**Evidence-based Practice Center Systematic Review Protocol**

**Project Title: Interventions to Modify Healthcare Provider Adherence to Asthma Guidelines**

Amendment Date(s) if applicable:

(Amendments Details–see Section VII)

## I. Background and Objectives for the Systematic Review

### Background

### Asthma Epidemiology and Practice Guidelines

Asthma is a respiratory disease characterized by variable and recurring symptoms, airflow obstruction, bronchial hyper-responsiveness, and inflammation of the airways.

In the United States, an estimated that 24.6 million people (8.2%) currently have asthma.[1] Students with asthma miss more than 14 million school days every year due to illness. Furthermore, certain U.S. population subgroups have higher prevalence rates of asthma in comparison to the national average: children (9.6%), poor children (13.5%), non-Hispanic black children (17.0%), women (9.7%), and poor adults (10.6%).[1]

The current approach to asthma management includes monitoring symptoms and lung function, encouraging the use of medications that control and prevent symptoms, controlling the triggers of asthma, educating the patient, and maintaining a collaborative patient-provider relationship that includes the use of written action plans.[2] The main goals of therapy is to minimize current impairment and future risk.

The National Asthma Education and Prevention Program (NAEPP) of the National Heart, Lung, and Blood Institute (NHLBI) has published comprehensive guidelines for diagnosing and managing asthma. The most recent guidance was published in 2007 (previous versions were published in 1991, 1997, and 2002): *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma* is also known as EPR-3.[2] This guideline provides treatment recommendations with the strength of the evidence base for children 0–4, 5–11, and >12 years of age and adults. EPR-3 is based on a systematic review and expert opinion.

Adhering to NAEPP guideline recommendations has been shown to be efficacious in a variety of pediatric populations, including among high-risk populations, such as inner-city, poor, and/or African-American populations.[3-5] The available evidence suggests that most people with asthma can be symptom-free if they receive appropriate medical care, use inhaled corticosteroids when prescribed, and modify their environment to reduce or eliminate exposure to allergens and irritants.

### Current Practices and Decisional Uncertainty

Despite the evidence of efficacy in improving outcomes, their long-standing presence (>20 years) and their wide availability, there is extensive evidence that the NAEPP recommendations are not routinely being followed.[6,7] In one study, only 34.2 percent of patients reported being given a written asthma action plan, while only 68.1 percent had been taught the appropriate response to symptoms of an asthma attack.[7] In the same study, only about one-third of children or adults were using long-term control medicine such as inhaled corticosteroids. Additional evidence shows that clinicians are classifying asthma

appropriately in only a few patients, resulting in substandard care. Suboptimal asthma outcomes, such as unplanned care (e.g., emergency room visits), also persist despite the NAEPP guidelines.[8-13] In 2005, there were approximately 679,000 emergency room visits due to asthma in children under 15 years of age.[14] Currently, asthma is the third leading cause of hospitalization among children in this age group.[14]

With the growing number of published clinical practice guidelines (CPGs) across a variety of diseases, there has been more focused attention on why best practices are not followed (i.e., adhered to) by clinicians. In 1999, Cabana et al.[15] proposed a theoretical framework to understand why physicians do not comply with CPGs. They identified the following barriers: lack of awareness, disagreement with the CPG recommendations, doubts about the effectiveness of the CPG recommendations, lack of confidence in being able to carry out the best practice, inability to overcome the inertia of previous practice behaviors, and external barriers (e.g., time constraints during a visit, the CPGs are not user-friendly, patient preferences, etc.). There is a growing understanding that one of the shortcomings of asthma CPGs published by the National Institutes of Health (NIH) is the limited extent to which clinicians are provided with the tools and resources necessary to follow the recommended care.[16] This limitation may be due to the general lack of interventions developed specifically to address the barriers outlined by Cabana et al. It is possible that with the publication of two additional asthma CPGs and the development of a Guideline Implementation Panel, more physicians have been exposed to the NIH asthma CPGs, resulting in greater awareness of the CPGs, fewer disagreements with CPG recommendations, and greater confidence in carrying out recommended asthma care. Given that Cabana et al. found these barriers to be primarily related to how long physicians have been in practice, it is not unreasonable that physician attitudes and perceptions have changed over the past 16 years and through the four iterations of the NIH asthma CPGs.[17,18] However, there are some barriers outlined by Cabana et al. that likely would not be solved by increased exposure to asthma CPGs, including the inability of health care providers to overcome practice inertia and external barriers (e.g., time constraints during a visit, CPGs that are not user-friendly, patient preferences, etc.).[19]

