VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE PRIMARY CARE MANAGEMENT OF ASTHMA

Department of Veterans Affairs
Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent Department of Veterans Affairs or TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Version 3.0 – 2019

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The Primary Care Management of Asthma Work Group

With support from:

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&
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I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the Health Executive Committee (HEC) "…on the use of clinical and epidemiological evidence to improve the health of the population…" across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This CPG is intended to provide primary care providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of adults and children four years or older with asthma, thereby leading to improved clinical outcomes.

In 2009, the VA and DoD published a CPG for the Primary Care Management of Asthma (2009 VA/DoD Asthma CPG), which was based on evidence reviewed through February 2008. Since the release of that guideline, a growing body of research has expanded the general knowledge and understanding of asthma.

Consequently, a recommendation to update the 2009 VA/DoD Asthma CPG was initiated in 2018. The updated CPG includes objective, evidence-based information on the management of asthma. It is intended to assist primary care providers in all aspects of patient care, including, but not limited to, assessment, treatment, and follow-up. The system-wide goal of evidence-based guidelines is to standardized management pathways for health professionals to improve the health and well-being of patients with asthma. The expected outcome of successful implementation of this guideline is to:

- Assess the patient's condition and determine, in collaboration with the patient, the best treatment method
- Optimize each individual's health outcomes and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient- (and family-) centered care (PCC)

II. Background

A. Description of Asthma

Asthma is a common medical problem frequently managed by primary care providers. It usually presents in the primary care setting with typical symptoms of wheezing, coughing, and dyspnea. In some cases, asthma exacerbations can be severe and potentially life threatening. Airway inflammation and bronchial hyperreactivity are considered the primary underlying pathologic processes. Asthma is characterized by airway obstruction that is usually at least partially reversible. Despite these unifying characteristics, asthma is a very heterogeneous condition. There is significant variability in presenting symptoms, degree of airway obstruction, level of impairment, responsiveness to medication, and frequency/severity of exacerbations. Patients with asthma also vary with respect to age at diagnosis, symptom triggers, psychosocial factors, and comorbid medical conditions. The heterogeneous nature of asthma can complicate diagnostic and treatment decisions. A one-size-fits-all approach may lead to inadequate treatment or exposure to unnecessary risks and burdens of therapies.

CPGs attempt to reduce inappropriate practice variability by providing recommendations based on scientific evidence. The varied nature of asthma, however, also makes clinical research and the application of that research to individual patients challenging. CPGs also provide a conceptual framework for the treatment of an illness. The paradigm for asthma treatment has evolved to recognize both the diversity among patients and variability of symptoms within an individual patient over time. Early asthma guidelines determined levels of severity based on pretreatment symptom burden and matched controller therapy to a specific severity level. The goal in this paradigm was to provide adequate medication for the severity of the disease while minimizing the risks and burdens of therapy. The current paradigm addresses attaining control of current symptoms, but it also considers the therapy necessary for maintaining control of symptoms and reducing the risk of loss of control from exacerbations. Therapy can be stepped up or down over time to achieve these goals while minimizing risks and burdens of the therapy. The current conceptual framework for asthma care also addresses quality of life and considers patients' values and preferences. Therapeutic choices are based on shared decision making (SDM) and are periodically reviewed over time.

B. Classification of Asthma Severity and Control

Asthma severity is commonly classified as mild intermittent, mild persistent, moderate persistent, or severe persistent. This CPG did not determine if applying a particular classification system for asthma severity led to improved outcomes. We do recognize, however, that this classification system is widely used by clinicians, researchers, and other guideline developers and provides a common reference for communication. Table B-1 provides information to assist in assignment of the severity level during the initial evaluation of a newly diagnosed patient. This table was carried forward from the 2009 VA/DoD Asthma CPG. The Algorithm within this CPG refers to Table B-1 for the initial management of newly diagnosed patients. Decision points in the algorithm are determined by the CPG's key recommendations and also by current standards of care. The system for the initial classification of asthma severity reflects a standard of care that has been carried forward from the 2009 VA/DoD Asthma CPG. Asthma severity can also be classified once a patient is stabilized based on the medication required to maintain control of symptoms.

Quality asthma care involves not only assessing initial severity but also requires regular follow-up in which control of symptoms are assessed and therapy is adjusted to maintain effective control. This CPG did not validate a particular methodology for determining level of control but recognizes that clinicians benefit from a systematic approach when assessing asthma control. Therefore, Table B-2 was carried forward from the 2009 VA/DoD Asthma CPG. The Algorithm within this CPG refers to Table B-2 for ongoing follow-up of patients and can assist providers in making determinations to adjust therapy.

C. Epidemiology and Impact in the General Population

The national public health impact of asthma is significant. Based on health statistics from the 2016 National Health Interview Survey, over 20 million adults and six million children had a diagnosis of asthma in the United States (U.S.).[2] According to the 2015 National Ambulatory Medical Care Survey, over 6% of all office-based physician visits included asthma as a diagnosis.[2] Additionally, this 2015 survey reported 1.7 million emergency department (ED) visits with asthma as the primary diagnosis. The morbidity caused by chronic asthma impacts society. Uncontrolled asthma leads to activity limitation and missed days of school and/or work. In 2007, the estimated cost of asthma from loss of productivity was 3.8 billion

dollars.[3] Beyond morbidity, asthma is still a cause of death in the U.S. In 2016, 3,518 people died from asthma.[4]

D. Asthma in the Department of Defense and the Department of Veterans Affairs Populations

Since 2004, medical standards for appointment, enlistment, or induction into the military services have listed asthma as a disqualifying condition unless exempted via medical waiver. The current DoD instruction 6130.3, last updated in 2018, states the following with respect to asthma and disqualification for service:[5]

- History of airway hyperresponsiveness including asthma, reactive airway disease, exercise-induced bronchospasm or asthmatic bronchitis, after the 13th birthday.
    - Symptoms suggestive of airway hyperresponsiveness include but are not limited to cough, wheeze, chest tightness, dyspnea or functional exercise limitations after the 13th birthday.
    - History of prescription or use of medication (including but not limited to inhaled or oral corticosteroids, leukotriene receptor antagonists, or any beta agonists) for airway hyperresponsiveness after the 13th birthday.

Additional information can be found in Appendix D.

Despite these accessioning standards, asthma remains a common pre-service condition leading to discharge from the military within the first six months of military service. Perhaps more relevant to this guideline is that military members are commonly first diagnosed with asthma as adults, after they have begun military service. The reasons for this may involve occupational exposures, including deployment-related exposures, and increased smoking rates among active duty personnel compared to civilian counterparts. Retention standards for active duty personnel diagnosed with asthma vary by military service. Generally, Service Members with well-controlled asthma may remain on active duty. Uncontrolled asthma impacts military readiness; asthma-related disability is commonly evaluated in the separation and medical retirement process. Additionally, several studies have reported higher rates of new-onset asthma in Service Members that have deployed to the Middle East during Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF).[6] This makes it likely that primary care providers in both the DoD and VA will encounter patients with a diagnosis of asthma or with symptoms suggestive of the diagnosis that will warrant evaluation and treatment. This guideline is designed to assist these primary care providers in the diagnosis and management of asthma.

III. About this Clinical Practice Guideline

This guideline represents a significant step toward improving the diagnosis and management of asthma in the VA and DoD. As with other CPGs, however, challenges remain, including evidence gaps, the need to develop effective strategies for guideline implementation, and the need to evaluate the effect of guideline adherence on clinical outcomes. This guideline is intended for VA and DoD primary care practitioners treating patients four years of age and older (see Scope of this Clinical Practice Guideline for more information).

As elaborated upon in the qualifying statement on page one, this CPG is not intended to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns evolve. This CPG is based on information available by July 24, 2018 and is intended to provide a general guide to best practices. The guideline can assist care providers, but the use of a CPG must always be considered as a recommendation for the care of an individual patient, within the context of a provider's clinical judgment and patient values and preferences.

A. Methods

The current document is an update to the 2009 VA/DoD Asthma CPG. The methodology used in developing the 2019 CPG follows the *Guideline for Guidelines*, an internal document of the VA and DoD EBPWG that was updated in January 2019.[7] The *Guideline for Guidelines* can be downloaded from http://www.healthquality.va.gov/policy/index.asp. This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts from within the VA and DoD, known as the Work Group and, ultimately, the development and submission of a new or updated Asthma CPG.

The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations and writing and publishing a guideline document to be used by providers within the VA/DoD healthcare systems as well as those within the community who treat individuals within the VA and DoD. Specifically, the Champions and Work Group members for this guideline were responsible for identifying the key questions (KQs) with the most clinical relevance, importance, and interest for the primary care management of asthma. The Champions and the Work Group also provided direction on inclusion and exclusion criteria for the evidence review and assessed the level and quality of the evidence. The amount of new scientific evidence that had accumulated since the previous version of the CPG was also taken into consideration in the identification of the KQs. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

The VA Office of Quality, Safety and Value, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified four clinical leaders, Andrew I. Philip, MD and Amir Sharafkhaneh, MD, PhD from the VA and MAJ Nikhil Huprikar, MD and MAJ Cristian S. Madar, MD, MPH from the DoD, as Champions for the 2019 CPG.

The Lewin Team, including The Lewin Group, Duty First Consulting, ECRI Institute, and Sigma Health Consulting, LLC, was contracted by the VA and DoD to support the development of this CPG and conduct the evidence review. The first conference call was held in March 2018, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality, Safety and Value and the DoD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review (SR) about the assessment and management of patients at risk for asthma. The group also

identified a list of clinical specialties and areas of expertise that are important and relevant to the management of asthma, from which Work Group members were recruited. The specialties and clinical areas of interest included: primary care, family medicine, pediatrics, pulmonology, pediatric pulmonology, critical care medicine, nursing, social work, pharmacology, and respiratory care.

The guideline development process for the 2019 CPG update consisted of the following steps:

1. Formulating and prioritizing KQs and defining critical outcomes
2. Convening patient focus groups
3. Conducting the systematic evidence review
4. Convening a face-to-face meeting with the CPG Champions and Work Group members
5. Drafting and submitting a final CPG on the management of asthma to the VA/DoD EBPWG

Appendix A provides a detailed description of each of these tasks.

a. Grading Recommendations

The Champions and Work Group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the evidence base and assign a strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[8]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.,:
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

Using these four domains, the Work Group determined the relative strength of each recommendation as "Strong" or "Weak." A "Strong" recommendation generally indicates a high confidence in the quality of the available scientific evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient or provider values and preferences, and understood influence of other implications (e.g., resource use, feasibility). If the Work Group has less confidence after the assessment across these domains and believes that additional evidence may change the recommendation, it generally assigns a "Weak" recommendation. It is important to note that the GRADE terminology used to indicate the assessment across the four domains (i.e., "Strong" versus "Weak") should not be confused with the clinical importance of the recommendation. A weak recommendation may still be important to the clinical care of a patient with asthma.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a specific topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong for (or "We recommend offering this option …")
- Weak for (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence…")
- Weak against (or "We suggest not offering this option …")
- Strong against (or "We recommend against offering this option …")

The grade of each recommendation made in the 2019 CPG can be found in the section on Recommendations. Additional information regarding the use of the GRADE system can be found in Appendix A.

b. Reconciling 2009 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current, which typically requires revisions of previous guidelines based on new evidence, or as scheduled and subject to time-based expirations.[9] For example, the U.S. Preventive Services Task Force (USPSTF) has a process for refining or otherwise updating its recommendations pertaining to preventive services.[10]

The Asthma Guideline Work Group focused largely on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Work Group considered, without complete review of the relevant evidence, the current applicability of other recommendations that were included in the 2009 VA/DoD Asthma CPG, subject to evolving practice in today's environment.

A set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE).[11,12] These categories, along with their corresponding definitions, were used to account for the various ways in which older recommendations could have been updated. In brief, the categories took into account whether or not the evidence that related to a recommendation was systematically reviewed, the degree to which a recommendation was modified, and the degree to which a recommendation is relevant in the current care environment and within the scope of the CPG. Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The categories for the recommendations included in the 2019 version of the guideline can be found in the section on Recommendations. The categories for the recommendations carried forward from the 2009 VA/DoD Asthma CPG are noted in Appendix I.

The CPG Work Group recognized the need to accommodate the transition in evidence rating systems from the 2009 VA/DoD Asthma CPG to the current CPG. In order to report the strength of all recommendations using a consistent format (i.e., the GRADE system) the CPG Work Group converted the USPSTF strengths of

the recommendation accompanying the carryover recommendations from the 2009 guideline to the GRADE system. As such, the CPG Work Group considered the strength of the evidence cited for each recommendation in the 2009 VA/DoD Asthma CPG as well as the intervention's harms and benefits, values and preferences, and other implications, where possible. The CPG Work Group referred to the available evidence as summarized in the body of the 2009 VA/DoD Asthma CPG and did not systematically re-assess the evidence. In some instances, relevant peer-reviewed literature published since the 2009 VA/DoD Asthma CPG was considered along with the original evidence base for the specific recommendation. Where such newer literature was considered when converting the strength of the recommendation from the USPSTF to the GRADE system, it is referenced in the discussion that follows the corresponding recommendation, as well as in Appendix H.

The CPG Work Group recognizes that, while there are sometimes practical reasons for incorporating findings from a previous SR, previous recommendations,[13] or recent peer-reviewed publications into an updated CPG, doing so does not involve an original, comprehensive SR and, therefore, may introduce bias.

c. Peer Review Process

The CPG was developed through an iterative process in which the Work Group produced multiple drafts of the CPG. The process for developing the initial draft is described in more detail in Drafting and Submitting the Final Clinical Practice Guideline.

Once a near-final draft of the guideline was agreed upon by the Champions and Work Group members, the draft was sent out for peer review and comment. The draft was posted on a wiki website for a period of 14 business days. The peer reviewers comprised individuals working within the VA and DoD healthcare systems as well as experts from relevant outside organizations designated by the Work Group members. Organizations designated by the Work Group to participate in the peer review and who provided feedback include the following:

- American College of Physicians

The VA and DoD Leadership reached out to both the internal and external peer reviewers to solicit their feedback on the CPG. Reviewers were provided a hyperlink to the wiki website where the draft CPG was posted. All feedback from the peer reviewers was discussed and considered by the Work Group. Modifications made throughout the CPG development process were made in accordance with the evidence.

B. Summary of Patient Focus Group Methods and Findings

When forming guideline recommendations, consideration should be given to the values and preferences of those most affected by the recommendations: patients and their caregivers. Patients bring perspectives, values, and preferences into their healthcare experience that can vary from those of clinicians. These differences can affect decision making in various situations, and should thus be highlighted and made explicit due to their potential to influence a recommendation's implementation.[14,15] Focus groups can be used as an efficient method to explore ideas and perspectives of a group of individuals and collect qualitative data on a thoughtfully predetermined set of questions.

Therefore, as part of the effort to update this CPG, VA and DoD Leadership, along with the Asthma CPG Work Group, held a patient focus group on June 22, 2018 at the Womack Army Medical Center in Fort Bragg, NC. The aim of the focus group was to further understand and incorporate the perspective of patients who are living with asthma and who are covered and/or receiving their care through the VA and/or DoD healthcare systems, as these patients are most affected by the recommendations put forth in the CPG. The focus group delved into the patients' perspectives on a set of topics related to their asthma management, including their priorities, challenges they have experienced, and the information they received regarding their care, as well as the impacts of their care on their lives.

It is important to note the focus group comprised a convenience sample of Veterans, Service Members, and their dependents. Perspectives of children with asthma were provided through parent participation in the focus group. The Work Group recognizes the lack of generalizability and other limitations inherent in the small sample size. Less than 10 people in total were included in the focus group to be consistent with the requirements of the federal Paperwork Reduction Act, 1980. The Work Group acknowledges that the sample included in the focus group is not representative of all patients within the VA and DoD healthcare systems. Further, time limitations for the focus group prevented exhaustive exploration of all topics related to asthma management in VA and DoD and the patients' broader experiences with their care. Thus, the Work Group made decisions regarding the priority of topics to discuss at the focus group. These limitations, as well as others, were considered during guideline development as the information collected from the discussion was being used. Recruitment for participation in the focus group was managed by the Champions and VA and DoD Leadership, with assistance from coordinators at the facility at which the focus group took place.

The following concepts are ideas and suggestions about aspects of care that are important to patients who are living with asthma and emerged as recurring themes during the discussions (Table 1). These concepts were important parts of the participants' care and added to the Work Group's understanding of patient values and perspectives. Additional details regarding the patient focus group methods and findings can be found in Appendix G.

Table 1. Asthma CPG Focus Group Concepts

Asthma CPG Patient Focus Group Concepts	
A.	Ensure that patient history and symptoms are taken into account when assessing pulmonary issues. Once a patient is diagnosed with asthma, help the patient understand his or her triggers.
B.	For every patient, establish and maintain an asthma action plan in conjunction with the patient. Leverage multiple types of clinical expertise (e.g., pulmonologists, clinical pharmacists) when educating the patient on their condition, their asthma action plan, and treatment adherence.
C.	Work with the patient to identify an effective treatment for asthma, considering co-occurring conditions. Be mindful that different patients may respond to medications differently.
D.	Be mindful that, in some cases, a diagnosis of asthma or the inability to achieve control of asthma symptoms may affect an active duty Service Member differently than a civilian.
E.	Ensure that various types of clinicians are engaged as appropriate (e.g., specialists provide pulmonary expertise as needed based on patient condition, clinical pharmacists provide education). Leverage telehealth, mobile applications, and other information technology to the extent that it is available and helpful for the patient.
F.	Acknowledge the seriousness of asthma and its impact on the life of the patient. Discuss the patient's goals for asthma treatment and help each patient work toward those goals.

C. Conflicts of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest (COI) in the past 24 months. Verbal affirmations of no COI were used as necessary during meetings throughout the guideline development process. The project team was also subject to random web-based surveillance (e.g., Centers for Medicare and Medicaid Services open payments, ProPublica).

If a project team member reported a COI (actual or potential), then it was reported to the Office of Evidence Based Practice. It was also discussed with the Asthma CPG Champions in tandem with their review of the evidence and development of recommendations. The Office of Evidence Based Practice and the Asthma CPG Champions determined whether or not action, such as restricting participation and/or voting on sections related to the conflict or removal from the Work Group, was necessary. If it was deemed necessary, action to mitigate the COI was taken by the Champions and Office of Evidence Based Practice, based on the level and extent of involvement. No conflicts of interest were identified for the Asthma CPG Work Group members or Champions. Disclosure forms are on file with the VA Evidence Based Practice Program office and available upon request.

D. Scope of this Clinical Practice Guideline

This guideline is designed to assist primary care providers (including general internal medicine and family medicine physicians, pediatricians, physician assistants, nurse practitioners, nurses, respiratory therapists, pharmacists, asthma educators, social workers, case managers, and others) in managing or co-managing patients four years of age and older undergoing treatment for asthma. Moreover, the patient population of interest for this CPG consists of patients who are living with asthma and are eligible for care in the VA and DoD healthcare delivery systems who are being treated in an ambulatory or clinical setting. It includes Veterans as well as deployed and non-deployed active duty Service, Guard, and Reserve Members and their dependents. Patients receiving care in the urgent or emergency care setting or in the hospital, pregnant women, and children younger than four years are not included in the scope of this CPG.

Regardless of setting, any patient in the healthcare system should ideally have access to the interventions that are recommended in this guideline after taking into consideration the patient's specific circumstances. Guideline recommendations are intended to be patient centered. Thus, treatment and care should take into account a patient's needs and preferences. Good communication between healthcare professionals and the patient is essential and should be supported by evidence-based information tailored to the patient's needs. Use of an empathetic and non-judgmental approach facilitates discussions sensitive to gender, culture, ethnic, and other differences. The information that patients and caregivers are given about treatment and care should be culturally appropriate and available to people with limited literacy skills. It should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family involvement should be considered, if appropriate.

E. Highlighted Features of this Clinical Practice Guideline

The 2019 edition of the VA/DoD Asthma CPG is the second update to the original CPG. It provides practice recommendations for asthma as well as guidance for specialty referral. A particular strength of this CPG is the multidisciplinary stakeholder involvement from its inception, ensuring representation from the broad

spectrum of clinicians engaged in the treatment and management of asthma with and without co-occurring conditions.

The framework for recommendations in this CPG considered factors beyond the strength of the evidence, including balancing desired outcomes with potential harms of the intervention, equity of resource availability, the potential for variation in patient values and preferences, and other considerations (e.g., resource use, subgroup considerations) as appropriate. Applicability of the evidence to VA/DoD populations was also taken into consideration. An algorithm accompanies the guideline to provide an overview of the recommendations in the context of the flow of patient care and to assist with training providers (see Algorithm). The algorithm may be used to help facilitate translation of guideline recommendations into effective practice.

