_info\\_details.cfm?icde=0&projectnumber=6K08AT000782-05](http://projectreporter.nih.gov/project_info_details.cfm?icde=0&projectnumber=6K08AT000782-05). Accessed June 7, 2012.
7. Ball A. Breath controlled computer game controller for asthma therapy. Somerville, MA: Abid, Inc.; 2010. [http://projectreporter.nih.gov/project\\_info\\_description.cfm?aid=7928445&icde=12977959&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC](http://projectreporter.nih.gov/project_info_description.cfm?aid=7928445&icde=12977959&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC). Accessed June 7, 2012.
8. Feldman J. Adaptation of a behavioral treatment for Latinos with panic disorder and asthma. New York, NY: Yeshiva University; 2012. [http://projectreporter.nih.gov/project\\_info\\_description.cfm?aid=8197939&icde=12977992&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC](http://projectreporter.nih.gov/project_info_description.cfm?aid=8197939&icde=12977992&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC). Accessed June 7, 2012.
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## Appendix G. Relevant Funding Opportunities

Organization	Web site	Details of selected funding opportunities
American Asthma Foundation Research Program	<a href="http://www.americanasthmafoundation.org/grants/">http://www.americanasthmafoundation.org/grants/</a>	<ul style="list-style-type: none"> <li>• <i>Senior Investigator Award</i> \$750,000 (\$250,000 per year for three years) and <i>Early Excellence Award</i> \$450,000 (\$150,000 per year for 3 years). Eligible countries: United States, Australia, Canada, Ireland, Israel, Sweden and the United Kingdom. Review criteria: <ul style="list-style-type: none"> <li>○ Innovation: cutting-edge research, new-to-the-field thinking</li> <li>○ Relevance to asthma: potential for new insights into causes and treatments</li> <li>○ Research proposal: importance and clarity</li> <li>○ Investigator: productivity and ingenuity</li> </ul> </li> </ul>
American Lung Association	<a href="http://www.lung.org/finding-cures/grant-opportunities/">http://www.lung.org/finding-cures/grant-opportunities/</a>	<ul style="list-style-type: none"> <li>• <i>Lung Health Dissertation Grant</i> (one grant available): \$21,000 per year. Pre-doctoral support for nurses or students with an academic career focused on the various disciplines of social science. Research areas of particular interest are: psychosocial, behavioral, health services, health policy, epidemiological, biostatistical and educational matters related to lung disease.</li> <li>• <i>Senior Research Training Fellowship</i> (8-10 grants available): \$32,500 per year. Post-doctoral support for MDs and/or PhDs receiving further academic training as scientific investigators. Research areas of particular interest are: adult pulmonary medicine, pediatric pulmonary medicine and lung biology.</li> <li>• <i>Clinical Patient Care Research Grant</i> (1-2 grants available): \$40,000 per year. Provides seed monies for junior investigators working on traditional clinical studies examining methods of improving patient care and/or treatment for lung disease.</li> <li>• <i>Social-Behavioral Research Grant</i>: (1-2 grants available): \$40,000 per year. Provides seed monies for junior investigators working on epidemiological and behavioral studies examining risk factors affecting lung health. This grant includes studies concerning the ethical, legal and economic aspects of health services and policies.</li> <li>• <i>American Lung Association / The CHEST Foundation Asthma Clinical Patient Care Grant</i>: (one grant available): \$40,000 per year. Provides seed monies for junior investigators working on traditional clinical studies examining methods for improving patient care and treatment for asthma.</li> </ul>
Asthma UK	<a href="http://www.asthma.org.uk/how-we-help/groundbreaking-research-for-researchers/apply-for-funding/">http://www.asthma.org.uk/how-we-help/groundbreaking-research-for-researchers/apply-for-funding/</a>	<ul style="list-style-type: none"> <li>• <i>Project Grants</i>: Every two years from 2013, we will invite applications for larger, longer duration grants to tackle challenges in stable research fields and research fields in flux aligned with our priority research areas.</li> <li>• <i>Innovation Grants</i>: In alternate years from 2014, we will offer small grants to explore original ideas in inherently novel priority asthma research areas.</li> <li>• <i>Priority Needs Grants</i>: Priority Needs Grants are the mechanism within Asthma UK's 2011 to 2016 Research Strategy which enables the charity to strategically commission projects in order to address or highlight important issues in asthma research and/or service delivery.</li> </ul>