Although most interventions targeted at improving asthma care and outcomes have been patient-focused,[20-23] there have been provider-targeted interventions to improve adherence to guidelines (e.g., educational seminars, prompts, etc.).[24-29] However, there is no consensus on what are the most effective physician-targeted interventions that improve adherence to guidelines, to what extent these interventions are currently used in clinical practice, nor is there a comprehensive source of information on these interventions. Having a centralized source of such information would be useful to those looking for readily available strategies to implement to improve physician care in their own setting.

## Potential Impact of a Comparative Effectiveness Review

Good-quality guidelines are currently available for the care of children or adults with asthma. Systematic reviews have been published on patient-targeted interventions,[30, 31] but little attention has been directed toward the effectiveness of clinician-focused strategies designed to enhance the implementation of NAEPP guidelines in clinical practice. In 2007, the Stanford University–University of California San Francisco Evidence-based Practice Center published a report on asthma care, entitled *Closing the Quality Gap: A Critical Analysis of Quality Improvement Strategies: Volume 5—Asthma Care*.[32] This report showed that, despite the availability of evidence-based guidelines for the management of pediatric and adult asthma, a significant gap remains between accepted best practices for asthma care and the actual care delivered to patients with asthma in the United States. The report authors examined the published literature through May 2006 to evaluate whether quality improvement strategies can be used to improve the processes and outcomes of outpatient care for children and adults with asthma. The interventions used in the studies that the report authors included in their analyses had been tested between 1976 and 2004, so new data most likely would not have been published after 2004. Furthermore, although pediatric studies were included in the report analyses, the interventions used in those studies were directed at patient adherence to provider-prescribed care, rather than at provider

adherence to asthma guidelines. Thus, the results of the 2007 report would not be relevant to this topic nomination.

## Expected Use of the Proposed Report

The results of the proposed report will be of use to health care providers, health care policymakers, and guideline developers seeking to improve the adherence of health care providers to asthma guidelines. The results will help provide an evidence base for future practice guidelines to influence patient management.

### II. The Key Questions

The key questions (below) to be answered by this systematic review were posted for public comment. No changes were made to these questions following the public comments.

| | |
|---|---|
| **KQ 1:** | In the care of pediatric or adult patients with asthma, what is the evidence that interventions designed to improve health care provider adherence to guidelines impact health care process outcomes (e.g., receiving appropriate treatment)? |
| **KQ 2:** | In the care of pediatric or adult patients with asthma, what is the evidence that interventions designed to improve health care provider adherence to guidelines impact clinical outcomes (e.g., hospitalizations, patient reported outcomes such as symptom control)? |
| **KQ 3:** | In the care of pediatric or adult patients with asthma, what is the evidence that interventions designed to improve health care provider adherence to guidelines impact health care process outcomes that then affect clinical outcomes? |

### PICOTS Criteria

#### Population(s)

- Physicians, nurses, nurse practitioners, physiotherapists/physical therapists, respiratory therapists, pharmacists and other health care providers treating children (0 to 18 years of age) or adults (over 18 years of age) with asthma

#### Interventions

- Interventions to improve adherence to guidelines. Includes: education, reminders, decision support (health information technology and paper-based), clinical pharmacy service interventions, organizational change, pay-for-performance/quality incentives, physician detailing, audit and feedback

#### Comparators

- Usual care, as defined by eligible study, and comparisons between interventions

#### Outcomes

- Health care process outcomes (including: prescriptions for controller medicine, environmental control practice recommendations, self-management education, asthma action plans, documentation of level of asthma severity, prescription of peak flow meter, and follow-up visits,)

- Clinical outcomes (including: symptom days, missed days of school and/or work, quality of life, emergency department visits/hospitalizations/urgent doctor visits, lung function tests, rescue use of short-acting B2 agonists, parental/patient perceptions/ratings of care, and side effects of drugs)
- The outcomes are non-directional. That is, outcomes considered good, as well as those considered to be potential harms or unintended consequences, will be considered.