F. Patient-centered Care

VA/DoD CPGs encourage clinicians to use patient- (and family-) centered care (PCC) approach that is individualized based on patient needs, characteristics, and preferences. Regardless of setting, all patients in the healthcare system should be able to access evidence-based care appropriate to that patient. When properly executed, PCC may decrease patient anxiety, increase trust in clinicians, and improve treatment adherence.[16-18] Improved patient-clinician communication and a PCC approach conveys openness and supports disclosure of current and future concerns.

As part of the PCC approach, clinicians should engage patients in SDM to review the outcomes of previous healthcare experiences with the patients who are living with asthma. They should ask each patient about any concerns he or she has or barriers to high quality care he or she might experience. Lastly, they should educate the patient on the actions that need to be taken and any decisions that need to be made and should involve the individual in decision making regarding management of asthma.

G. Shared Decision Making

Throughout this VA/DoD CPG, the authors encourage clinicians to focus on SDM. The SDM model was introduced in *Crossing the Quality Chasm,* an Institute of Medicine (IOM) (now called the National Academy of Medicine [NAM]) report, in 2001.[19] It is readily apparent that patients, together with their clinicians, make decisions regarding their plan of care and management options. Clinicians must be adept at presenting information to their patients regarding individual treatments, expected outcomes, and levels and/or locations of care. Clinicians are encouraged to use SDM to individualize treatment goals and plans based on patient capabilities, needs, goals and preferences.

H. Co-occurring Conditions

Co-occurring medical and mental health conditions are important to recognize because they can modify the management of asthma, patient or provider treatment priorities, and clinical decisions. Further, the appropriate providers need to be involved in the management of the patient's asthma and ongoing healthcare based on the co-occurring medical and mental health conditions of each patient. Providers should expect that many Veterans, Service Members, and their families will have one or more co-occurring health conditions. Because of the nature of the management of asthma, which sometimes takes place in parallel with ongoing care for co-occurring conditions, it is generally best to manage asthma in collaboration with the care for other health conditions that are being treated in primary or specialty care.

I. Implementation

This CPG and algorithm are designed to be adapted by individual healthcare providers with consideration of local needs and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the course of an episode of care.

Although this CPG represents the recommended practice on the date of its publication, medical practice is evolving and this evolution requires continuous updating based on published information. New technology and more research will improve patient care in the future. The CPG can assist in identifying priority areas for research and informing optimal allocation of resources. Future studies examining the results of CPG implementation may lead to the development of new evidence particularly relevant to clinical practice.

IV. Guideline Work Group

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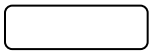
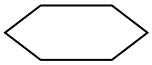
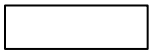
V. Algorithm

This CPG follows an algorithm which is designed to facilitate understanding of the clinical pathway and decision-making process used in the management of asthma. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision making and has the potential to change patterns of resource use. Although the Work Group recognizes that not all clinical practices are linear, the simplified linear approach depicted through the algorithm and its format allows the provider to assess the critical information needed at the major decision points in the clinical process. It includes:

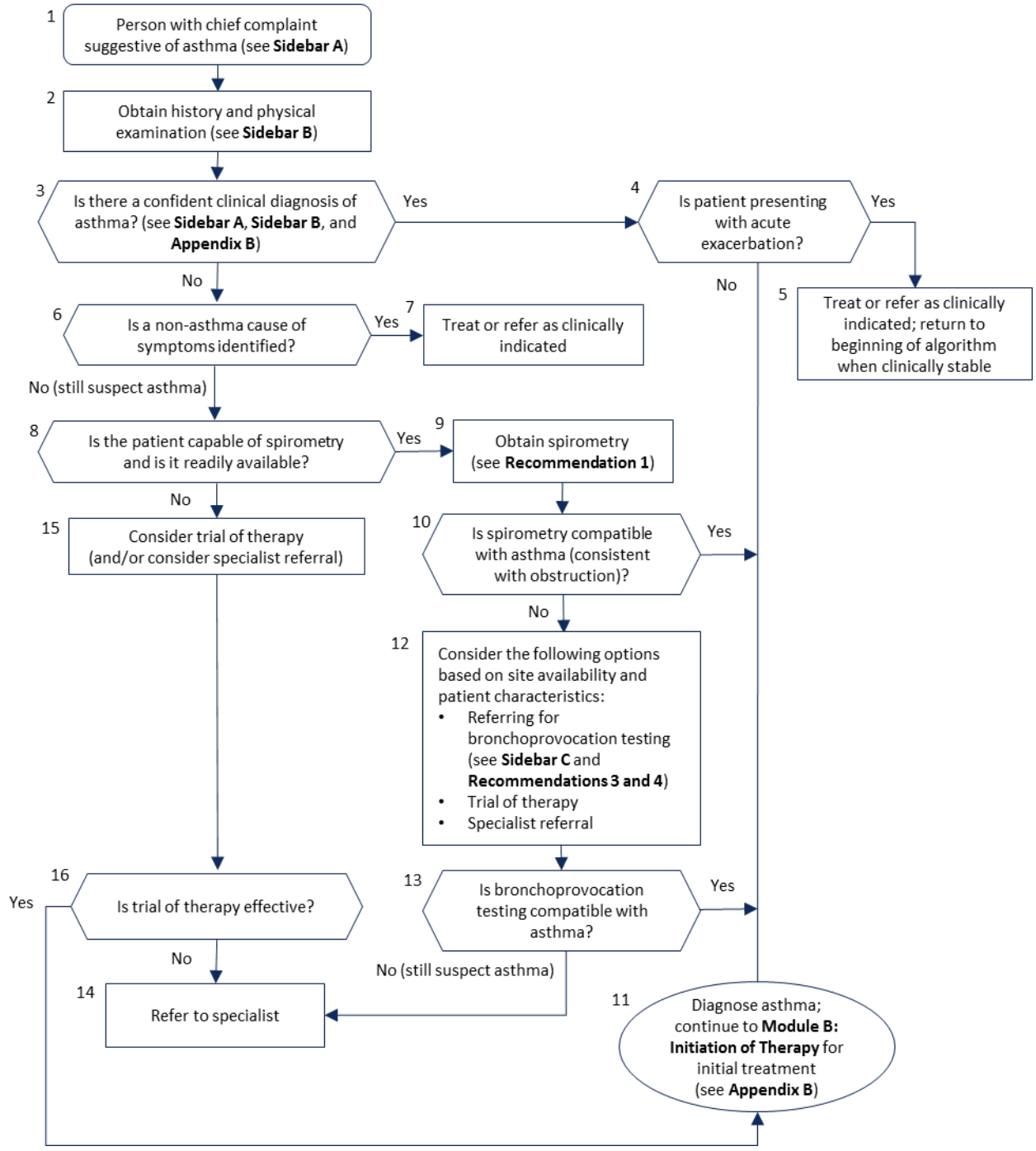
- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

For each guideline, there is corresponding clinical algorithm that is depicted by a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[20]

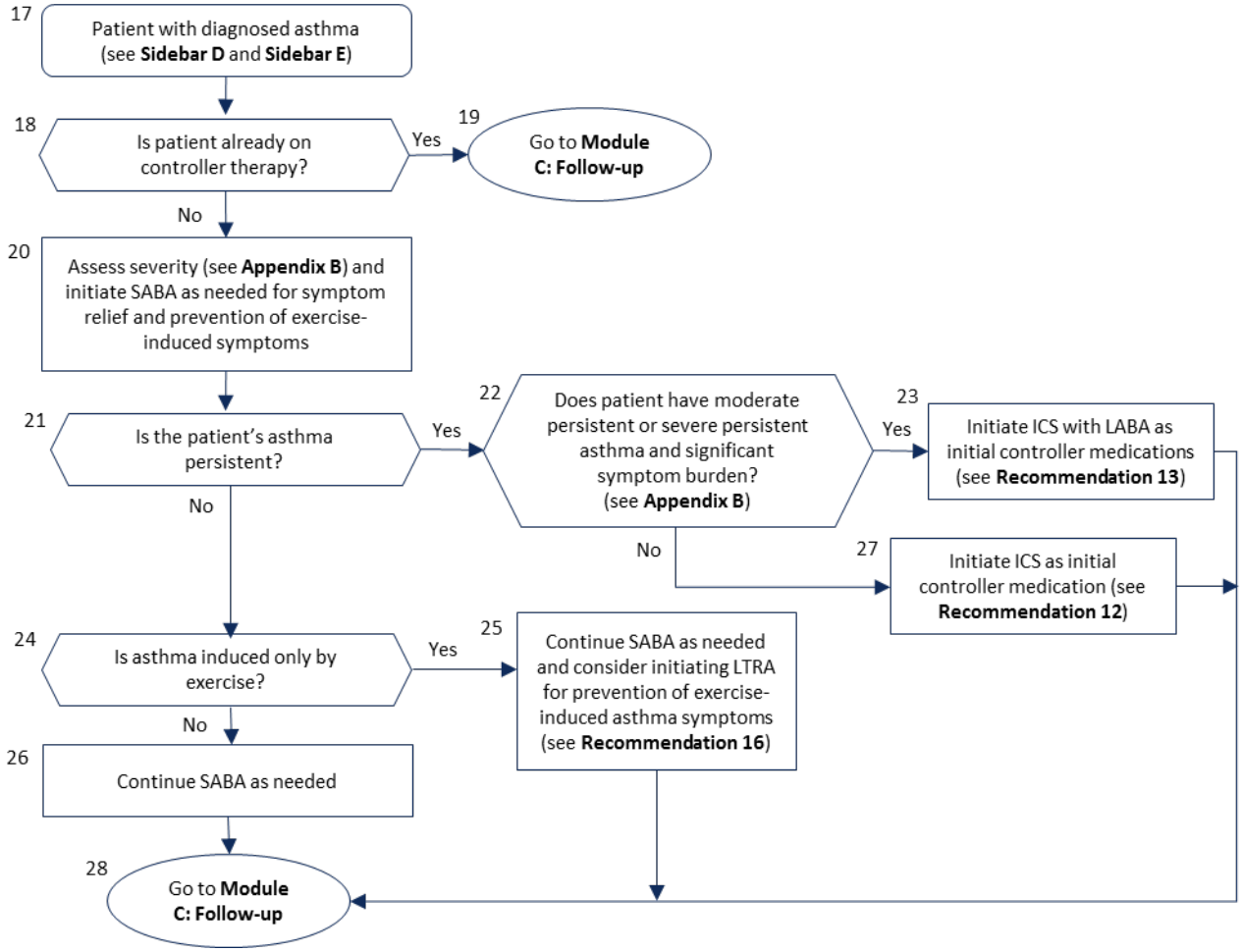
Shape	Description
	Rounded rectangles represent a clinical state or condition
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No
	Rectangles represent an action in the process of care
	Ovals represent a link to another section within the guideline.

Appendix L contains alternative text descriptions of Module A, Module B, and Module C.

A. Module A: Assessment and Diagnosis of Asthma

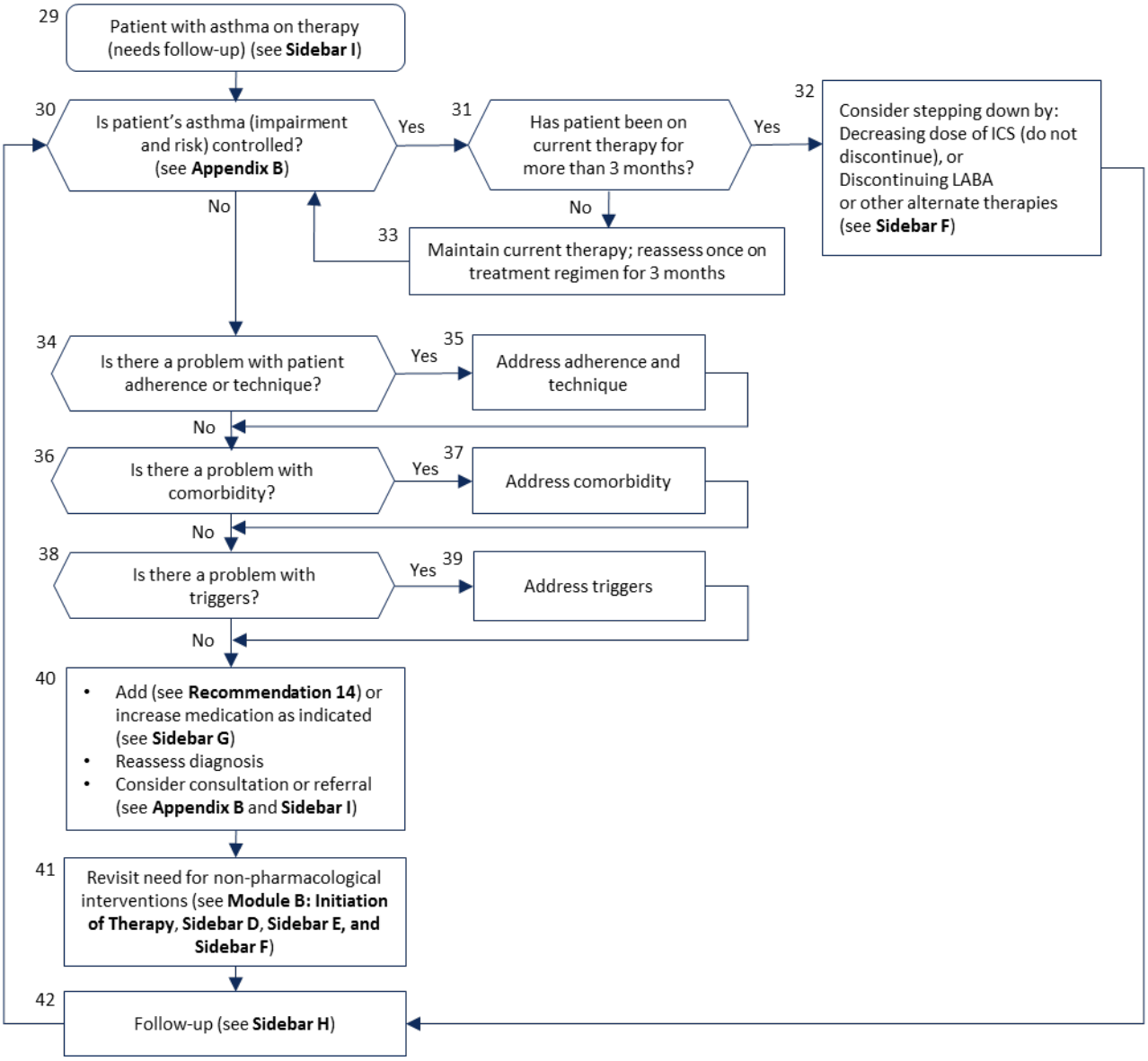


B. Module B: Initiation of Therapy



Abbreviations: ICS: inhaled corticosteroid; LABA: long-acting beta agonist; LTRA: leukotriene receptor antagonist; SABA: short-acting beta agonist

C. Module C: Follow-up



Abbreviations: ICS: inhaled corticosteroid; LABA: long-acting beta agonist

Sidebar A: Asthma Symptoms

Adult: More than 6 weeks of symptoms or recurrent episodes of cough, wheeze, shortness of breath
Child: Cough or wheeze for more than 2 weeks or recurrent episodes of wheeze/significant cough

Sidebar B: Assessment

- Symptoms (see **Sidebar A**)
- Pattern (exercise, nocturnal symptoms)
- Precipitating triggers
- Aggravating factors/risk factors (see **Recommendations 6 and 7**)
  - Adults and children: Overweight/obesity, atopy, secondhand smoke exposure in children, history of lower respiratory infection
  - Adults: Depression, current smokers, OIF/OEF combat deployment
- Comorbidities
- Response to treatment
- If not previously done, consider X-ray if other diagnoses are being considered

Abbreviations: OIF/OEF: Operation Iraqi Freedom/Operation Enduing Freedom

Sidebar C: Considerations for Bronchoprovocation Testing

- Bronchoprovocation should be done using methacholine challenge
- In some situations in the DoD, patients will need to have bronchoprovocation testing
- Bronchoprovocation should not be ordered for children; refer to specialist only
- See **Recommendations 3 and 4**

Abbreviations: DoD: Department of Defense

Sidebar D: Asthma Education

Patients and caregivers should be informed of the diagnosis of asthma. Their understanding should be assessed, and they should be given the opportunity to ask questions in order to take an active role in their medical care. More robust follow-up must be provided for those with asthma in order to provide "cornerstone" treatment which may consist of the following (see **Recommendations 9 and 10**):

- Symptoms (see **Sidebar A**)
- Pattern (exercise, nocturnal symptoms)
- Precipitating triggers
- Aggravating factors/risk factors (see **Recommendations 6 and 7**)
- Nature of asthma
- Goals of treatment
- Medication use (e.g., what it does, how to use it, potential side effects)
- How to recognize loss of asthma control and what steps to take to regain control of symptoms
- When and how to seek emergency care for asthma exacerbations
- Consider a personalized written asthma action plan (see **Recommendation 8**)
- Consider care management team approach (may consist of dietary changes, emergent responses, updated medications, monthly follow-up for those with more severe symptoms, etc.)

Sidebar E: Care Management

Multidisciplinary care management:

- Multidisciplinary care management (see **Recommendation 17**)
- CBT (see **Recommendation 19**)
- Triggers for worsening control should be identified and if possible steps taken to reduce exposure
- Comorbidities
- Medical comorbidities should be identified and addressed

Lifestyle changes:

- Smoking cessation
- Regular exercise (see **Recommendation 18**)
- Weight management
- Avoidance of triggers

Psychosocial considerations and impact on asthma:

- Patient ability to absorb financial burden of medication cost
- Time away from work, home responsibilities for follow-up (e.g., office visits, testing)

Abbreviations: CBT: cognitive behavioral therapy

Sidebar F: Considerations for Stepping Down Therapy

- Do not step down in patients that cannot be closely monitored (e.g., planned travel) or at risk of severe exacerbations (e.g., pregnancy, acute illness)
- Step down (not discontinue) ICS dose
- Discontinue LABA
- In low risk patients who are still well-controlled on low-dose ICS for at least three months, consider discontinuing ICS using caution
- Refer to **Appendix F, Tables F-1 and F-2** for discussion of specific medications

Abbreviations: ICS: inhaled corticosteroid; LABA: long-acting beta agonist

Sidebar G: Considerations for Stepping Up Therapy

Preferred therapy:

- Initial therapy:
  - ICS (see **Recommendation 12**)
  - Combination of ICS and LABA as initial controller treatment for patients with moderate-to-severe persistent asthma and significant symptom burden (see **Recommendation 13**)
- Step-up therapy:
  - If on low-medium ICS mono-therapy, add LABA (see **Recommendation 14**)
  - If considering 3-drug therapy or high-dose ICS, specialty referral is recommended (see **Sidebar I**)

In the case of contraindication/intolerance to preferred treatment, refer to **Appendix F, Table F-1** for options.
Refer to **Appendix F, Table F-2** for relative ICS dose ranges.