Organization	Web site	Details of selected funding opportunities
Australian Association of Asthma Foundations	<a href="http://www.asthmaaustralia.org.au/research/grants.php">http://www.asthmaaustralia.org.au/research/grants.php</a>	<ul style="list-style-type: none"> <li><i>Grants in the Area of Asthma:</i> These grants are investigator led projects relating to asthma and may be in basic sciences, clinical fields, epidemiology, public health etc. Grants will be awarded to applicants who best fulfill the grant selection criteria and who are employed at an institution with appropriate research facilities, under the supervision of a responsible investigator.</li> </ul>
British Lung Foundation	<a href="http://www.lunguk.org/research/grants_available_how_to_apply">http://www.lunguk.org/research/grants_available_how_to_apply</a>	<ul style="list-style-type: none"> <li><i>Leeds Trust Project Grant 2012:</i> The British Lung Foundation is offering a grant of £100,000 for research into ANY lung disease. Principal applicants can be based anywhere in the UK.</li> <li><i>Early Career Investigator Awards:</i> One award of £800 is being offered by the British Lung Foundation. A runner-up prize of £200 will also be available. Both prizes are designed to help the careers of the most promising early-career investigators carrying out original research in respiratory medicine and respiratory science during the past year. A selection committee judges the awards based on abstracts presented at the British Thoracic Society Winter Meeting. More information can be found at the British Thoracic Society website.</li> </ul>
Buteyko Breathing Educators Association	<a href="http://www.buteykoeducators.org/content.aspx?page_id=0&amp;club_id=174916">http://www.buteykoeducators.org/content.aspx?page_id=0&amp;club_id=174916</a>	No funding opportunities identified
Buteyko-USA	<a href="http://www.buteyko-usa.com/Default.htm">http://www.buteyko-usa.com/Default.htm</a>	No funding opportunities identified
Buteyko Institute of Breathing and Health	<a href="http://www.buteyko.info/index.asp">http://www.buteyko.info/index.asp</a>	No funding opportunities identified
Central Council for Research in Yoga and Naturopathy	<a href="http://www.ccryn.org/grant%20research.html">http://www.ccryn.org/grant%20research.html</a>	<ul style="list-style-type: none"> <li><i>Grant-in-Aid:</i> Given to the premier Medical and Yoga and Naturopathy Institutes for conducting clinical research to establish efficacy of Yoga and Naturopathy in prevention and treatment of various diseases. Application available online (no further details).</li> </ul>
Grants.gov	<a href="http://www.grants.gov">http://www.grants.gov</a>	<ul style="list-style-type: none"> <li><i>Asthma in Older Adults (R03):</i> Issued by the NHLBI and the NIAID encourages applications that propose to study the pathophysiology, epidemiology, diagnosis, and/or management of asthma in older adults.</li> <li><i>Obesity and Asthma: Awareness and Management (R01):</i> Issued by the NINR to stimulate research to examine the interconnections of asthma and obesity including intervention studies targeting asthma or obesity and their effects on each one, and possible mechanisms of action are encouraged.</li> </ul>
National Asthma Campaign	<a href="http://www.nationalasthmacampaign.org/home.asp">http://www.nationalasthmacampaign.org/home.asp</a>	No funding opportunities identified
Royal College of General Practitioners	<a href="http://www.rcgp.org.uk/">http://www.rcgp.org.uk/</a>	No funding opportunities identified

**Abbreviations:** NHLBI=National Heart, Lung and Blood Institute; NIAID=National Institute of Allergy and Infectious Disease; NINR=National Institute for Nursing Research