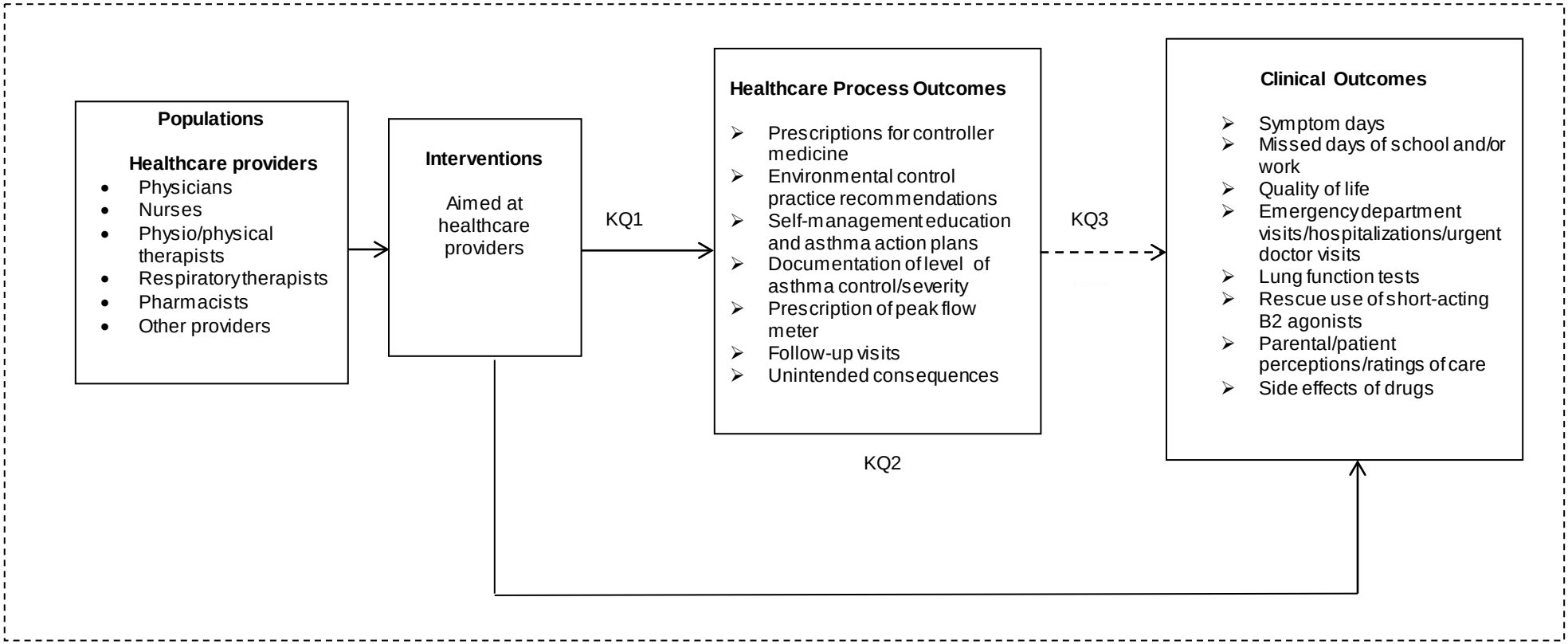
**Timing**

- Studies with all duration of follow-up will be included in the analysis.

**Setting**

- Outpatient settings in which health care providers work, but not emergency room or in-patient settings.

**Figure 1. Analytic framework for Guidelines on the Care of Adults and Children with Asthma**




**Alternative text for figure 1**

Figure 1 is our analytic framework presenting the Key Questions (KQ) in terms of the populations: physicians, nurses, physio/physical therapists, respiratory therapists, pharmacists, and other providers. Interventions are aimed at our given populations. Healthcare process outcomes are listed as: prescriptions for controller medicine, environmental control practice recommendations, self-management education and asthma action plans, documentation of level of asthma control/severity, prescription of peak flow meter, follow-up visits, and unintended consequences. Clinical



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outcomes include: symptom days, missed days of school and/or work, quality of life, emergency department visits/hospitalizations/urgent doctor visits, lung function tests, rescue use of short-acting B2 agonists, parental/patient perceptions/ratings of care, side effects of drugs.