Abbreviations: ICS: inhaled corticosteroid; LABA: long-acting beta agonist

Sidebar H: Considerations for Short Follow-up

- Recent hospitalization
- ED visit
- Step medication change
- Recent exacerbation
- Increasing use of rescue inhalers
- Inability to use inhaler correctly

Abbreviations: ED: emergency department

Sidebar I: Considerations for Specialty Referral

- Desensitization
  - In selected children
  - Atopy
  - Anaphylaxis
- Patients who may benefit from biological agents
- Consider adding a third drug
- Life-threatening exacerbation/intubation
- Multiple hospitalizations

VI. Recommendations

Topic	Sub-topic	#	Recommendation[a]	Strength[b]	Category[c]
Diagnosis and Assessment		1.	We suggest spirometry if there is a need to confirm a clinical diagnosis of asthma.	Weak for	Reviewed, New-replaced
		2.	In primary care, we suggest against whole-body plethysmography as part of the diagnostic evaluation of asthma.	Weak against	Reviewed, New-replaced
		3.	There is insufficient evidence to recommend for or against the routine use of bronchodilator response testing to exclude the initial diagnosis of asthma in the absence of airway obstruction.	Neither for nor against	Reviewed, New-replaced
		4.	If bronchoprovocation testing is considered, we suggest methacholine challenge testing.	Weak for	Reviewed, New-replaced
		5.	We recommend against offering computed tomography scan to diagnose asthma in patients with persistent airflow obstruction post-bronchodilator.	Strong against	Reviewed, New-added
		6.	In adults and children with asthma, we suggest identifying known risk factors of asthma-related outcomes including overweight/obesity, atopy, secondhand smoke exposure in children, and history of lower respiratory infection.	Weak for	Reviewed, New-replaced
		7.	In adults with asthma, we suggest identifying known risk factors of asthma-related outcomes including depression, current smokers, and Operation Iraqi Freedom/Operation Enduring Freedom combat deployment.	Weak for	Reviewed, New-replaced
Treatment and Management	*Asthma Education*	8.	We suggest offering a written asthma action plan to improve asthma-related quality of life.	Weak for	Reviewed, New-replaced
		9.	We suggest offering asthma education.	Weak for	Reviewed, New-replaced
		10.	There is insufficient evidence to recommend one particular asthma education program or education component(s) over others.	Neither for nor against	Reviewed, New-replaced
		11.	There is insufficient evidence to recommend for or against patient-oriented technologies (e.g., mobile apps, web based, or telemedicine) as a means to reduce the number or severity of asthma-related exacerbations.	Neither for nor against	Reviewed, New-replaced
	Pharmacotherapy	12.	For patients with persistent asthma, we recommend inhaled corticosteroids as initial controller medication.	Strong for	Reviewed, Amended
		13.	Among patients with moderate-to-severe persistent asthma and significant symptom burden, we suggest offering a combination of inhaled corticosteroid and long-acting beta agonist as initial controller treatment.	Weak for	Reviewed, New-replaced
		14.	For patients with asthma not controlled by inhaled corticosteroids alone, we suggest adding long-acting beta agonists as a step-up treatment over increasing inhaled corticosteroids alone or adding long-acting muscarinic antagonists or leukotriene receptor antagonists.	Weak for	Reviewed, New-replaced

Topic	Sub-topic	#	Recommendation[a]	Strength[b]	Category[c]
Treatment and Management (cont.)	*Pharmacotherapy (cont.)*	15.	In patients with controlled asthma on a stable medication regimen, we suggest either stepping down (not discontinuing) inhaled corticosteroids dose or discontinuing long-acting beta agonists.	Weak for	Reviewed, New-replaced
		16.	We suggest short-acting beta agonists or leukotriene receptor antagonists for prevention of exercise-induced bronchospasm.	Weak for	Not reviewed, Amended
	Non-pharmacotherapy	17.	We suggest a multidisciplinary treatment approach to improve asthma-related quality of life, asthma control, and treatment adherence.	Weak for	Reviewed, New-replaced
		18.	We suggest patients with asthma participate in regular exercise to improve quality of life and asthma control.	Weak for	Reviewed, Amended
		19.	We suggest offering cognitive behavioral therapy as a means of improving asthma-related quality of life and self-reported asthma control for adult patients with persistent asthma.	Weak for	Reviewed, New-added
	Monitoring and Follow-up	20.	We suggest against utilizing spirometry for routine monitoring of patients with stable asthma.	Weak against	Reviewed, New-replaced
		21.	There is insufficient evidence to recommend for or against routine use of fractional exhaled nitric oxide in monitoring patients in primary care settings to improve asthma-related clinical outcomes.	Neither for nor against	Reviewed, New-replaced
		22.	We suggest leveraging electronic health record capabilities such as trackers and reminders in the care of patients with asthma.	Weak for	Reviewed, New-added

[a] If not otherwise specified, the recommendation applies to the target population for this CPG, which includes adults and children four years or older. For more information regarding the scope of the CPG, please refer to Scope of this Clinical Practice Guideline.

[b] For additional information, please refer to Grading Recommendations.

[c] For additional information, please refer to Recommendation Categorization and Appendix I.

A. Diagnosis and Assessment

Recommendation

1. We suggest spirometry if there is a need to confirm a clinical diagnosis of asthma.
   (Weak for | Reviewed, New-replaced)

Discussion

The diagnosis of asthma is a clinical diagnosis based on history, physical examination, and findings suggestive of airway hyperactivity. While objective measurements of airway reactivity, specifically reversible obstruction post-bronchodilator, may be helpful in the diagnosis of asthma, the lack of objective reversibility does not disqualify the diagnosis. We suggest that spirometry be used when a confirmatory test is needed to support a clinical diagnosis of asthma. Although often considered a component of the diagnostic work-up for asthma, documentation of airflow obstruction may not be required in cases of clinical asthma that adequately respond to therapy. Current data is limited with very low quality evidence regarding the overall utility of spirometry. In a pediatric study conducted by Murray et al. (2017), a validated clinical questionnaire was compared to spirometry and demonstrated high specificity but poor sensitivity.[21] Furthermore, an adult study by Schneider, et al. (2009) showed a poor sensitivity (29%) for spirometry in primary care to identify patients with obstructive airway disease.[22] As the specificity of the test was relatively high (90%), the authors concluded that spirometry in primary care might have a role to confirm a clinical diagnosis of asthma, but is not useful to rule out asthma.

In specific populations with occupational hazards, such as active duty military populations, specific confirmatory testing and guidance may be dictated by DoD standards of medical fitness for duty. Alternative diagnoses may have significant impact on active duty Service Members, should be included in the diagnostic evaluation, and may require subspecialty evaluation. DoD service-specific regulations related to asthma can be found in Appendix D.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[21,22] The Work Group's confidence in the quality of the evidence is very low. The body of evidence had some limitations including use of an indirect asthma diagnosis through questionnaire. Other considerations regarding this recommendation included the benefits, such as improved diagnosis, outweighing the potential harm related to lack of sensitivity. Patients are expected to have similar values and preferences regarding this issue, as most will agree with the test for improved diagnosis. Thus, the Work Group decided upon a "Weak for" recommendation.

Recommendation

2. In primary care, we suggest against whole-body plethysmography as part of the diagnostic evaluation of asthma.
   (Weak against |Reviewed, New-replaced)

Discussion

Lung function measurements have traditionally been a cornerstone of the work-up for respiratory disorders. Spirometry is often the initial step in assessing lung function for suspected asthma, and more sophisticated measurement of lung volumes by body plethysmography is needed only in more complex

cases. A review of the literature identified one study with a relatively large sample size examining use of whole-body plethysmography in children.[23] The assessment of specific airway resistance using whole-body plethysmography provided modest ability to diagnose asthma when compared to clinical diagnosis and spirometry. The study was of low quality.

For all these tests, benefits and risks were determined to be balanced when the test is used in the primary care setting. There was some variation in the acceptability of these tests among users. The most important drawback is that these tests may not be helpful for primary care providers in diagnosing asthma, as they may not be easy to perform or interpret and may not be available in all practice settings.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[23] The Work Group determined that the confidence in the quality of the evidence was low. The body of the evidence had limitations including small sample sizes and limited reporting of details such as demographics and inclusion/exclusion criteria.[23] Although there is little evidence of benefit, there is also little risk of harm. Further, patient preferences regarding these tests are somewhat varied. Thus, the Work Group decided upon a "Weak against" recommendation. In summary, the above tests may not provide clarity in diagnosing asthma in a primary care setting. However, for this guideline, the evidence reviewed related to the above tests was limited to the examination of the benefit for diagnosing asthma in the primary care setting. Therefore, the Work Group did not review the evidence on addressing the use of these tests in other settings and for other purposes. The use of the above tests may help in the differential diagnosis of asthma in more specialized practice settings (e.g., a pulmonary practice).

Recommendation

3. There is insufficient evidence to recommend for or against the routine use of bronchodilator response testing to exclude the initial diagnosis of asthma in the absence of airway obstruction. **(Neither for nor against | Reviewed, New-replaced)**

Discussion

As a part of the guideline update, the Work Group reviewed evidence related to the most useful tests for a diagnosis of asthma and, more specifically, bronchodilator response testing. In the previous version of the guideline (2009 VA/DoD Asthma CPG), it was recommended that spirometry should be repeated post-bronchodilator to establish presence and degree of reversibility if there is airway obstruction present or if there is a suspicion of asthma. Although the systematic evidence review for this guideline update searched for studies conducted in the adult population looking at the use of bronchodilator response testing, no such studies met inclusion criteria. After reviewing evidence from Murray et al. (2017) [21] and Tse et al. (2013) [24] (both of which studied bronchodilator response testing in children), the Work Group determined that, due to the poor diagnostic performance of bronchodilator response testing (sensitivity, specificity, negative predictive value [NPV], positive predictive value [PPV]), we could neither recommend for nor against the use of this test as a diagnostic tool to exclude or confirm the diagnosis of asthma. Bronchodilator testing may be appropriate in specialized care settings; therefore, the Work Group decided to not recommendation against this test.

Upon review of the evidence, bronchodilator response testing showed unreliable diagnostic performance (sensitivity: 9-77%; specificity: 45-95%; NPV: 85-91%; PPV: 21-32%).[21] We determined that the benefits

and harm/burden of bronchodilator response testing are balanced. The confidence in the quality of evidence from the available studies reviewed was very low.

This is a *Reviewed, New-Replaced* recommendation. Due to the shortcomings of current available evidence evaluating bronchodilator response testing along with its poor diagnostic performance,[21,24] the Work Group determined that there is insufficient evidence to support or refute the use of this test alone as a diagnostic test in the diagnosis of asthma. While reversibility with bronchodilator use has long been accepted as objective data to confirm the diagnosis of asthma and reversible obstruction, failure to reverse or improve obstruction with bronchodilator testing does not exclude the diagnosis of asthma. Further studies on the use of bronchodilator response testing are warranted and needed.

Recommendation

4. If bronchoprovocation testing is considered, we suggest methacholine challenge testing. **(Weak for | Reviewed, New-replaced)**

Discussion

The Work Group did not develop a recommendation specifically addressing the usefulness of bronchoprovocation testing. However, if bronchoprovocation testing is considered, the Work Group suggests methacholine challenge testing. The Work Group reviewed five individual studies,[25-29] with 1,171 total patients, that reported on the performance of methacholine challenge testing for diagnosing asthma. The participants included both children and adults, and all five studies utilized some form of clinical diagnosis as a component of the reference test. The outcomes analyzed were sensitivity, specificity, NPV, and PPV. The studies reported a mean sensitivity of 76.2%, specificity of 76.2%, NPV of 81.1%, and PPV of 77%.

The Work Group also considered an analysis of potential benefits and harms related to methacholine challenge testing. Exposure to methacholine does incur some risk, as there is a possibility of inducing asthma exacerbation during the testing process and patients may have widely varying tolerance for the risk associated with this test. Additionally, methacholine challenge testing is time and resource intensive. While methacholine challenge testing will typically be available in most hospitals, it is unlikely to be available in smaller ambulatory clinics. While bronchoprovocation testing is not mandatory in the standard diagnostic workup for asthma, it may be useful for the clarification of the diagnosis of asthma in select cases. In this setting, we suggest methacholine challenge testing over other forms of bronchoprovocation. Depending upon the patient characteristics, the clinician's experience, and the clinical resourcing of the individual facility, it may be appropriate for methacholine challenge testing to be ordered by the specialist or in conjunction with a specialty referral.

Additionally, the Work Group reviewed the evidence related to effectiveness of eucapnic voluntary hyperpnea testing compared to exercise challenge testing in the SR by Dryden et al. (2010),[30] which found that the mean sensitivity and specificity of eucapnic voluntary hyperpnea testing did not approach the levels needed to make a recommendation for this testing. The evidence review conducted as part of this guideline update did not identify evidence related to exercise challenge testing except as a comparator to other testing modalities.

As this is a *Reviewed, New-Replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[25-30] The Work Group determined that the confidence in the quality of evidence in support of methacholine challenge testing for diagnosis of asthma was low. The benefits and harms related to methacholine challenge testing were balanced. Although there are some potential harms, it can be beneficial in the diagnosis for some patients and is preferable to other bronchoprovocation tests. Thus, the Work Group decided upon a "Weak For" recommendation.

Recommendation

5. We recommend against offering computed tomography scan to diagnose asthma in patients with persistent airflow obstruction post-bronchodilator.
   (Strong against | Reviewed, New-added)

Discussion

Zhang et al. (2014) conducted a prospective cohort study investigating the use of high-resolution computed tomography (CT) to evaluate various measures of airway remodeling in adult patients with asthma.[31] The study found a statistically significant difference in bronchial wall thickness between asthma and control groups in only one of five anatomic levels. No differences were seen between the study and control group for any other measures. The strength of evidence of this study was determined to be very low due to serious limitations in study quality, indirectness, and imprecision.

As this is a *Reviewed, New added* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[31] The Work Group determined the confidence in the quality of evidence related to this recommendation was very low in support of CT in diagnosing asthma. Studies have found increased cancer risks related to radiation exposure, particularly in the pediatric population.[32,33] Radiation exposure related to imaging studies is a concern often raised by adult patients. The International Commission on Radiologic Protection estimates that 3–6 radiation-induced cancers will occur over a 15–20 year period per 100,000 persons screened.[34] The harms of using CT scanning to diagnose asthma greatly outweigh any potential benefit for its use. Thus, the Work Group decided upon a "Strong Against" recommendation. In addition, access to CT scanning and acceptability of CT scanning may be highly variable for patients due to geographic and cost issues. CT has been used to evaluate other post-deployment dyspnea, but is not needed to confirm asthma.

Recommendation

6. In adults and children with asthma, we suggest identifying known risk factors of asthma-related outcomes including overweight/obesity, atopy, secondhand smoke exposure in children, and history of lower respiratory infection.
   (Weak for | Reviewed, New-replaced)
7. In adults with asthma, we suggest identifying known risk factors of asthma-related outcomes including depression, current smokers, and Operation Iraqi Freedom/Operation Enduring Freedom combat deployment.
   (Weak for | Reviewed, New-replaced)

Discussion

As these are *Reviewed, New-Replaced* recommendations, the Work Group systematically reviewed evidence related to risk factors that predict onset and exacerbations of asthma in the evidence review conducted as part of this guideline update.[6,35-46] The evidence for each identified risk factor is discussed as follows:

OIF/OEF Combat Deployment

Combat deployment is a risk factor unique to Service Members and Veterans. Rivera et al. (2018) found a statistically significant association between OIF/OEF combat deployment and incidence of new-onset asthma in adults.[6] The longitudinal cohort study involved 75,770 military participants over 12 years. The primary outcome of interest in the systematic evidence review was self-reported physician-diagnosed new-onset asthma at follow-up. The Work Group found that burn-pit exposure was associated with no greater increase in the risk for development of asthma than non-burn-pit deployment.[6]

The Work Group also considered the "Defense Health Board: Deployment Pulmonary Health" report (2015).[47] This report cites a fairly heterogeneous body of references, most of which did not meet criteria for the evidence review of this CPG (see Appendix A for more information on the methodology of the SR). However, the Work Group acknowledges that there has been significant attention given to association between exposure to potential inhalational hazards during deployment and possible adverse pulmonary health outcomes, and that the Defense Health Board seeks to further develop recommendations for post-deployment screening and surveillance for pulmonary disease. Additional research is ongoing, which may modify our understanding of a possible association between OIE/OEF combat deployment and asthma. Clear data on the association between other deployments and asthma were not identified and reviewed as part of the systematic evidence review carried out as part of this guideline update.

Obesity

The Work Group found evidence that overweight/obesity is a risk factor for asthma-related outcomes. Ahmadizar et al. (2016), an SR of five studies, found that overweight/obesity was associated with an increased risk of asthma exacerbation in children.[35] An SR of six cohort studies by Egan et al. (2013) found that overweight and obesity were associated with an increased risk of new-onset asthma in children (relative risk [RR]= 1.35 for overweight, RR= 1.5 for obesity).[36] Severe obesity (body mass index [BMI]>50) in adults was found to be significantly associated with poorly controlled asthma in a retrospective cohort study of 2.8 million participants over 4.5 years.[37] Additionally, Schatz et al. (2015) found a statistically significant association between obesity and short-acting beta agonist use, as well as ED visits and hospitalizations for asthma in adults.[38] A retrospective cohort study of 72,086 patients by Luthe et al. (2018) found obesity to be associated with longer length of stay for adults with asthma-related hospitalizations, as well as increased risk of need for mechanical ventilation (odds ratio [OR]= 1.77).[48] The Work Group determined that the overall strength of evidence for overweight/obesity as a risk factor for asthma-related outcomes was very low.

Atopy

The Work Group reviewed the evidence from two retrospective cohort studies conducted in adults,[39,40] as well as two SRs of studies conducted in children.[41,42] The overall strength of evidence was very low. The studies showed that adults with a history of atopy and allergic rhinitis had a higher risk of new-onset

asthma. The evidence also demonstrated a higher risk of hospitalization and hospital readmission in children with asthma with allergic diseases.

Secondhand Smoke Exposure in Children

Three SRs examined an evidence base of over 200,000 patients.[41,43,44] The evidence demonstrated that secondhand smoke exposure in children was associated with a higher risk of severe asthma exacerbation, as indicated by hospital admission, ED or urgent care visit (strength of evidence [SOE]: very low). Additionally, children exposed to secondhand smoke were at increased risk for having lower forced expiratory volume/forced vital capacity (FEV1/FVC) ratio (SOE: moderate) and new-onset asthma (SOE: low).

Although secondhand smoke can pose risks in adults, the evidence review did not identify studies that met inclusion criteria that looked at the effect of secondhand smoke in adults.

Lower Respiratory Tract Infection

A prospective cohort study of 5,197 patients found that children with a history of early-life lower respiratory tract infection were at a higher risk of developing new-onset asthma by age 10.[45] A retrospective cohort study of 1,554 adults found that bronchitis and sinusitis were significantly associated with new-onset asthma, while pneumonia was not (SOE: Low).[39]

Depression

Zhang et al. (2016) found that adults with both depression and combined psychologic dysfunction (PD) had an increased risk of asthma exacerbation.[46] There was also an increased risk of unscheduled medical visits, ED visits, and hospitalizations for patients with depression and PD (SOE: low).

Current Smoking

In a retrospective cohort study of 1,554 patients, Jamrozik et al. (2009) found a statistically significant association between current smoking and risk of new-onset asthma in adults (OR= 1.9; SOE: low).[39] Tobacco smoking is associated with accelerated decline of lung function in patients with asthma

and increases in asthma severity based on guidance from another organization cited in the 2009 VA/DoD Asthma CPG.[49] As smoking is a known risk factor, recent research is limited.

Other Factors

The systematic evidence review conducted for this CPG update did not identify evidence related to metabolic syndrome, anxiety disorder, or depression in children as risk factors for asthma-related outcomes. Additionally, while several of the risk factors identified above are considered modifiable, the Work Group did not specifically review evidence related to the impact of modification of these risk factors. Further research is needed to investigate whether interventions aimed at decreasing these risk factors may help reduce risk of poor outcomes in patients with asthma.

The Work Group did not specifically review evidence related to gastroesophageal reflux disease (GERD) as a risk factor for asthma. Studies that were included in the 2009 CPG did not meet current inclusion criteria for the 2018 CPG or have sufficient quality of evidence upon which to make a recommendation for screening for GERD.

Although the Work Group did not specifically review evidence for the following risk factors, indoor and outdoor allergens have been identified by other expert review panels.[50] However, this information was not included in the systematic evidence review carried out for this CPG (and therefore did not contribute to the recommendation or its strength). In drafting these recommendations, the Work Group also considered an analysis of potential benefits, harms, and patient values related to screening for the risk factors identified above. In general, patients are likely to be amenable to providing this information as part of the medical history, and there is little harm in asking about these risk factors/behaviors. However, additional screening can require further time and resources. The Work Group also recommended that certain screening questions may be more appropriately targeted towards specific populations (e.g., screening for OIF/OEF deployment would not be necessary in children). While further review is needed to investigate whether interventions to modify these risk factors may improve outcomes in patients with asthma, there is value to the clinician in being aware of factors that will put the patient at risk of frequent or severe asthma exacerbations.

B. Treatment and Management

a. Asthma Education

Recommendation

8. We suggest offering a written asthma action plan to improve asthma-related quality of life. **(Weak for | Reviewed, New-replaced)**

Discussion

This weak recommendation was based on low quality evidence from the SR by Gatheral et al. (2017).[51] This SR and meta-analysis of 15 randomized controlled trials (RCTs) comparing personalized asthma action plans (PAAPs) in adults with asthma to no PAAPs found no significant effects on asthma exacerbations or healthcare utilization. One of the randomized trials in the review did show a statistically significant difference in asthma control as measured by changes from baseline control on questionnaire scores. Three of the RCTs reviewed showed a statistically significant but modest improvement in quality of life scores. Additionally, the evidence review conducted as part of this guideline update included trials by Khan et al. (2014) and Wong et al. (2013) which compared written asthma action plans (WAAPs) to no WAAPs in children with asthma.[52,53] No differences in asthma exacerbations or healthcare utilization were detected in either of these studies. Wong et al. (2013) also did not detect a difference in asthma control or quality of life scores.[53] The overall confidence in the quality of the evidence was low. There were wide confidence intervals for most outcomes.

The term WAAP has been replaced in more recent literature by PAAP. The change in terminology emphasizes that these asthma action plans are individualized for particular patients; furthermore, the patient participates in the process of developing the plan. They are not typically stand-alone interventions, but rather an integrated component of asthma self-management education. PAAPs are also integrated into regular medical follow-up and are periodically reviewed and adjusted. Formats for PAAPs can vary significantly, but their main feature includes instructions to help patients maintain control of their asthma and to recognize and respond to loss of control.

The patient focus group that was conducted for this CPG update suggested that patients are receptive to the use of a PAAP. It provides an organized approach for day-to-day maintenance and a plan for what to

do when loss of symptom control occurs. Reviewing the PAAP with providers can provide an opportunity to ask questions, express concerns, and share values and preferences. Adherence to the plans may be poor or diminish over time, but the plans themselves are not likely to be viewed as burdensome by patients. Providers, on the other hand, may see PAAPs as a burden. The time to complete and review them with patients competes with other priorities during the office visit. Lack of strong evidence for their effectiveness in the recent medical literature may limit buy-in by providers. Providers who are required to provide a PAAP to patients to meet a quality metric may see it as another form to complete and might not take a patient-centered approach. A PAAP may also be a requirement for school in pediatric patients. In this situation they may be seen as an essential communication tool between the primary care provider and school-based healthcare providers. Other considerations are the availability of printers and PAAP templates. Templates for PAAPs can simplify the process. Integration of PAAPs into the electronic health record (EHR) can also facilitate their regular review and adjustment. Currently, the DoD EHR has a linked PAAP template, but the VA EHR does not. Example asthma action plans can be found in Appendix E.

Our recommendation contrasts with the 2009 VA/DoD Asthma CPG, which strongly recommended the use of WAAPs. The relevant recommendations in the 2009 VA/DoD Asthma CPG were informed by SRs that did show improvement in asthma outcomes in adults [54] and children [55] with the use of asthma action plans as part of a multifaceted self-management program involving primary care provider review. The Gatheral et al. (2017) SR, which is used to support the current recommendation, aimed at isolating the effect that PAAPs have on asthma outcomes.[51] It is possible that PAAPs may be a key component of effective multifaceted interventions, but primary care providers would more likely be using PAAPs without the additional benefits of multifaceted self-management programs.

As this recommendation is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[51] After reviewing the evidence, the Work Group determined that the confidence in the quality of the evidence for the effect of PAAP on asthma outcomes was lower than what would be required for a strong evidence-based recommendation. Our Work Group's "Weak for" recommendation reflects both the low quality of the evidence and the fact that benefit was seen only in quality of life, not for other outcomes such as exacerbations and healthcare utilization. The confidence intervals for these outcomes were large, so it is possible that PAAPs might affect them. Further research with sufficiently powered studies is required to improve the confidence in the effect of this intervention on asthma outcomes.

Recommendations

9. We suggest offering asthma education.
   (Weak for | Reviewed, New-replaced)

10. There is insufficient evidence to recommend one particular asthma education program or education component(s) over others.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

The evidence base for asthma education considered by the Work Group included 16 RCTs [56-71] and one SR encompassing 12 RCTs.[72] Unfortunately, the evidence for the benefit of asthma education is only indirect. This is because asthma education is part of routine care, and it would be impractical or unethical for research studies to have a group with no education. However the evidence reviewed supports "more" or "better" education, indirectly supporting the benefit of asthma education in general.

Plaza, et al. (2015), for example, shows an overall benefit of education (including basic asthma information, a PAAP, and a review of inhaler technique) over usual care alone.[56] In this case, education contributed to improved asthma control, number of exacerbations, unscheduled medical visits, and asthma-related quality of life at one year, but no difference was detected in number of ED visits or hospitalizations.

Studies as a whole show inconsistent benefit of asthma education across several outcomes, including asthma control, asthma-related quality of life, exacerbation frequency, healthcare utilization, and adherence. Therefore, the overall assessment of the importance of asthma education as a whole on critical outcomes is largely based on the likelihood of benefit versus the likelihood of harm. Education is unlikely to cause harm, and burdens imposed by education programs are likely to be limited, such as the commitment of necessary time and resources. Benefit, on the other hand, is highly probable, but likely to be highly variable based on patient values and preferences, particularly when considering patient age, highest level of education, geographic location, and cultural background.

Various studies addressed the impact of specific constituents of asthma education, but no single component or method was clearly superior to others. Approaches to education that were studied included print materials; personalized action plans; review of inhaler indications and technique; review of triggers; and phone-based, as well as clinic-based, close follow-up. Educational interventions also varied on cultural approaches, duration of interventions, and individual versus group methods.

It remains unclear if education customized to cultural background is beneficial. Two of the better quality RCTs, for example, evaluated an evidence-based, culturally sensitive family education program for children aged 5-12 years with poorly controlled asthma in Puerto Rico and found conflicting results.[57,58] The first study randomized 221 participants to receive five flyers with educational information. The authors found statistically significant improvement in asthma control at four months as well as a decrease in ED visits and hospitalizations at six months.[57] The second study randomized 404 participants to an expanded version of culturally sensitive asthma education that included home visits and telephone calls.[58] The study was limited by suboptimal implementation of the intervention, but nonetheless there was no statistically significant difference between groups in asthma control, self-reported ED visits, or hospitalizations at six months.

In addition, it is uncertain what duration of asthma education is most beneficial. Indinnimeo et al. (2009) showed long-term education, including a clinic diary and educational games for children, decreased the number of reported asthma attacks but did not significantly change use of systemic steroids, ED visits, or hospitalizations at 12 months.[64] A shorter duration study by Gagne et al. (2017) showed that a decision aid added to asthma education did not improve asthma control by the Asthma Control Scoring System (ACSS) at two months.[59] Another study by Morell et al. (2014) showed that two five-minute educational

interventions three months apart successfully improved asthma control and decreased general practitioner visits for exacerbations at six months.[63]

It also remains unclear whether individual or group education is more effective. Goeman et al. (2013) compared individualized, person-centered education tailored to responses from a patient questionnaire to passive education. They found a statistically significant difference favoring individualized, person-centered education for asthma control and asthma-related qualify of life, but there was no significant difference in adherence or exacerbations at 12 months.[62] Taskin Yilmaz and Cinar (2015) found that a group education session along with a printed education manual improved asthma control, exacerbation frequency, and asthma-related quality of life at four months compared to usual care.[61] However, Arikan-Ayyildiz et al. (2016) found that their group education program did not significantly improve asthma control, healthcare utilization, or self-reported exacerbations at three months compared to usual care.[60]

The literature reviewed also showed conflicting results regarding benefit of asthma education outside the clinic setting, particularly when considering home-based and school-based education interventions. The most convincing evidence exists for school-based asthma education as a means to improve asthma outcomes in children with asthma. Cicutto et al. (2013) randomized participants across 170 schools to receive school-based asthma self-management education delivered by a public health nurse, with 1,172 children completing the study.[67] At 12 months, there was a statistically significant improvement in asthma-related quality of life as well as urgent care or ED use. Halterman et al. (2011) randomized 523 children to a school-based program wherein a school nurse administered asthma medications in addition to in-home counseling sessions and follow-up telephone calls.[71] The authors found a statistically significant difference favoring the intervention for number of days with rescue medication use and exacerbations requiring prednisone.

Meanwhile, some smaller studies failed to show benefit to school-based interventions. For example, Praena-Crespo et al. (2017) randomized 381 grade school students to an asthma sport and health education program with teaching integrated with physical education classes.[70] The authors found no statistically significant difference for asthma control or asthma-related quality of life. Similarly, three other studies did not find a statistically significant improvement in critical asthma outcomes for school-based programs.[66,68,69]

One SR assessed the impact of home-based asthma education interventions on asthma outcomes.[72] The authors assessed 12 RCTs enrolling 2,342 children with asthma and did not find a statistically significant benefit to home-based education on the primary outcome of number of patients with exacerbations requiring ED visits at six months or at 18 months or on exacerbations requiring oral corticosteroids. Thus, the evidence did not support a recommendation for home-based asthma education.

As Recommendation 9 is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[56-72] The Work Group offers a weak recommendation in favor of offering asthma education; the overall confidence in the quality of evidence is low. The benefits of this recommendation slightly outweigh the harms and burdens. Education requires resources, particularly time and labor, yet some benefit was seen with even the brief, five-minute interventions. We anticipate a large variation in patient values and preferences regarding education, particularly by age and education levels. Other

considerations that impact this recommendation include subgroup considerations, such as geographic location and cultural background. Thus, the Work Group decided upon a "Weak for" recommendation.

As Recommendation 10 is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[57-64,66-72] The Work Group recommends neither for nor against one particular asthma education program or education component(s) over others. The overall confidence in the quality of evidence was low. Data was insufficient to isolate benefit or superiority of one particular component of education over others, and most studies required a broader interpretation of educational interventions as a whole. The benefits of most individual education components likely outweigh any potential harms, though there is likely to be some variation in patient preference and values. Other implications include acceptability of different education components, particularly with regard to children with asthma and the role their parents may be required to play, in addition to anticipated concerns regarding resource requirements. Thus, the Work Group decided upon a "Neither for nor against" recommendation.

Recommendation

11. There is insufficient evidence to recommend for or against patient-oriented technologies (e.g., mobile apps, web based, or telemedicine) as a means to reduce the number or severity of asthma-related exacerbations.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Review of the literature revealed no supporting evidence to recommend either for or against patient-oriented technologies as a method to reduce the number or severity of asthma-related exacerbations. Four SRs and 10 individual studies were identified and provided very low confidence in the quality of the evidence.[73-86] The evidence mixed for asthma severity, treatment adherence, and asthma control and were limited by small sample sizes and short follow-ups.

An SR of 12 RCTs by Hui et al. (2017) examined use of mobile application and showed a positive impact of these tools on asthma control.[73] The most optimal mobile applications included multiple features to support patient self-management. Another SR of six RCTs by Kew and Cates (2016) examined the use of technology-enabled check-ups compared to face-to-face visits; however, findings were inconclusive.[76] Miller et al. (2017) conducted an SR of 11 RCTs comparing mobile technology to paper-based monitoring or standard treatment.[74] Mobile technology showed an impact on unscheduled visits and medication adherence when compared to standard treatment, but the findings were inconclusive when compared to paper-based monitoring. The last SR of 39 RCTs by Normansell et al. (2017) showed a positive impact of electronic inhalers trackers on treatment adherence, but was inconclusive on the clinically relevant outcome on asthma control, number of exacerbations, or health care utilization.[75] Most individual studies identified were relatively small, with short follow-up, and/or inconclusive for critical outcomes.[77-86]

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[73-86] The Work Group's confidence in the quality of the evidence is very low. Due to the lack of strong data coupled with the large variation in patient preferences regarding mobile technology applications, the Work Group decided upon a "Neither for nor against"

recommendation on the use of patient-oriented technologies as a means to reduce the number and severity of asthma-related exacerbations.

b. Pharmacotherapy

Recommendation

12. For patients with persistent asthma, we recommend inhaled corticosteroids as initial controller medication.
    (Strong for | Reviewed, Amended)

Discussion

An SR and meta-analysis of RCTs, comparing inhaled corticosteroids (ICS) against leukotriene receptor antagonists (LTRA), showed a significant decrease in asthma exacerbations requiring systemic steroids and hospitalizations favoring ICS.[87] While a few other studies had differing findings, these were smaller and lower quality studies.[88,89] The use of ICS was also associated with a decrease in incident pneumonia according to a study by Bansal et al. (2015).[90] When prescribing ICS, the lowest effective dose to control asthma should be utilized to minimize potential side effects. Broersen et al. (2015) showed that there is a risk for adrenal suppression with the use of ICS, although this risk is lower when compared to systemic steroids.[91] Decreased linear growth in children associated with use of ICS is also a consideration. Loke et al. (2015) analyzed an RCT comparing ICS versus non-ICS control with a 4.3 year mean follow-up, showing a mean decrease in final adult height by 1.2 cm.[92] Several studies show that higher doses of ICS are associated with a more significant decrease in height velocity.[87,92,93] Reviews of studies by Kramer et al. (2013) and Singh et al. (2016) do not sufficiently show benefit for any specific ICS, compared to another ICS, in regard to efficacy or side-effect profile.[94,95] However, evidence may emerge in the near future that supports the superiority of a specific ICS.

Despite general consistency in the evidence supporting the use of ICS as initial maintenance therapy for patients with persistent asthma, there is some variability in provider, patient, and patient's guardian preferences regarding this treatment. Potential medical profile and career implications may need to be considered for active duty Service Members. Although most medical providers accept the use of ICS therapy, the patient or parent/guardian of a child with asthma may be hesitant to use ICS due to concerns for potential medication side effects. Detailed education and discussion about the benefits versus potential side effects of ICS therapy may be required in these situations. Moreover, the diagnosis of asthma in some children may not be obvious to the parent/guardian, which may lead to hesitancy in using ICS.

LTRA has indications for use in patients with asthma and allergic rhinitis. The 2009 VA/DoD Asthma CPG recommendations included the use of LTRA as an alternative to ICS for mild persistent asthma. This recommendation is not carried forward based upon additional evidence for the benefits of ICS therapy significantly mitigating the risks of a severe asthma exacerbation compared to LTRA. Given the overlap in allergic rhinitis and asthma, patients may be prescribed LTRA alone for allergic rhinitis, and have poorly controlled asthma long term if ICS is not considered.

Certain aspects of asthma care are beyond the scope of this review, as they are part of standard care and therefore do not require a literature review. Standard of care for asthma treatment involves well-known

protocols that provide guidelines for the initial and subsequent categorization of asthma severity (see Appendix B) as well as the use of short-acting beta agonist (SABA) rescue inhaler. These protocols typically also include a step care approach (see Module C of the algorithm).

As this is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[87-95] The Work Group's confidence in the quality of the evidence is moderate. The body of evidence had some limitations such as high attrition and limited information on allocation concealment. Other considerations regarding this recommendation included the benefits, specifically a decrease in hospitalizations and a decrease in exacerbations requiring systemic steroids, outweighing the potential harm of adrenal suppression and decreased linear growth velocity, which was small with overall limited clinical relevance. Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Strong for" recommendation.

Recommendation

13. Among patients with moderate-to-severe persistent asthma and significant symptom burden, we suggest offering a combination of inhaled corticosteroid and long-acting beta agonist as initial controller treatment.
    (Weak for | Reviewed, New-replaced)

Discussion

The Work Group made a strong recommendation for ICS as initial controller therapy medication (see Recommendation 12). The evidence for addition of a long-acting beta agonist (LABA) to an ICS as a controller medication is low for preventing exacerbations,[96] but moderate for symptom control.[97] This was true for adults [98] and children.[99] Therefore, this recommendation applies specifically to patients with moderate-to-severe persistent asthma and significant symptom burden (see Appendix B for additional information on assessment of asthma severity). Most of the studies identified through the systematic evidence review were for the addition of LABA to already existing therapy, but at least one reference addressed using ICS/LABA as first-line therapy.[97] LABA was superior to LTRA when combined with ICS [89,100,101] and LTRA was superior to the addition of theophylline.[102] There was no evidence that one specific brand of LABA was superior to another.[103-105] One SR [106] and another single study [107] suggested that long-acting muscarinic antagonists (LAMA) may be added to ICS as initial controller medication in adults to reduce the risk of asthma exacerbations, but it was not conclusive that this combination was superior to the ICS/LABA combination. There were concerns that beta agonist use alone was detrimental; however, when long-acting agents are used in combination with an ICS, the safety profile is similar to placebo.[108] Despite this safety profile, some patients do experience some side effects (including the patients that participated in the patient focus group conducted as part of this guideline update), which makes the benefit slightly outweigh any harms encountered. Despite general consistency in the evidence to recommend a LABA, there were some suggestions that a LAMA could be substituted in adults.[106,107]

This recommendation is similar to several recommendations in the 2009 VA/DoD Asthma CPG and is common practice among providers. Some patient subgroups, such as the elderly and young children, may be more sensitive to the adverse effects of LABA. There may also be a cost savings when a combination is given to reduce the number of co-pays (in circumstances in which co-pays apply). There may also be some

compliance improvements with the combination, although this question was not addressed by the evidence review. The level of symptoms that might trigger the addition of LABA to ICS is an individual decision that needs to be part of the SDM process between the provider and the patient. The considerations for addition might be very different in an active duty member of the military versus a sedentary office worker.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[89,96-108] The Work Group's confidence in the quality of the evidence is low for the addition of LABA to ICS as initial controller treatment for patients with moderate-to-severe persistent asthma and significant symptom burden. The body of evidence had some limitations, such as confounders in the analysis. Other considerations regarding this recommendation included weighing the potential harm of adverse events, which was small, against potential benefit. Patient values and preferences were thought to be somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

Recommendation

14. For patients with asthma not controlled by inhaled corticosteroids alone, we suggest adding long-acting beta agonists as a step-up treatment over increasing inhaled corticosteroids alone or adding long-acting muscarinic antagonists or leukotriene receptor antagonists.
    (Weak for | Reviewed, New-replaced)

Discussion

In patients who are uncontrolled on ICS alone, we recommend adding a LABA over other treatment options. The 2009 VA/DoD Asthma CPG found the addition of a LABA to ICS therapy was more efficacious than increasing the intensity of ICS treatment. However, the Work Group at that time recommended increasing ICS preferentially to adding an LABA as step-up therapy for patients not controlled on ICS alone, citing safety concerns reported at the time with the use of LABA in persistent asthma. Since that time, additional research has validated the effectiveness and safety of this combination approach for asthma management with the U.S. Food and Drug Administration (FDA) subsequently withdrawing the black box labeling requirements for ICS/LABA combination products.[109] Methods to determine comparative daily dosages of the approved ICS products at low, medium, and high intensities are complex and follow FDA-approved measurements. The section on Additional Information on Drugs Used in Treatment of Asthma provides information on available products. The Work Group did not perform a focused review of all the individual studies included in the SRs that met inclusion criteria for the systematic evidence review conducted for this CPG, but relied on the authors' discussion and conclusions. ICS/LABA has been shown to reduce exacerbations and decrease treatment withdrawals due to adverse events when compared to higher dose ICS. An SR by Zhao et al. (2015) of 35 RCTs with a network meta-analysis comparing combination low-dose ICS/LABA to monotherapy with low- and high-dose ICS (high dose was defined as anything greater than low dose) showed a 31% decrease in exacerbation with fewer adverse events for ICS/LABA compared to higher dose ICS in pediatric patients.[100] An SR by Dwan et al. (2016) showed statistically significant improvements in Asthma Control Test (ACT) scores, spirometry, nighttime peak expiratory flow rate (PEFR), and number of adverse events in adults and children with ICS/LABA compared to higher dose ICS while changes in exacerbations, and other quality of life outcomes, were not statistically significant and/or were inconclusive.[105] Peters et al. (2016) conducted an RCT in patients 12 years of age

and older that resulted in decreases in exacerbations and improvements in Asthma Control Questionnaire 6 (ACQ-6) scores that were statistically significant while the outcomes of safety and side effects were inconclusive.[98]

The SRs of the evidence comparing different ICS/LABA products were not statistically significant and were inconclusive for the outcomes of exacerbations, quality of life, asthma control, serious adverse events, and spirometry.[104,105] Furthermore, Bernstein et al. (2011) conducted a 12-week, open-label, non-inferiority efficacy and safety trial in patients 12 years of age and older comparing two ICS/LABA combinations (mometasone furoate/formoterol versus fluticasone propionate/salmeterol) that showed both products were effective and safe.[103]

Typically, the decision to use three or more medications is made in specialty care environments with patients with confirmed asthma diagnoses. Patients who have uncontrolled asthma while on two medications, one of which is an ICS, may benefit from referral to specialty care for further evaluation.

The Work Group reviewed evidence related to the effectiveness and safety of other treatments compared to ICS/LABA. Much of the evidence included in the SRs and/or RCTs was of low or moderate quality and many results were not statistically significant and/or inconclusive. In patients for whom LABA is contraindicated or intolerable (see Table F-1 for product-specific warnings), other combination options using non-preferred drugs may be used.