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## III. Methods

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

**Table 4: List of Inclusion/Exclusion**

| | Inclusion | Exclusion |
|---|---|---|
| | Human subjects | Animal studies/models |
| **Populations** | Physicians, nurses, nurse practitioners, physiotherapists/physical therapists, respiratory therapists, pharmacists, and other health care providers treating children or adults with asthma | • Study does not address asthma |
| **Intervention** | Interventions to improve adherence to guidelines including education, reminders, decision support (health information technology and paper-based), clinical pharmacy service interventions, organizational change, pay-for-performance/quality incentives, physician detailing, audit, and feedback | Studies that do not assess an intervention will be excluded. |
| **Comparisons of interest** | Usual care, as defined in each eligible study, and comparisons between interventions | • If there is no comparison, the study will be excluded. |
| **Outcomes** | **Health care process outcomes**<br>➢ Prescriptions for controller medicine<br>➢ Environmental control practice recommendations<br>➢ Self-management education and asthma action plans<br>➢ Documentation of level of asthma control/severity<br>➢ Prescription of peak flow meter<br>➢ Follow-up visits<br><br>**Clinical outcomes**<br>➢ Symptom days<br>➢ Missed days of school and/or work<br>➢ Quality of life<br>➢ Emergency department visits/hospitalizations/urgent doctor visits<br>➢ Lung function tests<br>➢ Rescue use of short-acting B2 agonists<br>➢ Parental/patient perceptions/ratings of care<br>➢ Side effects of drugs<br><br>The outcomes will be nondirectional; that is, all outcomes will be considered whether they are beneficial or cause potential harms or unintended consequences | We will exclude studies that do not report an outcome of interest, such as those studies that report only acceptability of intervention. |
| **Type of Study** | We will include meeting abstracts<br><br>Randomized and quasi-randomized controlled trials and cross-over studies<br>Non-randomized studies including non- | We will exclude studies that:<br>• Do not address adherence to guideline<br>• Do not target health care providers |



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| | randomized controlled trial or cross-over studies, controlled before-after studies, interrupted-time-series, historically controlled studies, cohort studies, case-control studies, cross-sectional studies, and case series. | • Do not evaluate intervention designed to influence adherence of health care providers to guidelines<br>• We will exclude studies with no original data (e.g., reviews, editorials, comments, and letters). |
| **Timing and Setting** | Studies with all durations of follow-up will be included in the analysis<br>Outpatient settings in which health care providers work, but not emergency room or inpatient settings | We will exclude studies addressing inpatient or emergency department guideline or setting only |

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

We will develop a search strategy for MEDLINE, accessed via PubMed, based on an analysis of the medical subject headings (Mesh) terms for all potential relevant publications and text words of key articles identified a priori. The search will be updated during the peer review process. We will search the following databases for primary studies: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Educational Resources Information Center (ERIC), PsycInfo, and Research and Development Resource Base in Continuing Medical Education (RDRB/CME). If possible, we will also search the EPOC register. Our preliminary search strategy for MEDLINE is shown in **Appendix A.**

We will also review the reference lists of each included article, relevant review articles and related systematic reviews. We will not have any date or language restrictions.

**C. Data Abstraction and Data Management**

Abstracts will be reviewed independently by two investigators, and will be excluded if both investigators agree that the article meets one or more of the exclusion criteria (see inclusion and exclusion criteria listed in Table 3). Differences between investigators regarding abstract inclusion or exclusion will be tracked and resolved through consensus adjudication. Citations promoted on the basis of abstract review will undergo another independent parallel review using full-text of the articles to determine if they should be included in the final qualitative and quantitative systematic review and meta-analysis. The differences regarding article inclusion will be tracked and resolved through consensus adjudication.

We will use a systematic approach for extracting data to minimize the risk of bias in this process. We will create standardized forms for data extraction, which will be pilot tested. By creating standardized forms for data extraction, we will maximize consistency in identifying all pertinent data available for synthesis. Each article will undergo double review by study investigators for data abstraction. The second reviewer will confirm the first reviewer's data abstraction for completeness and accuracy. Reviewer pairs will be formed to include personnel with both clinical or domain, and methodological expertise. A third reviewer will audit a random sample of articles by the first two reviewers to ensure consistency in the data abstraction of the articles. Reviewers will not be masked to the articles' authors, institution, or journal. For all articles, reviewers will extract information on general study characteristics (e.g., study design, study period, and follow-up), study participants (e.g., type of provider, type of practice etc.), eligibility criteria, interventions (e.g., type of intervention), outcome measures and the method of ascertainment, and the results of each outcome, including measures of variability.