Although the majority of the evidence reviewed supported this recommendation, the overall confidence in the quality of the evidence is rated low because of issues concerning study designs and small sample sizes in a portion of the reviewed literature. ICS/LABA is established practice and generally well accepted by both patients and providers although some patients cannot tolerate the side effects of LABA. The patients in the focus group articulated understanding of how the medications improve symptoms and decrease exacerbations but acknowledged obstacles to following treatment regimens. Combination products simplify treatment plans and support improved adherence by avoiding the need for multiple devices or delivery systems. Availability of once-daily dosing of some ICS/LABA products may be appropriate for patients with persistent non-adherence. The addition of LABA to lower doses of ICS is particularly acceptable in the pediatric population because of documented concerns of the effects of ICS on growth velocity and other possible adverse events.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[98,100-106,110,111] The Work Group's confidence in the quality of the evidence is low to support the recommendation to add LABA preferentially over other medications when intensifying treatment in patients on ICS with uncontrolled asthma. The body of evidence had some limitations including flawed study designs, small sample sizes, and confounders in the analysis. The benefits of this recommendation, including improved outcomes of better asthma control, decreased exacerbations, and lower side effects requiring discontinuation outweigh the potential harm of adverse events, which was small. Patient and caregiver values, preferences, and safety concerns were somewhat varied, particularly in the pediatric population, but these were balanced with the desire for good asthma control and fewer severe exacerbations. Thus, the Work Group decided upon a "Weak for" recommendation.

Single Maintenance and Reliever Therapy (SMART) Compared to Other Treatment Options

Use of a combination inhaler containing budesonide and formoterol as both maintenance and quick relief therapy (SMART) has been explored in both pediatric and adult populations. An SR of 16 studies (15 of which described this treatment approach) [106] as well as an RCT [98] revealed statistically significant and positive effects on the occurrence of serious exacerbations requiring systemic corticosteroids when compared to same dose ICS, higher dose ICS, same dose ICS/LABA and higher dose ICS/LABA. While this research is positive, at this time, ICS/formoterol combination is not approved for the treatment of acute bronchospasm. Therefore, the Work Group does not recommend this as a current therapeutic option.

Recommendation

15. In patients with controlled asthma on a stable medication regimen, we suggest either stepping down (not discontinuing) inhaled corticosteroids dose or discontinuing long-acting beta agonists. **(Weak for | Reviewed, New-replaced)**

Discussion

Standard practice for outpatient management of asthma involves a stepwise approach (see Module C of the algorithm). Treatment decisions are made based on response to controller therapies. Within this approach is the concept of stepping down therapy in patients that have demonstrated control of asthma symptoms over time. The goal of stepping down therapy is to maintain patients on the minimum dose of medication to effectively control their symptoms and risks for exacerbations while mitigating medication side effects. Asthma control questionnaires include, for example, the ACQ and the ACT. It is standard practice to make decisions about stepping down therapy after a patient has maintained asthma control on a regimen for at least three months (see Module C of the algorithm). Clinicians routinely take patient factors into consideration when making decisions about stepping down. Historical information like prior step down failure or poor adherence with therapy may influence the decision. Even when a patient is on a stable regimen for three or more months, there are instances in which stepping down is ill advised. In clinical practice, stepping down is avoided during pregnancy, times of stress, planned travel, or peak allergen seasons.

The stepping down of asthma therapy is an established part of asthma care for patients with controlled disease; however, the evidence base for this practice is relatively limited. This recommendation is based on four SRs [112-115] and two RCTs [116,117]. The strongest evidence was to avoid complete discontinuation of ICS in adults due to increased exacerbations and asthma symptoms.[114] With respect to stepping down ICS therapy to a lower dose ICS versus continuing a stable dose ICS, the evidence was inconclusive for the outcomes of exacerbations, asthma control, and quality of life.[115] However, the same SR demonstrated that stepping down the ICS component of a LABA/ICS versus continuing a stable dose ICS/LABA resulted in equivalent levels of asthma control and asthma-related quality of life. Considering evidence for lower adverse effects at lower ICS dosage, this observation of equivalence supports the decrease in ICS dosage among well-controlled patients. Impact on exacerbations was not statistically significant. Stepping down a patient on LABA/ICS to ICS alone versus continued stable dose LABA/ICS was studied in both the SR by Ahmad et al. (2015) [112] and the RCT by Rogers et al. (2018).[117] The SR found statistically significant differences favoring continued LABA/ICS therapy with respect to asthma control and asthma-related quality of life.[112] A more recent RCT examining the same LABA step-

off found no statistically significant difference in outcomes between groups.[117] Both studies were inconclusive with respect to exacerbations after LABA step-off.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[112-117] Based on the findings of the systematic evidence review conducted on step-down therapy as part of this guideline update, the Work Group decided upon a "Weak for" recommendation in favor of stepping down therapy in the specific scenarios reviewed above based on low quality evidence. The Work Group determined that the benefits of stepping down therapy slightly outweighed the harms/burdens of continued therapy in patients with controlled asthma on a stable medication regimen. Each step down of asthma therapy should be considered as a therapeutic trial warranting close patient follow-up. All decisions on step-down therapy must be individualized taking into consideration the patient's clinical history and risk factors for exacerbations, as well as their values and preferences.

Recommendation

16. We suggest short-acting beta agonists or leukotriene receptor antagonists for prevention of exercise-induced bronchospasm.
    (Weak for | Not reviewed, Amended)

Discussion

Exercise-induced bronchospasm (EIB), commonly referred to in the medical literature as exercise-induced asthma or exercise-induced bronchoconstriction, can be diagnosed in two distinct groups of patients. The first group consists of those patients with established asthma who, during exercise, have a component of bronchospasm that limits their activities. It is reported to occur in up to 90% of patients with asthma and is usually a self-limited process that resolves with cessation of exercise.[118]

There is a separate group of patients who do not have underlying asthma but may develop symptomatic bronchospasm with prolonged exercise. These patients are generally competitive athletes and can include active duty military who exercise on a regular basis. The evaluation of these patients always demonstrates normal resting spirometry but with airway hyperreactivity upon bronchoprovocation testing.

In addition to medications, a non-pharmacologic approach to reduce EIB includes warming up prior to exercise. This is usually done in conjunction with the use of a SABA 15-20 minutes prior to vigorous exercise. A regular exercise program is indicated in patients with asthma to avoid deconditioning and improve cardiovascular health.

For patients with EIB, treatment with either a SABA or LTRA has been proven beneficial.[119,120] Traditionally, a SABA just before exercise was considered first-line treatment for EIB; but review of the evidence shows that LTRAs, at least two hours before exercise, also provide equivalent outcomes in EIB symptom reduction with an effect that extends up to 24 hours.[119,120] Prevention of EIB is desired both to optimize function of daily activities and avoid complications such as ED visits. Therefore, treatment with either a SABA or LTRA is of benefit and outweighs the minimal known side-effect profile of these medications. This recommendation is for the prevention of EIB and it should be noted that all patients with asthma should have access to a rescue inhaler (i.e., SABA) to treat symptoms should they occur.

While SABAs have been the mainstay of treatment of EIB, certain populations may benefit from the ease of using an LTRA due to dosing once daily in pill form (at least two hours prior to exercise) as opposed to using an inhaler just before exercise. This is particularly useful for patients with variable levels of activity throughout the day or concomitant allergic rhinitis.

As this is a *Not reviewed, Amended* recommendation, the Work Group based this recommendation on the evidenced cited in the previous guideline.[119,120] The Work Group's confidence in the quality of the evidence is low. Benefits outweigh harms, as there are few harms that a small number of patients may experience. Benefits include better asthma control during exercise. Patient values and preferences were somewhat varied. Thus, the Work Group decided upon a "Weak for" recommendation.

c. Non-pharmacotherapy

Recommendation

17. We suggest a multidisciplinary treatment approach to improve asthma-related quality of life, asthma control, and treatment adherence.
    (Weak for | Reviewed, New-replaced)

Discussion

The evidence base for this recommendation consisted of three SRs [121-123] and nine RCTs.[124-132] A multidisciplinary treatment approach for this recommendation is defined as at least one other healthcare professional in addition to the primary care provider. A myriad of other healthcare professionals provided interventions in these studies including nurses, clinical psychologists, pharmacists, community health workers, respiratory therapists, case managers, pulmonologists, physiotherapists, behavioral health personnel, nurse practitioners, physician assistants, and occupational therapists. Interventions were provided by either one supplemental person or multiple personnel. One component underlying all the included studies was focused patient education based upon the patient's needs.

Quality of life, per self-reported patient satisfaction, increased with chronic disease management/ education,[121] culturally specific education,[124] holistic self-management education,[125] community pharmacist education,[126,127] asthma management program education,[128] and behavioral modification education.[122,129-131] Though there was moderate quality evidence supporting cognitive behavioral therapy (CBT), CBT was not a specific program and included any model "including acceptance and mindfulness-based therapies."[122] There was no identifiable combination of team member disciplines preferable that was beneficial over another combination of team member disciplines.

Asthma control, per patient self-reported satisfaction, increased with chronic disease management/ education,[121] holistic self-management education,[125] community pharmacist education,[126] and behavioral modification education.[122] "A significant positive correlation was demonstrated between asthma control and asthma-related quality of life scores."[126] Improved asthma control from behavioral modification may be a secondary outcome as identified through patient self-reported increases in quality of life.[122]

Asthma treatment adherence, per patient self-reported satisfaction, increased with community pharmacist education.[123,132] Not all interventions were delivered exclusively by pharmacists, but all interventions had pharmacist input in the education. Primary interventions were behavioral modification

based upon goal setting, action planning, and feedback demonstrations (e.g., inhaler usage).[123] A patient diary-keeping method showed improvement in medication adherence only after "the 3rd follow-up to 4th follow-up"[132]

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed pertinent studies as part of this guideline update.[121-132] The Work Group determined the overall confidence in the quality of evidence to be low in the support of the recommendation. Thus, the Work Group decided upon a "Weak for" recommendation. The benefits of using a multidisciplinary treatment approach outweigh harms/burdens. Variation exists in the execution of the multidisciplinary treatment approach; but the one common underlying consistent component to all the included studies was focused patient education based upon the patient's needs. Resource use and feasibility of using a multidisciplinary treatment approach would be influenced by costs, resource availability, community support, and technological advancements (e.g., telemedicine platform). Since the studies were predominately adults, further research is warranted to include adolescent and pediatric populations.

Recommendation

18. We suggest patients with asthma participate in regular exercise to improve quality of life and asthma control.
    (Weak for | Reviewed, Amended)

Discussion

Patients with asthma should participate in regular exercise to improve quality of life and asthma control. As noted in the 2013 Cochrane SR [133] (which updated the 2005 review [134] cited in the 2009 VA/DoD Asthma CPG), "Physical training improved cardiopulmonary fitness…Although there was insufficient data for a meta-analysis on the effects of physical training on health related quality of life, the Carson study does provide evidence, however limited, that physical training has positive effects on the quality of life of asthma patients."[133] The 2013 Cochrane SR compared several studies, showing that the benefits of exercise outweigh the risks for patients with asthma.[133] The SR found that asthma symptom management, lung function, and mental health improved with regular aerobic exercise. Exercise training may also reduce the perception of breathlessness through a number of mechanisms including strengthening respiratory muscles. The SR also noted that exercise may reduce airway inflammation and increase patency of bronchioles, thereby having a protective effect against asthma development. In some patients with asthma, exercise can provoke bronchoconstriction; however, patients may also experience worsening breathlessness with a lack of conditioning. The 2013 Cochrane review also noted that studies have shown that people with asthma are able to exercise and improve their fitness and that limitations in exercise capacity can sometimes relate more to lack of fitness than to airflow limitation.

Based on the research conducted by Eichenberger et al. (2013), the quality of life of patients with asthma considerably improves with physical training and that changes through decrease in airway hyperactivity and improvement in lung function significantly contribute to this improvement.[118] In the research conducted by Flapper et al. (2008), which examined a physical exercise program along with self-management education, there were improvements in pediatric quality of life with outcomes of decreased school absenteeism of patients with asthma.[135] The 2013 Cochrane review also noted studies have shown that people with asthma are able to exercise and improve their fitness and that limitations in

exercise capacity can sometimes relate more to lack of fitness than to airflow limitation.[133] Thus, physical activity should be recommended as a supplementary therapy to medication.

As this is a *Reviewed, Amended* recommendation, the Work Group systematically reviewed the evidence identified in the evidence review conducted for this CPG update [118,133,135] and considered the assessment of the evidence put forth in the 2009 CPG.[134] There was some evidence of benefit and no evidence of adverse effects on asthma symptoms caused by physical training. Thus, there was no clinical reason for people with stable asthma to refrain from regular exercise.[133] Eichenberger et al. (2013) states about 90% of patients with asthma suffer from exercise-induced bronchoconstriction (i.e., airway narrowing and increased airway resistance during or after exercise) which might prevent patients with asthma from performing regular physical exercise.[118] The Work Group's confidence in the quality of the evidence is low, specifically regarding outcomes including asthma control/symptoms, exacerbations, and quality of life. Thus, the Work Group decided upon a "Weak for" recommendation that exercise will improve quality of life and asthma control in this population.

Recommendation

19. We suggest offering cognitive behavioral therapy as a means of improving asthma-related quality of life and self-reported asthma control for adult patients with persistent asthma.
    (Weak for | Reviewed, New-added)

Discussion

In an SR of six studies, Kew et al. (2016) found that CBT may improve quality of life, asthma control, and anxiety levels for adults with persistent asthma when compared to usual care or no intervention.[122] Studies included 214 adult participants with mean ages ranging from 39 to 53; no adolescents or children were included in the studies. There was much variation between studies in how CBT was delivered and what constituted usual care, meaning the most optimal method of CBT delivery, format, and target population requires further investigation.

While CBT may have modest benefits for people with asthma, the current body of literature reviewed offers little insight into the possible harms of CBT.[122] When indicated, healthcare providers are encouraged to address any questions or concerns their patients may have related to the possible harms and stigma associated with counseling services.[a] Furthermore, the majority of studies in the SR by Kew et al. (2016) included intensive interventions which may not be feasible for patients and program resources.[122] Brief consultation provided by mental health professionals integrated within the primary care setting may offer the best model for optimizing services; however, further research is needed in this area.[136]

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review as part of this guideline update.[122] The Work Group determined the confidence in the evidence was moderate in support of CBT as a means of improving asthma-related quality of life and self-reported asthma control for adult patients with persistent asthma. Other support for this recommendation stemmed from the Work Group's assessment that the

[a] See the VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder (2016) (available at: https://www.healthquality.va.gov/guidelines/MH/mdd/).

benefits of this recommendation slightly outweigh the associated harms and burdens. Further, behavioral health consultants already embedded within primary care clinics may be able to mitigate concerns related to resources and stigma. Finally, additional research is need to determine the optimal delivery method, format, and target population when treating patients with asthma in primary care. Thus, the Work Group decided upon a "Weak for" recommendation.

d. Monitoring and Follow-up

Recommendation

20. We suggest against utilizing spirometry for routine monitoring of patients with stable asthma. **(Weak against | Reviewed, New-replaced)**

Discussion

The diagnosis of asthma is a clinical diagnosis based on history, physical examination, and findings suggestive of airway hyperactivity. While objective measurements of airway reactivity, specifically reversible obstruction post-bronchodilator, may be helpful in the diagnosis of asthma, the lack of objective reversibility does not disqualify the diagnosis. Furthermore, the use of spirometry in routine monitoring of patients with asthma was not found to significantly improve patient outcomes on the standardized ACT. An RCT by Oei et al. (2011) demonstrated no statistically significant difference between patients who received spirometry every three months versus patients who received only routine medical follow-up.[137] Similarly, in patients with fixed obstruction and incomplete bronchodilator reversal, there is insufficient evidence to provide recommendations regarding follow-up spirometry. Review of the literature found a single cohort study in which children with asthma symptoms and a fixed, non-reversible airflow obstruction were unlikely to change at 12 months.[21] Associated literature regarding a similar evaluation of the adult population was not identified for review.

Although a recommendation related to routine monitoring of patients with stable asthma was included in the 2009 VA/DoD Asthma CPG, that recommendation was based on guidance from other organizations. Current literature does not support routine (e.g., quarterly) spirometry for stable patients with asthma in the general population. However, there may be specific requirements that need to be considered for active duty members of the military). While there are no obvious harms associated with spirometry, there may be added burden and many patients (especially the very young or elderly) may have difficulty performing an adequate/reproducible test. Accessibility for repeated visits may be burdensome to both patients and staff. In addition, not every facility may have easy access to proper equipment or trained personnel. At some facilities, a provider may need to wait for test results. If during this time the provider does not consider the symptoms to guide treatment, the harms of obtaining the test may outweigh the benefits. For these reasons, a recommendation of "Weak Against" was suggested.

Although the reviewed literature does not support routine use of spirometry in monitoring of patients with stable asthma, there does not appear to be significant variability in patient preference for this test.[137] The patient focus group revealed no comments or concerns regarding spirometry.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation identified through the systematic evidence review.[21,137] The Work Group's confidence in the quality of the evidence is low. The body of evidence had some limitations

including small sample sizes and unclear randomization. The benefits versus harms appeared to be balanced. Patient values and preferences were not varied. Thus, the Work Group decided upon a "Weak against" recommendation.

Recommendation

21. There is insufficient evidence to recommend for or against routine use of fractional exhaled nitric oxide in monitoring patients in primary care settings to improve asthma-related clinical outcomes. **(Neither for nor against | Reviewed, New-replaced)**

Discussion

Human lungs produce nitric oxide (NO) and a fraction of NO can be measured in exhaled breath (fractional exhaled nitric oxide [FeNO]). FeNO has been extensively studied in various diseases and specifically for asthma. The American Thoracic Society (ATS) published an extensive document about interpretation of exhaled NO level.[138]

Our evidence review focused on the role of routine measurement of FeNO on management of asthma and important clinical outcomes in the primary care setting. Two large SRs by Petsky et al. (2018) [139] and Wang et al. (2015) [44] looked at various important clinical outcomes. Asthma exacerbations occurred significantly less often in the FeNO group compared to control. The confidence in the quality of the data was assessed as moderate for both SRs. In contrast, several clinically important outcomes, including exacerbations requiring systemic steroid and healthcare utilization, did not differ significantly in the FeNO management groups compared to control.

An RCT by Szefler et al. (2008) evaluated various clinical outcomes when FeNO measurement-driven guideline management of asthma was compared to control.[140] The quality of the data was rated as moderate. Treatment adherence and healthcare utilization did not differ between the two groups.

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[44,139,140] The Work Group's confidence in the quality of the evidence is low. Significant differences in exacerbation outcomes were most likely driven by improvement in milder forms of exacerbations. The Work Group determined there was little harm with the use of FeNO. The Work Group also did not perceive any significant variation among patients to accept the test. However, implementation of a new test is resource intensive and not all centers may have easy and timely access to the testing. Thus, the Work Group decided upon a "Neither for nor against" recommendation.

In summary, use of FeNO in primary care practice may reduce milder forms of asthma exacerbations but this may not outweigh the issues related to resource use. Thus, the Work Group did not recommend for or against the use of FeNO in primary care management of asthma. The Work Group did not assess the value of FeNO in a subspecialty setting.

Recommendation

22. We suggest leveraging electronic health record capabilities such as trackers and reminders in the care of patients with asthma.
    (Weak for | Reviewed, New-added)

Discussion

Fiks et al. (2015) showed that families using an EHR-linked patient portal for pediatric patients had better outcomes with fewer missed days of work by parents.[141] The use of the portal was more effective in those patients with worse disease. A proprietary system showed some improvement in symptom-free days, but this improvement disappeared within six months.[71] Reminders to improve inhaler adherence were mostly ineffective; however the confidence the quality of evidence was very low.[75] Smith et al. (2012) showed reduced hospitalizations and increased prescriptions for recommended preventive therapies in primary care practices using electronic alerts compared to practices using routine care alone, although there was no overall effect on exacerbations.[142] Another cluster-randomized trial showed a reduced rate of uncontrolled asthma episodes in patients using an asthma management system.[143] While these tools may not be readily available, they may be helpful when they are available.

As this is a *Reviewed, New-added* recommendation, the Work Group systematically reviewed evidence related to this recommendation in the evidence review conducted as part of this guideline update.[71,75,141-143] The quality of the evidence was low. The harms were small, and therefore the group determined that the benefits slightly outweighed the harms. There is likely to be significant variation regarding patient preferences since many elderly patients might not feel comfortable using the technology. There may also be issues of licensure for proprietary systems and variation between different EHRs. Of note, the DoD and VA have both purchased the same EHR system, Cerner. The reminders and patient portals contained in the Cerner EHR may be able to supply the benefits outlined above. The low quality of the evidence, variation in outcomes, and variation in patient preferences caused the group to make a “Weak for” recommendation.

VII. Research Priorities

Several research priorities were identified through the development of this CPG. Regarding diagnosis and assessment, there is a need for tests that more clearly differentiate asthma from chronic obstructive pulmonary disease (COPD). Research to determine the effect of the use of FeNO as an assessment tool for children and adults with asthma on clinical outcomes was also identified as a priority. In general, the Work Group felt that more research is needed for supplemental tests to diagnose asthma and monitor treatment and adherence. Further, more research is needed regarding potential risk factors of asthma related outcomes (e.g., use of electronic cigarettes).

Research priorities for pharmacologic therapy included questions related to ICS use in children. Pediatric studies should test the risk-benefit balance of intermittent versus daily use of ICS. Other studies are needed to assess the safety profile of different types and forms of ICS in children, with a focus on systemic bioavailability and height growth. Use of higher dose ICS in cases of asthma exacerbation, as well as the testing of SMART therapy with drugs available in the U.S., were identified as research priorities. In addition to the management of acute exacerbations, more research is needed looking at stepping down or stepping off maintenance therapy during seasons with less exacerbations.

The Work Group identified the need to study the use of technology to support patients and providers in the management of asthma. Technology is a promising tool to improve patient-provider communication and has the potential to improve treatment adherence. Telehealth was identified as a research priority with studies that focus on the non-inferiority of telehealth versus in-person care, including auscultatory telehealth and mobile telehealth.

A lack of recent high quality research supporting the benefit of asthma action plans and asthma education was noted by the Work Group, and additional research in these areas is needed. For asthma action plans, research should focus on specific measures of benefit, the integration of technology into action plans, and the effectiveness of written action plans. As asthma action plans are often considered a standard of care, limiting the possibility to study them in RCTs, use of registries could be an alternative research design. Additional larger studies on asthma education are necessary to define which component, strategy, or setting for education leads to the greatest benefit. Similarly, high quality research is needed to define the size and composition of multi- or inter-disciplinary teams to improve asthma care. The Work Group identified a need for studies that assess the impact of exercise plans on asthma control and quality of life, as well as the impact of dietary changes, such as the Dietary Approaches to Stop Hypertension (DASH) eating plan, on asthma outcomes.

As risk factors for the onset or exacerbation of asthma are in part environmental, high quality care may not always be enough to improve patient outcomes. For instance, although a patient is treated for an exacerbation, they may return following care to a home with mold or dust mites. Additional research into social determinants of care (e.g., care teams that include social workers and lawyers) would be helpful in order to determine how to best take into account social determinants of health during asthma treatment.

Appendix A: Evidence Review Methodology

A. Developing the Key Questions

The CPG Champions, along with the Work Group, were tasked with identifying KQs to guide the systematic evidence review on management of asthma. These questions, which were developed in consultation with the Lewin Team, addressed clinical topics of the highest priority for the VA and DoD populations. The KQs follow the population, intervention, comparison, outcome, timing and setting (PICOTS) framework for evidence questions, as established by the Agency for Healthcare Research and Quality (AHRQ). Table A-1 provides a brief overview of the PICOTS typology.

Table A-1. PICOTS [144]

PICOTS Elements	Description
Patients, Population, or Problem	A description of the patients of interest. It includes the condition(s), populations or sub-populations, disease severity or stage, co-occurring conditions, and other patient characteristics or demographics.
Intervention or Exposure	Refers to the specific treatments or approaches used with the patient or population. It includes doses, frequency, methods of administering treatments, etc.
Comparison	Describes the interventions or care that is being compared with the intervention(s) of interest described above. It includes alternatives such as placebo, drugs, surgery, lifestyle changes, standard of care, etc.
Outcome	Describes the specific results of interest. Outcomes can include short, intermediate, and long-term outcomes, or specific results such as quality of life, complications, mortality, morbidity, etc.
Timing, if applicable	Describes the duration of time that is of interest for the particular patient intervention and outcome, benefit, or harm to occur (or not occur).
Setting, if applicable	Describes the setting or context of interest. Setting can be a location (such as primary, specialty, or inpatient care).

The Champions, Work Group, and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the systematic evidence review. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. Table A-2 contains the final set of KQs used to guide the systematic evidence review for this CPG.

Once the KQs were finalized, the Work Group prioritized the outcomes they had defined for each KQ based on how important the Work Group judged each outcome to be. Ranking outcomes by their relative importance can help focus attention on those outcomes that are considered most important for clinical decision making when making judgements regarding the overall quality of the evidence to support a recommendation.[145]

Using GRADE methodology, the Work Group rated each outcome on a 1-9 scale (7-9, critical for decision making; 4-6, important, but not critical, for decision making; and 1-3, of limited importance for decision making). Critical and important outcomes were included in the evidence review (see Outcomes); however, only outcomes judged to be critical were used to determine the overall quality of evidence (see Grading Recommendations).

a. Population(s)

- Adults and children four years of age and older who may be experiencing asthma

b. Interventions

- Key Question 1

  Tests

  - Diagnostic tests (e.g., chest x-ray, CT scan, full pulmonary function tests [PFTs])
  - In-office/primary care spirometry
  - Referral for specialized spirometry

- Key Question 2

  Tests

  - Spirometry with bronchodilator
  - Spirometry with methacholine challenge
  - Other tests

- Key Question 3

  Exposure

  - Comorbidities (e.g., GERD)
  - Burn pits
  - Aviation fuel
  - Sleep apnea
  - Smoking/vaping (including second-hand smoke)
  - Stress
  - Emotions
  - Respiratory infection
  - Other triggers/risk factors

- Key Question 4

  Pharmacotherapy:

  - **Inhaled steroids**
    - Beclomethasone (*QVAR*)
    - Budesonide (*PULMICORT*)
    - Ciclesonide (*ALVESCO*)
    - Flunisolide (*AEROSPAN*)
    - Fluticasone (*FLOVENT*, *ARMONAIR*, *ARNUITY*)
    - Mometasone (*ASMANEX*)

        - Triamcinolone acetonide (*AZMACORT*)
    - **Inhaled steroids/long-acting beta agonists**
        - Budesonide/Formoterol (*SYMBICORT*)
        - Fluticasone/Salmeterol (*ADVAIR*, *AIRDUO*)
        - Fluticasone/vilanterol (*BREO ELLIPTA*)
        - Mometasone/formoterol (*DULERA*)
    - **Short-acting beta agonists**
        - Albuterol (*VENTOLIN*, *PRO-AIR*, *PROVENTIL*)
        - Levalbuterol (*XOPENEX*)
    - **Long-acting anticholinergic/muscarinic receptor antagonists**
        - Tiotropium (*SPIRIVA*)
    - **Leukotriene receptor antagonist**
        - Montelukast (*SINGULAIR*)
        - Zafirlukast (*ACCOLATE*)
        - Zileuton (*ZYFLO*)
    - **Systemic corticosteroids**
        - Prednisone (*DELTASONE*)
        - Prednisolone (*PRELONE*)
        - Methylprednisone (*MEDROL*)
        - Dexamethasone (*DECADRON*)
    - **Other medications**
        - Cromolyn sodium
        - Theophylline
- Key Question 5

  Chronic daily ICS use:
    - **Inhaled steroids**
        - Beclomethasone (*QVAR*)
        - Budesonide (*PULMICORT*)
        - Ciclesonide (*ALVESCO*)
        - Flunisolide (*AEROSPAN*)
        - Fluticasone (*FLOVENT*, *ARMONAIR*, *ARNUITY*)
        - Mometasone (*ASMANEX*)
        - Triamcinolone acetonide (*AZMACORT*)

- **Inhaled steroids/long-acting**
  - Budesonide/Formoterol (*SYMBICORT*)
  - Fluticasone/Salmeterol (*ADVAIR*, *AIRDUO*)
  - Fluticasone/vilanterol (*BREO ELLIPTA*)
  - Mometasone/formoterol (*DULERA*)

- Key Question 6

  Pharmacotherapy, addition/modification of treatment: (e.g., adding medication, increasing dose)

  - **Inhaled steroids**
    - Beclomethasone (*QVAR*)
    - Budesonide (*PULMICORT*)
    - Ciclesonide (*ALVESCO*)
    - Flunisolide (*AEROSPAN*)
    - Fluticasone (*FLOVENT*, *ARMONAIR*, *ARNUITY*)
    - Mometasone (*ASMANEX*)
    - Triamcinolone acetonide (*AZMACORT*)
  - **Inhaled steroids/long-acting beta agonists**
    - Budesonide/Formoterol (*SYMBICORT*)
    - Fluticasone/Salmeterol (*ADVAIR*, *AIRDUO*)
    - Fluticasone/vilanterol (*BREO ELLIPTA*)
    - Mometasone/formoterol (*DULERA*)
  - **Short-acting beta agonists**
    - Albuterol (*VENTOLIN*, *PRO-AIR*, *PROVENTIL*)
    - Levalbuterol (*XOPENEX*)
  - **Long-acting anticholinergic/muscarinic receptor antagonists**
    - Tiotropium (*SPIRIVA*)
  - **Leukotriene receptor antagonist**
    - Montelukast (*SINGULAIR*)
    - Zafirlukast (*ACCOLATE*)
    - Zileuton (*ZYFLO*)
  - **Systemic corticosteroids**
    - Prednisone (*DELTASONE*)
    - Prednisolone (*PRELONE*)

        - Methylprednisone (*MEDROL*)
        - Dexamethasone (*DECADRON*)
    - **Other medications**
        - Cromolyn sodium
        - Theophylline

- Key Question 7

  Pharmacotherapy, reduction in number/dosage of medication (e.g., step down in therapy) (e.g., inhaled corticosteroids)

- Key Question 8

  Interdisciplinary treatment approaches:

    - Behavioral Health Optimization Program
    - Patient-centered medical home
    - Team-oriented treatment approach/use of coordination team
    - Psychotherapy
    - Behavioral health approaches
    - Lifestyle modifications
    - Inclusion of other healthcare professions in provision of care/education (e.g., clinical pharmacists)

- Key Question 9
    - Content/components of asthma action plan including non-urgent, management of acute exacerbation
    - Patient self-management approaches/strategies
    - Patient education (including on inhaler use)

- Key Question 10

  Monitoring/assessment/severity classification tools for provider decision regarding step-up or step-down in therapy

    - ACT
    - Spirometry
    - Peak flow
    - FeNO
    - Global Initiative for Asthma classification

- Key Question 11

  Provider-oriented technologies

  - EHR/decision support
  - Telehealth (e.g., for specialist consultation)

- Key Question 12

  Patient-oriented technologies

  - Telehealth (e.g., for specialist consultation)
  - Mobile apps/technology
  - Text messages
  - Web/internet-based management approaches

c. Comparators

- Key Question 1
  - No diagnostic test
  - Clinical assessment
  - Different diagnostic test
- Key Question 2
  - Standard spirometry alone
  - No test
  - Other tests
- Key Question 3
  - No exposure
- Key Question 4
  - Listed intervention compared to each other
- Key Question 5
  - Intermittent or no ICS or ICS/LABA use to manage chronic asthma
  - Use of different chronic medication to manage chronic asthma
  - Uncontrolled asthma
  - No asthma
  - Intermittent asthmatics
- Key Question 6
  - Other addition/modification in treatment (e.g., maintaining dose of ICS and adding another agent [e.g., leukotrienes, tiotropium, LABA, LAMA])

- Key Question 7
  - Maintenance of therapy (e.g., no reduction)
- Key Question 8
  - Usual care
  - Single provider care
  - Primary care
- Key Question 9
  - No self-management approach
  - No asthma action plan
  - Different self-management approach
- Key Question 10
  - No use of listed tools for the provider to make a treatment decision (e.g., step-up or step-down in therapy)
- Key Question 11
  - Usual care
  - No use of these tools
  - Use of a different tool
- Key Question 12
  - Usual care
  - No use of these tools
  - Use of a different tool

d. Outcomes

- Key Question 1
  - Critical outcomes
    - Diagnosis of asthma
    - Diagnosis of another condition
    - Indication for specialty referral
- Key Question 2
  - Critical outcomes
    - Diagnosis of asthma
    - Diagnosis of another condition
    - Indication for specialty referral

- Key Question 3
  - Critical outcomes
    - Number/severity of exacerbations
    - Asthma control/symptoms
    - Healthcare utilization
  - Important outcomes
    - Incidence of asthma
    - Achievement of physical activity goals
    - Quality of life
    - Pulmonary function
- Key Question 4
  - Critical outcomes
    - Safety/side effects
    - Quality of life
    - Number/severity of exacerbations
    - Asthma control/symptoms
    - Healthcare utilization
  - Important outcomes
    - Pulmonary function
- Key Question 5
  - Critical outcomes
    - Safety/side effects
    - Quality of life
    - Number/severity of exacerbations
    - Asthma control/symptoms
    - Healthcare utilization
  - Important outcomes
    - Pulmonary function
- Key Question 6
  - Critical outcomes
    - Safety/side effects
    - Quality of life

        - Number/severity of exacerbations
        - Asthma control/symptoms
        - Healthcare utilization
    - Important outcomes
        - Pulmonary function
- Key Question 7
    - Critical outcomes
        - Safety/side effects
        - Quality of life
        - Number/severity of exacerbations
        - Asthma control/symptoms
        - Healthcare utilization
    - Important outcomes
        - Pulmonary function
- Key Question 8
    - Critical outcomes
        - Treatment adherence
        - Quality of life
        - Number/severity of exacerbations
        - Asthma control/symptoms
        - Healthcare utilization
- Key Question 9
    - Critical outcomes
        - Treatment adherence
        - Quality of life
        - Number/severity of exacerbations
        - Asthma control/symptoms
        - Healthcare utilization
- Key Question 10
    - Critical outcomes
        - Treatment adherence
        - Quality of life

        - Number/severity of exacerbations
        - Asthma control/symptoms
        - Healthcare utilization
- Key Question 11
    - Critical outcomes
        - Ease of intervention use
        - Number/severity of exacerbations
    - Important outcomes
        - Patient satisfaction/experience
        - Feasibility
        - Access to healthcare
        - Treatment adherence
        - Asthma control/symptoms
        - Healthcare utilization
        - Cost of care/resource use
- Key Question 12
    - Critical outcomes
        - Ease of intervention use
        - Number/severity of exacerbations
    - Important outcomes
        - Patient satisfaction/experience
        - Feasibility
        - Access to healthcare
        - Treatment adherence
        - Asthma control/symptoms
        - Healthcare utilization
        - Cost of care/resource use

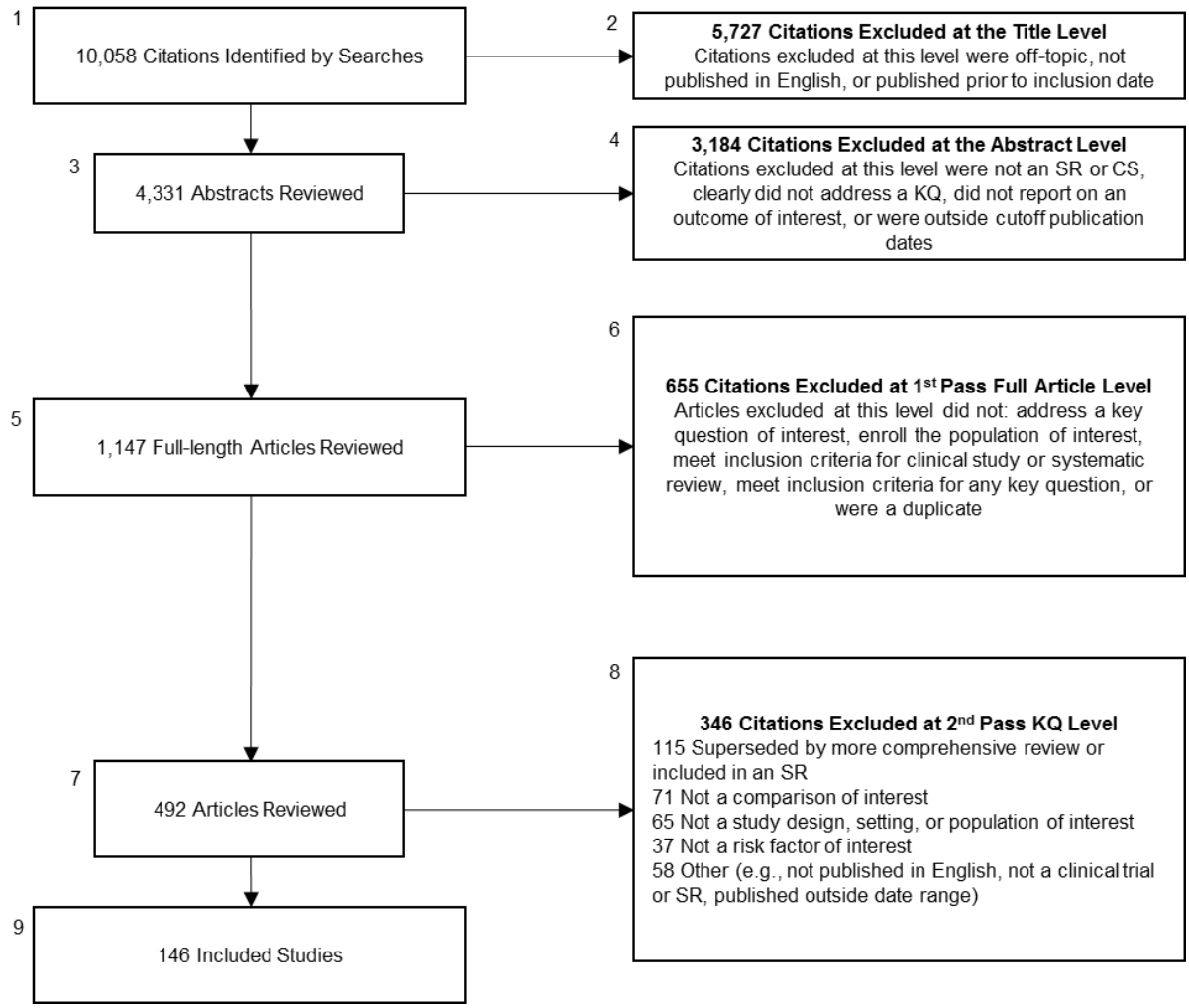
B. Conducting the Systematic Evidence Review

Based on the decisions made by the Champions and Work Group members regarding the scope, the KQs, and the PICOTS statements, the Lewin Team produced a systematic evidence review protocol prior to conducting the review. The protocol was reviewed and approved by the Champions and Work Group members. It described in detail the final set of KQs, the methodology to be used during the systematic evidence review process, and the inclusion/exclusion criteria to be applied to each potential study, including, but not limited to, study type, sample size, and PICOTS criteria.

Extensive literature searches identified 10,058 citations potentially addressing the KQs of interest to this evidence review. Of those, 5,727 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date, or not a full-length article). Overall, 4,331 abstracts were reviewed with 3,184 of those being excluded for the following reasons: not an SR or an accepted study design (see the General Criteria for Inclusion in Systematic Review and Key Question Specific Criteria), did not address a KQ of interest to this review, did not report on an outcome of interest, or published outside cut-off publication dates. A total of 1,147 full-length articles were reviewed. Of those, 655 were excluded at a first pass review for the following: not addressing a KQ of interest, not enrolling the population of interest, not meeting inclusion criteria for study design, not meeting inclusion criteria for any KQ, or being a duplicate. A total of 492 full-length articles were thought to address one or more KQs and were further reviewed. Of these, 346 were ultimately excluded. Reasons for their exclusion are presented in Figure A-1 below.

Overall, 146 studies addressed one or more of the KQs and were considered as evidence in this review. Table A-2 indicates the number of studies that addressed each of the questions.