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All information from the article review process will be entered into the DistillerSR database by the individual completing the review. Reviewers will enter comments into the system whenever applicable. The DistillerSR database will be used to maintain the data, as well as to create detailed evidence tables and summary tables.

### D. Assessment of Risk of Bias of Individual Studies

The risk of bias of included trials will be conducted independently and in duplicated based on the Cochrane Collaboration's Risk of Bias Tool.[33] For non-randomized studies, we will use the Newcastle Ottawa Scale.[34] We will supplement these tools with additional assessment questions, such as use of appropriate analysis, based on recommendations in the Methods Guide for Conducting Comparative Effectiveness Reviews.[35]

### E. Data Synthesis

Qualitative synthesis will be completed, grouped by type of intervention (i.e., provider-based, practice-based, system-based). Where possible, synthesis will consider subgroups including:

- Type of provider
- Type of practice
- Practice location (e.g., inner-city, rural, non-U.S., etc.)

We will conduct meta-analyses of summary data when there are sufficient data (at least 3 trials or observational studies) and studies are sufficiently homogenous with respect to key variables (population characteristics, study duration). Randomized controlled trials and non-randomized studies will be analyzed separately. All analyses will be intention to treat. Statistical significance (will be set at a two sided alpha of 0.05.

We will calculate a weighted mean difference using a random effects model with the DerSimonian and Laird formula for continuous outcomes.[36] We will calculate a pooled effect estimate of the relative risk between trial arms from RCTs for dichotomous outcomes, with each study weighted by the inverse variance, using a random effects model with the DerSimonian and Laird formula for calculating between-study variance. We will evaluate for statistical heterogeneity among studies using an $I^2$ statistic, and anticipate statistical heterogeneity.

A value greater than 50% will be considered to have substantial statistical heterogeneity. If we find substantial heterogeneity, we will attempt to determine potential reasons by conducting metaregression if covariate information (age, sex, and dose) is available.

Publication bias may be examined using Begg's and Eggers tests including evaluation of the asymmetry of funnel plots for each comparison of interest for the outcomes where meta-analyses are conducted.[37] All meta-analyses will be conducted using STATA (Intercooled, version 11, StataCorp, College Station, TX). Studies that are not amenable to pooling will be summarized qualitatively.

### F. Grading the Strength of Evidence for Each Key Question

Two reviewers independently will grade the strength of evidence on each of the key questions by adapting an evidence grading scheme recommended by the Methods Guide for Conducting Comparative Effectiveness Reviews.[38] In assigning evidence grades we will consider the four required domains including risk of bias of included studies, directness, consistency and precision. We will also consider additional domains such as the impact of plausible confounders and publication bias. Evidence will be graded for the outcomes in the KQs. We will classify evidence pertaining to KQs 1–3 into four basic



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categories: 1) "high" grade (indicating high confidence that the evidence reflects the true effect, and further research is very unlikely to change our confidence in the estimate of the effect); 2) "moderate" grade (indicating moderate confidence that the evidence reflects the true effect, and further research may change our confidence in the estimate of the effect and may change the estimate); 3) "low" grade (indicating low confidence that the evidence reflects the true effect, and further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate); and 4) "insufficient" grade (evidence is unavailable).

### G. Assessing Applicability

Applicability will be assessed separately for the different outcomes of benefit and harm for the entire body of evidence guided by the PICOS framework as recommended in the *Methods Guide for Comparative Effectiveness Reviews of Interventions.*[35] We will also consider factors that may limit applicability of the findings (e.g., a study conducted in a non-U.S. health care setting, providers not common to the U.S. health care system, etc.).

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## V. Summary of Protocol Amendments

In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

## VI. Review of Key Questions

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

## VII. Key Informants

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

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

## VIII. Technical Experts

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



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

## IX. Peer Reviewers

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

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

## X. EPC Team Disclosures

Co-principal investigator is a consultant on a study funded by Glaxo-Smith-Kline assessing care quality in COPD. There are no other interests to disclose for the EPC research team.



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