Figure A-1. Study Flow Diagram



Abbreviations: CS: clinical study; KQ: key question; SR: systematic review

Alternative Text Description of Study Flow Diagram

Figure A-1. Study Flow Diagram is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion/exclusion process. Arrows point down to boxes that describe the next literature review step and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

1. Box 1: 10,058 citations identified by searches
    a. Right to Box 2: 5,727 citations excluded at the title level
        i. Citations excluded at this level were off-topic, not published in English, or published prior to inclusion date
    b. Down to Box 3
2. Box 3: 4,331 abstracts reviewed
    a. Right to Box 4: 3,184 citations excluded at the abstract level
        i. Citations excluded at this level were not an SR or clinical study, clearly did not address a KQ, did not report on an outcome of interest, or were outside cutoff publication dates
    b. Down to Box 5
3. Box 5: 1,147 full-length articles reviewed
    a. Right to Box 6: 655 citations excluded at 1st pass full article level
        i. Articles excluded at this level did not: address a key question of interest, enroll the population of interest, meet inclusion criteria for clinical study or SR, meet inclusion criteria for any key question, or were a duplicate
    b. Down to Box 7
4. Box 7: 492 articles reviewed
    a. Right to Box 8: 346 citations excluded at 2nd pass KQ level
        i. 115 superseded by more comprehensive review or included in an SR
        ii. 71 not a comparison of interest
        iii. 65 not a study design, setting, or population of interest
        iv. 37 not a risk factor of interest
        v. 58 other (e.g., not published in English, not a clinical trial or SR, published outside date range)
    b. Down to Box 9
5. Box 9: 146 included studies

Table A-2. Evidence Base for KQs

Question Number	Question	Number of Studies & Type of Studies
1	What are the most useful tests for a diagnosis of asthma/criteria for specialist referral?	1 SR and 13 diagnostic studies
2	In patients with a fixed obstruction, what diagnostic tests suggest a diagnosis of asthma?	2 cross-sectional studies and 1 prospective cohort study
3	What risk factors (e.g., comorbidities, environmental and occupational exposures) predict: a. Onset of asthma? b. Exacerbations of asthma?	7 SRs and 11 cohort studies
4	What is the comparative effectiveness of initial treatment for asthma? a. How does this vary for mild vs. severe asthma? b. What initial treatments allow patients (e.g., Active Duty military, athletes) to achieve physical activity goals?	3 SRs and 4 RCTs
5	In patients with asthma, what are the long-term potential benefits vs. side effects of chronic inhaled steroid use?	8 SRs and 2 RCTs
6	For patients with treated but uncontrolled asthma, what addition/modification in pharmacologic intervention is effective at controlling asthma?	8 SRs and 6 RCTs
7	In patients with well-controlled asthma, what is the safety and efficacy of step down therapy?	4 SRs and 2 RCTs
8	In patients with asthma, what interdisciplinary treatment approaches improve or prevent the decline of asthma-related outcomes?	4 SRs and 20 RCTs
9	For patients with asthma, what self-management approaches, asthma action plan components, or patient education affect asthma-related outcomes?	5 SRs and 22 RCTs
10	For patients with asthma, what monitoring, assessment, or severity classification tools affect asthma-related outcomes?	2 SRs and 2 RCTs
11	For patients with asthma, what provider-oriented technologies (e.g., decision-support) affect relevant asthma-related outcomes?	1 SR and 5 RCTs
12	For patients with asthma, what patient-oriented technologies (e.g., mobile apps) affect relevant asthma-related outcomes?	4 SRs and 10 RCTs
	Total Evidence Base	**146 studies** **(1 study addressed 2 questions)**

Abbreviations: RCT: randomized controlled trial; SR: systematic review

a. General Criteria for Inclusion in Systematic Review

- Clinical studies or SRs published on or after January 1, 2008 to July 24, 2018. If multiple SRs addressed a KQ, we selected the most recent and/or comprehensive review. SRs were supplemented with clinical studies published subsequent to the SR.
- Studies must be published in English.
- Publication must have been a full clinical study or SR; abstracts alone were not included. Similarly, letters, editorials, and other publications that are not full-length clinical studies were not accepted as evidence.
- SRs must have searched MEDLINE or EMBASE for eligible publications, performed a risk of bias assessment of included studies, and assessed the quality of evidence using a recognizable rating system, such as GRADE or something compatible (e.g., the one used by the AHRQ Evidence-based Practice Centers). If an existing review did not assess the overall quality of the evidence, evidence from the review must be reported in a manner that allowed us to judge the overall risk of bias, consistency, directness, and precision of evidence. We did not use an existing review as evidence if we were not able to assess the overall quality of the evidence in the review.
- Intervention studies must assess diagnostic tests, pharmacologic or non-pharmacologic treatment, interdisciplinary care, self-management, asthma action plan, education, providers or patient-facing technologies and be a prospective, RCT with an independent control group. Randomized crossover trials were included only if data from the first period (prior to treatment crossover) was reported separately.
- Study must have enrolled at least 20 patients (10 per study group) unless otherwise noted (see Key Question Specific Criteria below)
- Study must have enrolled at least 85% of patients who meet the study population criteria: children or adults who may have asthma.
- Study must have reported on at least one outcome of interest.

b. Key Question Specific Criteria

- For KQ 1 and 2, SRs of acceptable study designs, RCTs and diagnostic cohort studies that compare a diagnostic test to clinical assessment, a different diagnostic test, or no diagnostic test were required.
- For KQ 3, SRs of acceptable study designs and comparative observational studies, such as large prospective (>100 patients/arm) or retrospective (>200 patients/arm) cohort or case-controlled studies were required.
- For KQs 4-12, SRs of acceptable study designs and RCTs were required. If there was insufficient evidence from these study designs for any KQ, we considered evidence from large prospective (>100 patients/arm) or retrospective (>200 patients/arm) cohort or case-controlled studies.

Information regarding the bibliographic databases, date limits, and platform/provider can be found in Table A-3, below. Additional information on the search strategies, including topic-specific search terms and search strategies can be found in Appendix K.

Table A-3. Bibliographic Database Information

Name	Date Limits	Platform/Provider
Cochrane Database of Systematic Reviews (Cochrane Reviews)	January 1, 2008 to July 24, 2018	Wiley
Cochrane Central Register of Controlled Trials	January 1, 2008 to July 24, 2018	Wiley
Database of Abstracts of Reviews of Effects	January 1, 2008 to July 24, 2018	Wiley
EMBASE (Excerpta Medica)	January 1, 2008 to July 23, 2018	Elsevier
Health Technology Assessment Database (HTA)	January 1, 2008 to July 24, 2018	Wiley
MEDLINE/PreMEDLINE	January 1, 2008 to July 23, 2018	Elsevier
PsycINFO	January 1, 2008 to July 24, 2018	OvidSP
PubMed (In-process and Publisher records)	January 1, 2008 to July 24, 2018	National Library of Medicine

C. Convening the Face-to-face Meeting

In consultation with the COR, the Champions, and the Work Group, the Lewin Team convened a three and one half day face-to-face meeting of the CPG Champions and Work Group members on October 15–18, 2018. These experts were gathered to develop and draft the clinical recommendations for an update to the 2009 VA/DoD Asthma CPG. Lewin presented findings from the evidence review in order to facilitate and inform the process.

Under the direction of the Champions, the Work Group members were charged with interpreting the results of the evidence review and were asked to categorize and carry forward recommendations from the 2009 VA/DoD Asthma CPG, modifying the recommendations as necessary. The members also developed new clinical practice recommendations not presented in the 2009 VA/DoD Asthma CPG based on the 2018 evidence review. The subject matter experts were divided into three smaller subgroups at this meeting.

As the Work Group members drafted clinical practice recommendations, they also assigned a grade for each recommendation based on a modified GRADE and USPSTF methodology. Each recommendation was graded by assessing the quality of the overall evidence base, the associated benefits and harms, the variation in values and preferences, and other implications of the recommendation.

In addition to developing recommendations during the face-to-face meeting, the Work Group members also revised the 2009 VA/DoD Asthma CPG algorithms to reflect the new and amended recommendations. They discussed the available evidence as well as changes in clinical practice since 2009, as necessary, to update the algorithms.

D. Grading Recommendations

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[8]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence

- Values and preferences
- Other implications, as appropriate, e.g.,:
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

The following sections further describe each domain.

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid event, resolution of symptoms, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse event, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that the majority of clinicians will offer patients therapeutic or preventive measures as long as the advantages of the intervention exceed the risks and adverse effects. The certainty or uncertainty of the clinician about the risk-benefit balance will greatly influence the strength of the recommendation.

Some of the discussion questions that fall under this domain include:

- Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?
- Are the desirable anticipated effects large?
- Are the undesirable anticipated effects small?
- Are the desirable effects large relative to undesirable effects?

Confidence in the quality of the evidence reflects the quality of the evidence base and the certainty in that evidence. This second domain reflects the methodological quality of the studies for each outcome variable. In general, the strength of recommendation follows the level of evidence, but not always, as other domains may increase or decrease the strength. The evidence review used for the development of recommendations, conducted by ECRI, assessed the confidence in the quality of the evidence base using GRADE methodology and assigned a rating of "High," "Moderate," "Low," or "Very Low." The outcomes judged to be critical were used to determine the overall quality of evidence. Per GRADE, if the quality of evidence differs across the critical outcomes, the lowest quality of evidence for any of the relevant critical outcomes determines the overall quality of the evidence for a recommendation; the overall confidence cannot be higher than the lowest confidence in effect estimates for any outcome that is determined to be critical for clinical decision making.[15,145]

The elements that go into the confidence in the quality of the evidence include:

- Is there high or moderate quality evidence that answers this question?
- What is the overall certainty of this evidence?

Values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. More precisely, it refers to the processes that individuals use in considering the potential benefits, harms, costs, limitations, and inconvenience of the therapeutic or preventive measures in relation to one another. For some, the term "values" has the closest connotation to these processes. For others, the connotation of "preferences" best captures the notion of choice. In general, values and preferences increase the strength of the recommendation when there is high concordance and decrease it when there is great variability. In a situation in which the balance of benefits and risks are uncertain, eliciting the values and preferences of patients and empowering them and their surrogates to make decisions consistent with their goals of care becomes even more important. A recommendation can be described as having "similar values," "some variation," or "large variation" in typical values and preferences between patients and the larger populations of interest.

Some of the discussion questions that fall under the purview of values and preferences include:

- Are you confident about the typical values and preferences and are they similar across the target population?
- What are the patient's values and preferences?
- Are the assumed or identified relative values similar across the target population?

Other implications consider the practicality of the recommendation, including resource use, equity, acceptability, feasibility and subgroup considerations. Resource use is related to the uncertainty around the cost effectiveness of a therapeutic or preventive measure. For example statin use in the frail elderly and others with multiple co-occurring conditions may not be effective and, depending on the societal benchmark for willingness to pay, may not be a good use of resources. Equity, acceptability, feasibility, and subgroup considerations require similar judgments around the practically of the recommendation.

The framework below (Table A-4) was used by the Work Group to guide discussions on each domain.

Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgment
Balance of desirable and undesirable outcomes	▪ Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa? ▪ Are the desirable anticipated effects large? ▪ Are the undesirable anticipated effects small? ▪ Are the desirable effects large relative to undesirable effects?	▪ Benefits outweigh harms/burden ▪ Benefits slightly outweigh harms/ burden ▪ Benefits and harms/burden are balanced ▪ Harms/burden slightly outweigh benefits ▪ Harms/burden outweigh benefits
Confidence in the quality of the evidence	▪ Is there high or moderate quality evidence that answers this question? ▪ What is the overall certainty of this evidence?	▪ High ▪ Moderate ▪ Low ▪ Very low
Values and preferences	▪ Are you confident about the typical values and preferences and are they similar across the target population? ▪ What are the patient's values and preferences? ▪ Are the assumed or identified relative values similar across the target population?	▪ Similar values ▪ Some variation ▪ Large variation
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	▪ Are the resources worth the expected net benefit from the recommendation? ▪ What are the costs per resource unit? ▪ Is this intervention generally available? ▪ Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? ▪ Is there lots of variability in resource requirements across settings?	▪ Various considerations

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which combines the four domains.[146] GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances where strong recommendations are warranted even when the quality of evidence is low.[8] In these types of instances where the balance of desirable and undesirable outcomes and values and preferences played large roles in determining the strength of a recommendation, this is explained in the discussion section for the recommendation.

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong For (or "We recommend offering this option …")
- Weak For (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence…")
- Weak Against (or "We suggest not offering this option …")
- Strong Against (or "We recommend against offering this option …")

Note that weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and clinician or they may be qualified with an explanation about the issues that would lead decisions to vary.

E. Recommendation Categorization

a. Recommendation Categories and Definitions

A set of recommendation categories was adapted from those used by NICE.[11,12] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2009 VA/DoD Asthma CPG. The categories and definitions can be found in Table A-5.

Table A-5. Recommendation Categories and Definitions*

Evidence Reviewed	Recommendation Category	Definition
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012) [11] and Garcia et al. (2014) [12]
Abbreviation: CPG: clinical practice guideline

b. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether or not they were based on an updated review of the evidence. If evidence had been reviewed, recommendations were categorized as "New-added," "New-replaced," "Not changed," "Amended," or "Deleted."

"Reviewed, New-added" recommendations were original, new recommendations that were not in the 2009 VA/DoD Asthma CPG. "Reviewed, New-replaced" recommendations were in the previous version of the guideline, but were modified to align with the updated review of the evidence. These recommendations could have also included clinically significant changes to the previous version. Recommendations categorized as "Reviewed, Not changed" were carried forward from the previous version of the CPG unchanged.

To maintain consistency between 2009 recommendations, which were developed using the USPSTF methodology (http://www.uspreventiveservicestaskforce.org), and 2019 recommendations, which were developed using the GRADE methodology, it was necessary to modify the 2009 recommendations to include verbiage to signify the strength of the recommendation (e.g., "We recommend," "We suggest"). Because the 2009 recommendations inherently needed to be modified at least slightly to include this language, the "Not changed" category was not used. For recommendations carried forward to the updated CPG with review of the evidence and slightly modified wording, the "Reviewed, Amended" recommendation category was used. This allowed for the wording of the recommendation to reflect GRADE methodology as well as for any other non-substantive (i.e., not clinically meaningful) language

changes deemed necessary. The evidence used to support these recommendations was carried forward from the previous version of the CPG and/or was identified in the evidence review for the update.

Recommendations could have also been designated "Reviewed, Deleted." These were recommendations from the previous version of the CPG that were not brought forward to the updated guideline after review of the evidence. This occurred if the evidence supporting the recommendations was out of date, to the extent that there was no longer any basis to recommend a particular course of care and/or new evidence suggests a shift in care, rendering recommendations in the previous version of the guideline obsolete.

c. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous version of the CPG without an updated SR of the evidence. Due to time and budget constraints, the update of the Asthma CPG could not review all available evidence on management of asthma, but instead focused its KQs on areas of new or updated scientific research or areas that were not previously covered in the CPG.

For areas of research that have not changed, and for which recommendations made in the previous version of the guideline were still relevant, recommendations could have been carried forward to the updated guideline without an updated SR of the evidence. The support for these recommendations in the updated CPG was thus also carried forward from the previous version of the CPG. These recommendations were categorized as "Not reviewed." If evidence had not been reviewed, recommendations could have been categorized as "Not changed," "Amended," or "Deleted."

"Not reviewed, Not changed" recommendations refer to recommendations from the previous version of the Asthma CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations which were modified from the 2009 VA/DoD Asthma CPG with the updated GRADE language, as explained above.

Recommendations could also have been categorized as "Not reviewed, Deleted" if they were determined to be out of scope. A recommendation was out of scope if it pertained to a topic (e.g., population, care setting, treatment, and condition) outside of the scope for the updated CPG as defined by the Work Group.

The categories for the recommendations included in the 2019 version of the guideline are noted in the Recommendations. The categories for the recommendations from the 2009 VA/DoD Asthma CPG are noted in Appendix I.

F. Drafting and Submitting the Final Clinical Practice Guideline

Following the face-to-face meeting, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2009 VA/DoD Asthma CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2009 VA/DoD Asthma CPG for inclusion in the update. During this time, the Champions and Work Group also made additional revisions to the algorithms, as necessary.

After developing the initial draft of the updated CPG, an iterative review process was used to solicit feedback on and make revisions to the CPG. Once they were developed, the first two drafts of the CPG were posted on a wiki website for a period of 14-20 business days for internal review and comment by the Work Group. All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG.

Draft 3 of the CPG was made available for peer review and comment. This process is described in the section titled Peer Review Process. After revisions were made based on the feedback received during the peer review and comment period, the Champions presented the CPG to the EBPWG for their approval. Changes were made based on feedback from the EBPWG and the guideline was finalized.

The Work Group also produced a set of guideline toolkit materials which included a provider summary, pocket card, and patient summary. The final 2019 Asthma CPG was submitted to the EBPWG in September 2019.

Appendix B: Assessments of Asthma Severity and Control

A. Initial Assessment of Asthma Severity

Table B-1. Initial Assessment of Asthma Severity[a,b,c]

Severity (Assess over a period of at least 4-6 weeks)		Classifying Asthma Severity and Initiating Therapy			
		Intermittent	Mild	Persistent Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2 times/month	>2 times/month but ≤once/week	>1 time/week but not nightly	Nightly
	Use of quick-relief for symptom control	≤2 days/week	>2 days/week but not daily, and not more than once on any day	Daily	Several times/day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk	Exacerbations requiring systemic corticosteroids (consider severity and interval since last episode)	0-1 times/year	Age 4 years: ≥2 exacerbations in 6 months requiring oral or intravenous corticosteroids, OR >4 wheezing episodes/1 year, lasting >1 day AND risk factors for persistent asthma		
			Age ≥5 years and adult: ≥2 exacerbations per year requiring oral or intravenous corticosteroids		

[a] Severity classification does not apply to the active duty population due to different occupational requirements.

[b] Treatment should be based on symptoms (see Recommendation 12 and Recommendation 13), not on the initial assessment of asthma severity. However, this table can be used as reference regarding terminology that is often used to describe severity of asthma based on level of impairment and risk.

[c] This table has been carried forward from the 2009 VA/DoD Asthma CPG. It has been modified from guidance from other organizations (the National Heart, Lung, and Blood Institute [2007] [49] and the Global Initiative for Asthma [2007] [147]).

B. Assessment of Asthma Control

Table B-2. Asthma Control (All Ages)*

Components of Control		Assessing Asthma Control and Adjusting Therapy All Ages	
		Controlled	Not Controlled
Impairment	Daytime Symptoms	≤2 brief symptomatic episodes per week	>2 symptomatic episodes per week
	Nighttime awakening	≤ 2 nights/month	>2 nights/month
	Interference with normal activities	None	Some Limitation
	SABA use for symptom control (not for prevention of EIB)	≤2 treatments/week	>2 treatments/week
	ACT score ages ≥4 years	≥ 20	≤19
Risk	Exacerbation requiring oral systemic steroids	0-1 times/year	≥2 times/year
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.	

*This table has been carried forward from the 2009 VA/DoD Asthma CPG. It has been modified from guidance from other organizations (the National Heart, Lung, and Blood Institute [2007] [49] and the Global Initiative for Asthma [2007] [147]).

Abbreviations: ACT: Asthma Control Test; EIB: exercise-induced bronchospasm; FEV1/FVC: forced expiratory volume/forced vital capacity; SABA: short-acting beta agonist

C. Indications for Specialist Referral

Patients may benefit from referral for assistance in asthma management in the following circumstances:

- Patient has had a recent life-threatening asthma exacerbation
- Patient is not meeting the goals of asthma therapy after 3–6 months of treatment; an earlier referral or consultation is appropriate if the primary care provider concludes that the patient is unresponsive to therapy
- If considering three-drug therapy or high dose of ICS, consider referral to specialty care
- Patient required more than two bursts of oral corticosteroids in one year or had an exacerbation requiring hospitalization
- Other conditions that complicate asthma or its diagnosis (e.g., recurrent sinusitis, nasal polyps, allergic bronchopulmonary aspergillosis [ABPA], severe rhinitis, vocal cord dysfunction, GERD, COPD) that do not respond to appropriate management
- Additional diagnostic testing is indicated (e.g., allergy skin testing, rhinoscopy, complete pulmonary function studies, bronchoscopy)
- Patient is being considered for immunotherapy or specialized medication such as biological agents
- Patient requires additional education and guidance on complications of therapy, problems with adherence, or allergen avoidance (asthma educator)
- Patient/parent requests consultation with a subspecialist

D. Identifying Alternative Diagnoses

Table B-3. Clinical Features Differentiating COPD and Asthma

Clinical Features	COPD	Asthma
Smoker or ex-smoker	Nearly all	Possibly
Symptoms under age 35	Rare	Often
Chronic productive cough	Common	Uncommon
Breathlessness	Persistent and progressive	Variable
Nighttime waking with breathlessness and/or wheeze	Uncommon	Common
Commonly associated with atopic symptoms and seasonal allergies	Uncommon	Common
Significant diurnal or day-to-day variability of symptoms	Uncommon	Common
Favorable response to inhaled glucocorticoids	Inconsistent	Consistent

Abbreviations: COPD: chronic obstructive pulmonary disease

Table B-4. Identifying Alternative Diagnoses Based on Symptoms and Tests

Diagnosis	Symptoms	Test: Results	Radiographic Findings (CT, chest X-ray)	Pulmonary Function Tests
COPD	▪ See VA/DoD COPD CPG[a]; see Table B-3	▪ Arterial blood gas: hypercapnia	▪ Bullous disease ▪ Hyperinflation	▪ Lack of reversibility
Allergic rhinitis	▪ Seasonal or chronic rhinorrhea/nasal obstruction ▪ Daytime and/or morning cough	▪ Trial of antihistamines ▪ Allergy testing ▪ Nasal steroids	▪ N/A	▪ Normal for allergies ▪ Allergic rhinitis common comorbid conditions in asthma
GERD	▪ Heartburn ▪ Irritable after feeding (children) ▪ Commonly asymptomatic	▪ Trial of H2-blocker or proton pump inhibitors ▪ Consider gastrointestinal referral for pH probe: reflux	▪ N/A	▪ N/A
Congestive heart failure/ coronary artery disease	▪ Fatigue ▪ Orthopnea ▪ Paroxysmal nocturnal dyspnea ▪ Dyspnea on exertion ▪ Edema ▪ Weight gain ▪ Hypertension ▪ Diabetes ▪ Coronary artery disease	▪ Echocardiogram: ▪ Low left ventricular ejection fraction ▪ Diastolic dysfunction ▪ B-type natriuretic peptide: elevated	▪ Cardiomegaly ▪ Pulmonary congestion ▪ Pleural effusion	▪ Reversible obstruction uncommon
Vocal cord dysfunction	▪ Poor response to asthma medication ▪ Inspiratory wheeze/stridor ▪ Episodic dyspnea ▪ Rapid onset/relief ▪ Emotional trigger	▪ Laryngoscopy: inspiratory vocal cord closure	▪ Normal	▪ Usually normal; 25% may have blunted inspiratory flow volume loop
Allergic bronchopulmonary aspergillosis	▪ Brownish sputum, wheezing, shortness of breath, fever, malaise	▪ Blood: eosinophilia ▪ Serum precipitins to aspergillus ▪ Very elevated IgE	▪ Recurrent fleeting infiltrates, bronchiectasis	▪ Obstruction

[a] See the VA/DoD Clinical Practice Guideline for the Management of Chronic Obstructive Pulmonary Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/copd/

Diagnosis	Symptoms	Test: Results	Radiographic Findings (CT, chest X-ray)	Pulmonary Function Tests
Sarcoidosis – Multisystem inflammatory disorder; granulomatous changes primarily found in lung	▪ Asymptomatic, shortness of breath, wheezing, cough	▪ Hilar adenopathy ▪ Non-caseating granulomas on biopsy	▪ Stage 0 – None ▪ Stage I – Hilar adenopathy ▪ Stage II – Adenopathy + infilitrates ▪ Stage III – Infiltrates	▪ Normal, restriction, 20% show obstruction
Bronchiectasis – Airway enlargement due to previous infections	▪ Chronic productive cough, wheezing, shortness of breath	▪ None	▪ High resolution CT: localized infiltrates, airway enlargement	▪ Normal or mild obstruction
Pulmonary embolus	▪ Unresponsive to bronchodilator ▪ Hemodynamic compromise ▪ Sudden chest pain ▪ Presence of risk factors ▪ Tachycardia	▪ D-dimer: elevated ▪ Arterial blood gas: hypoxemia	▪ CT: Chest pulmonary embolus protocol ▪ Ventilation/ perfusion mismatch ▪ Chest X-ray normal	▪ N/A
Cystic fibrosis	▪ Recurrent productive cough	▪ Sweat chloride test abnormal	▪ Hyperinflation, cystic changes	▪ Lack of reversibility

Abbreviations: COPD: chronic obstructive pulmonary disease; CT: computed tomography; DoD: Department of Defense; GERD: gastroesophageal reflux disease; IgE: immunoglobulin E; N/A: not applicable; VA: Department of Veteran Affairs

Table B-5. Identifying Alternative Diagnosis Based on Symptoms and Tests: Pediatric-Specific Causes (in Addition to Table B-4)

Diagnosis	Symptoms	Test	Radiographic Finding (CT, chest X-ray)
Foreign body	▪ Unilateral wheeze ▪ Sudden onset ▪ Choking history ▪ Age: 6 months to 6 years	▪ Bronchoscopy	▪ Chest X-ray – Unilateral hyperinflation or atelectasis ▪ Failure to deflate on expiratory or decubitus chest X-ray
Bronchopulmonary dysplasia	▪ Premature birth ▪ History of prolonged mechanical ventilation/oxygen requirement in neonatal period. If responsive to bronchodilators and steroids, treat as asthma	▪ N/A	▪ Chest X-ray: May appear identical to asthma patients
Laryngomalacia	▪ Inspiratory wheeze ▪ Onset prior to 6 weeks of age ▪ Improves when prone ▪ No bronchodilator response	▪ Laryngoscopy	▪ N/A

Diagnosis	Symptoms	Test	Radiographic Finding (CT, chest X-ray)
Subglottic stenosis	▪ History of intubation ▪ Biphasic wheeze, loudest in neck ▪ No bronchodilator response	▪ Bronchoscopy	▪ N/A
Trachea/bronchomalacia	▪ Inspiratory or expiratory monophonic wheeze ▪ No bronchodilator response	▪ Bronchoscopy	▪ N/A
Bronchiolitis (asthma exacerbation caused by viruses)	▪ Diffused wheeze and/or bronchi	▪ No response to beta-2 agonist ▪ Respiratory syncytial virus testing	▪ N/A
Recurrent upper respiratory infection	▪ Common cold symptoms	▪ Reduction of respiratory symptoms after bulb suction or decongestion	▪ N/A

Abbreviations: CT: computed tomography; N/A: not applicable

Appendix C: Details of a Comprehensive History and Physical Exam

A. Details of a Comprehensive History

- The history should focus on the characterization of symptoms related to airway obstruction or airway hyper-responsiveness:
  - Cough
  - Wheezing
  - Shortness of breath
  - Chest tightness
  - Sputum production
- The pattern of symptoms should be characterized:
  - Onset
  - Duration
  - Frequency
  - Diurnal variation
  - Seasonality
- Precipitating and aggravating factors should be explored:
  - Viral infections
  - Exercise
  - Environmental indoor allergens: mold, house dust mites, cockroaches, pets, rodents
  - Environmental outdoor allergens: pollens, molds
  - Secondary tobacco exposure
  - Occupational chemicals, irritants, or allergens
  - Irritants: strong odors, air pollution, chemicals , dusts/particulates , vapors, gases, and aerosols
  - Emotions and/or stress
  - Drugs (e.g., aspirin, nonsteroidal anti-inflammatory drugs)
  - Sulfites in food
  - Cold air
  - Characteristics of the home and/or office: carpeting, wood burning stoves, chemicals
  - Comorbid conditions (e.g., sinusitis, rhinitis, GERD)
- The development of disease and prior symptoms, diagnosis, and treatment should be explored:
  - Age of onset and/or diagnosis
  - Early life airway injury such as bronchopulmonary dysplasia or pneumonia

  - Present or recent management: frequency of SABA use and response, requirement for oral steroids, frequency, and response
- Family history:
  - Asthma
  - Allergy
  - Rhinitis
  - Sinusitis
  - Nasal polyps
  - Eczema
- Social history:
  - Daycare, workplace, school characteristics
  - Social factors interfering with adherence such as substance abuse
  - Social support networks
  - Level of education
  - Employment
- History of prior exacerbations:
  - Prodrome
  - Rapidity of onset
  - Duration
  - Frequency
  - Severity (e.g., hospitalizations, intensive care unit [ICU] admissions, intubations)
  - Life-threatening exacerbations (e.g., intubation, ICU)
  - Number and severity of exacerbations in last 12 months
  - Usual pattern and management
- Impact of the disease on the patient and family:
  - Unscheduled care (e.g., ED, urgent care, hospitalization)
  - Missed school days
  - Limitations in activity including work, sports, and play
  - Nocturnal awakenings
  - Effect on growth, development, behavior
  - Economic impact

- The history should include an assessment of the patient's and family's perceptions of disease:
  - Patient's/parent's/spouse's/partner's knowledge of and belief in disease and treatment
  - Ability of patient and family/support system to cope with disease
  - Level of support
  - Economic resources
  - Sociocultural beliefs

B. Details of a Comprehensive Physical Exam

Physical examination of the upper respiratory tract, neck, chest, heart, and skin may support the diagnosis of asthma. However, the absence of supportive findings does not exclude the diagnosis of asthma.

- Vital signs: hypertension, increased BMI
- Eyes: erythema of the conjunctiva
- Nasopharynx: increased nasal secretions, mucosal swelling, nasal polyps
- Oropharynx: enlarged tonsils, cobblestoning of the posterior pharynx, evidence of upper airway obstruction
- Ears: evidence of otitis media in children
- Neck: adenopathy or mass, jugular vein distension, stridor
- Chest: wheezing at rest, prolonged phase of forced exhalation, hyperexpansion of the thorax, use of accessory muscles, chest deformity, crackles, dullness to percussion
- Heart: rate, rhythm, presence of murmurs, presence of gallops,
- Abdomen: organomegaly
- Skin: presence of atopic dermatitis
- Extremities: edema, clubbing, pulses

Table C-1. Physical Findings

Physical Findings	Asthma	Comorbid Conditions	Alternative Diagnosis
Eyes	N/A	Conjunctivitis	N/A
Ears	N/A	Otitis media	N/A
Oropharynx	Normal	Cobblestoning	Evidence of upper airway obstruction
Neck	Normal	N/A	Mass, stridor, increased jugular vein distension
Chest	Wheeze, prolonged expiration	N/A	Crackles, dullness to percussion
Heart	Normal	N/A	Murmurs or gallops
Abdomen	N/A	N/A	Organomegaly, mass, or bruit
Skin	Atopic dermatitis	N/A	N/A
Extremities	N/A	N/A	Edema, clubbing

Abbreviations: N/A: not applicable

Appendix D: DoD Service-Specific Regulation Concerning Asthma

A. General

Uniformed service members will be evaluated for fitness according to service regulations and policies. Asthma is specifically addressed in these regulations and policies. The services' parent regulations as of this document's publication date are as follows:

- Army: AR40-501, Standards of Medical Fitness, June 14, 2017
- Air Force: AFI 48-123, Medical Examinations And Standards, January 26, 2018
- Navy: NAVMED P-117, The Manual of the Medical Department, June 1, 2018
- Marine Corps: NAVMED P-117, article 15-5, June 1, 2018
- Coast Guard: Medical Manual, COMDTINST M6000.1B

B. Deployment Issues

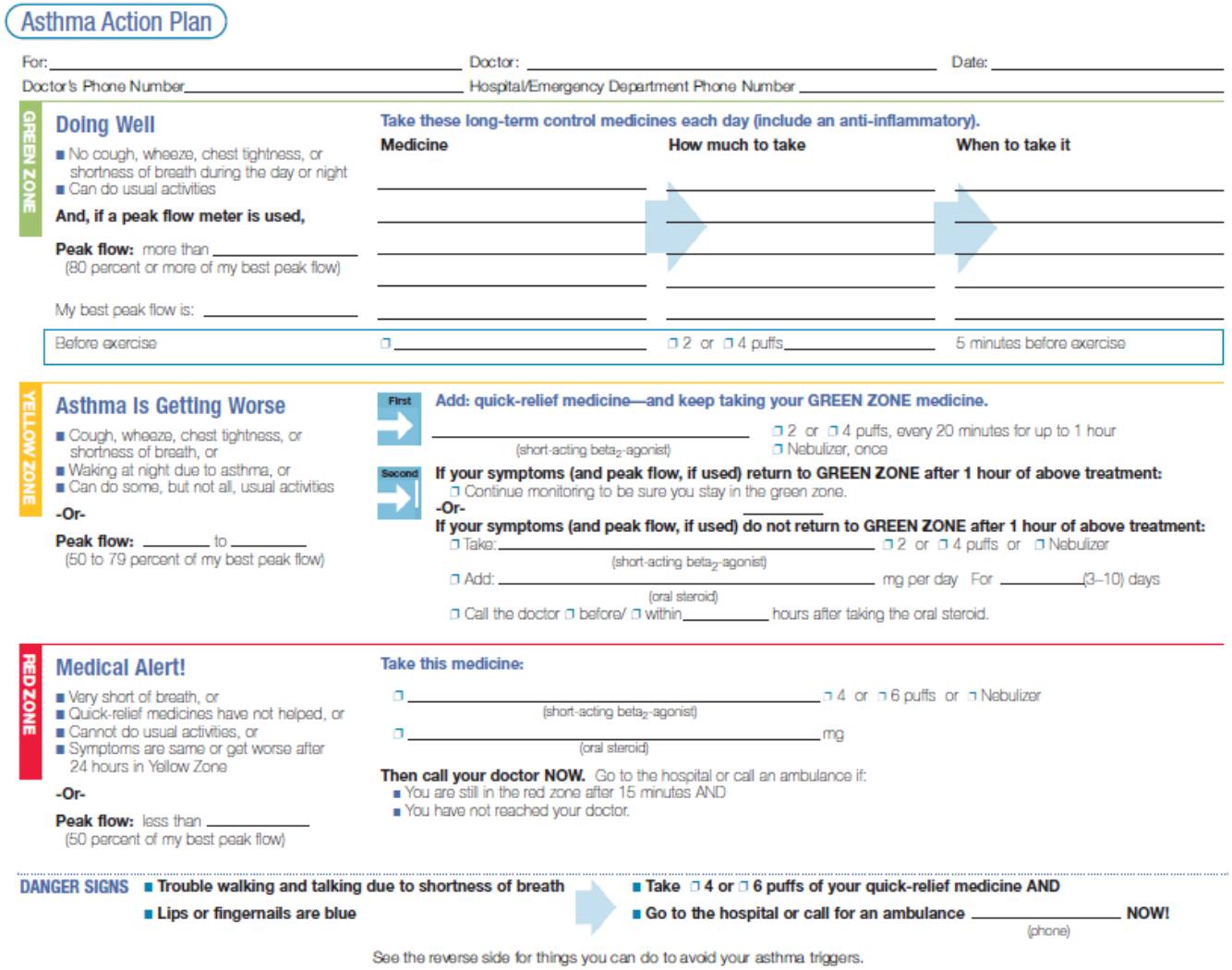
Uniformed service members deploying or stationed outside of the Continental United States (CONUS) may be required to meet more stringent health requirements than their services parent regulations. Healthcare providers assessing service members for deployment should procure the Standard of Fitness to the deployed area of responsibility prior to clearing a service member for deployment or stationing outside of CONUS.

Individuals possessing a disqualifying medical condition must obtain an exception to policy in the form of a medical waiver prior to being medically cleared for deployment. The list of deployment-limiting conditions is not comprehensive; there are many other conditions that may result in denial of medical clearance for deployment based upon the totality of individual medical conditions and the medical capabilities present at that individual's deployed location.

Appendix E: Example Asthma Action Plan Templates

The following are example asthma action plan templates for adults from the National Heart, Lung, and Blood Institute [148] and the DoD.[149] For an example of an asthma action plan template that can be used for children, please check with your local and state health and education departments.

A. National Heart, Lung, and Blood Institute Asthma Action Plan Example Template[148]



Asthma Action Plan

For: _____ Doctor: _____ Date: _____

Doctor's Phone Number _____ Hospital/Emergency Department Phone Number _____

GREEN ZONE

Doing Well

- No cough, wheeze, chest tightness, or shortness of breath during the day or night
- Can do usual activities

And, if a peak flow meter is used,

Peak flow: more than _____ (80 percent or more of my best peak flow)

My best peak flow is: _____

Take these long-term control medicines each day (include an anti-inflammatory).

Medicine	How much to take	When to take it
Before exercise	❒ _____	❒ 2 or ❒ 4 puffs _____	5 minutes before exercise

YELLOW ZONE

Asthma Is Getting Worse

- Cough, wheeze, chest tightness, or shortness of breath, or
- Waking at night due to asthma, or
- Can do some, but not all, usual activities

-Or-

Peak flow: _____ to _____ (50 to 79 percent of my best peak flow)

First

Add: quick-relief medicine—and keep taking your GREEN ZONE medicine.

_____ (short-acting beta$_2$-agonist) ❒ 2 or ❒ 4 puffs, every 20 minutes for up to 1 hour ❒ Nebulizer, once

Second

If your symptoms (and peak flow, if used) return to GREEN ZONE after 1 hour of above treatment:

❒ Continue monitoring to be sure you stay in the green zone.

-Or-

If your symptoms (and peak flow, if used) do not return to GREEN ZONE after 1 hour of above treatment:

❒ Take: _____ (short-acting beta$_2$-agonist) ❒ 2 or ❒ 4 puffs or ❒ Nebulizer

❒ Add: _____ (oral steroid) mg per day For _____ (3–10) days

❒ Call the doctor ❒ before/ ❒ within _____ hours after taking the oral steroid.

RED ZONE

Medical Alert!

- Very short of breath, or
- Quick-relief medicines have not helped, or
- Cannot do usual activities, or
- Symptoms are same or get worse after 24 hours in Yellow Zone

-Or-

Peak flow: less than _____ (50 percent of my best peak flow)

Take this medicine:

❒ _____ (short-acting beta$_2$-agonist) ❒ 4 or ❒ 6 puffs or ❒ Nebulizer

❒ _____ (oral steroid) mg

Then call your doctor NOW. Go to the hospital or call an ambulance if:

- You are still in the red zone after 15 minutes AND
- You have not reached your doctor.

DANGER SIGNS

- **Trouble walking and talking due to shortness of breath**
- **Lips or fingernails are blue**

- **Take ❒ 4 or ❒ 6 puffs of your quick-relief medicine AND**
- **Go to the hospital or call for an ambulance _____ (phone) NOW!**

See the reverse side for things you can do to avoid your asthma triggers.

How To Control Things That Make Your Asthma Worse

This guide suggests things you can do to avoid your asthma triggers. Put a check next to the triggers that you know make your asthma worse and ask your doctor to help you find out if you have other triggers as well. Then decide with your doctor what steps you will take.

Allergens

❒ **Animal Dander**

Some people are allergic to the flakes of skin or dried saliva from animals with fur or feathers.

The best thing to do:

- Keep furred or feathered pets out of your home.

If you can't keep the pet outdoors, then:

- Keep the pet out of your bedroom and other sleeping areas at all times, and keep the door closed.
- Remove carpets and furniture covered with cloth from your home. If that is not possible, keep the pet away from fabric-covered furniture and carpets.

❒ **Dust Mites**

Many people with asthma are allergic to dust mites. Dust mites are tiny bugs that are found in every home—in mattresses, pillows, carpets, upholstered furniture, bedcovers, clothes, stuffed toys, and fabric or other fabric-covered items.

Things that can help:

- Encase your mattress in a special dust-proof cover.
- Encase your pillow in a special dust-proof cover or wash the pillow each week in hot water. Water must be hotter than 130° F to kill the mites. Cold or warm water used with detergent and bleach can also be effective.
- Wash the sheets and blankets on your bed each week in hot water.
- Reduce indoor humidity to below 60 percent (ideally between 30—50 percent). Dehumidifiers or central air conditioners can do this.
- Try not to sleep or lie on cloth-covered cushions.
- Remove carpets from your bedroom and those laid on concrete, if you can.
- Keep stuffed toys out of the bed or wash the toys weekly in hot water or cooler water with detergent and bleach.

❒ **Cockroaches**

Many people with asthma are allergic to the dried droppings and remains of cockroaches.

The best thing to do:

- Keep food and garbage in closed containers. Never leave food out.
- Use poison baits, powders, gels, or paste (for example, boric acid). You can also use traps.
- If a spray is used to kill roaches, stay out of the room until the odor goes away.

❒ **Indoor Mold**

- Fix leaky faucets, pipes, or other sources of water that have mold around them.
- Clean moldy surfaces with a cleaner that has bleach in it.

❒ **Pollen and Outdoor Mold**

What to do during your allergy season (when pollen or mold spore counts are high):

- Try to keep your windows closed.
- Stay indoors with windows closed from late morning to afternoon, if you can. Pollen and some mold spore counts are highest at that time.
- Ask your doctor whether you need to take or increase anti-inflammatory medicine before your allergy season starts.

Irritants

❒ **Tobacco Smoke**

- If you smoke, ask your doctor for ways to help you quit. Ask family members to quit smoking, too.
- Do not allow smoking in your home or car.

❒ **Smoke, Strong Odors, and Sprays**

- If possible, do not use a wood-burning stove, kerosene heater, or fireplace.
- Try to stay away from strong odors and sprays, such as perfume, talcum powder, hair spray, and paints.

Other things that bring on asthma symptoms in some people include:

❒ **Vacuum Cleaning**

- Try to get someone else to vacuum for you once or twice a week, if you can. Stay out of rooms while they are being vacuumed and for a short while afterward.
- If you vacuum, use a dust mask (from a hardware store), a double-layered or microfilter vacuum cleaner bag, or a vacuum cleaner with a HEPA filter.

❒ **Other Things That Can Make Asthma Worse**

- Sulfites in foods and beverages: Do not drink beer or wine or eat dried fruit, processed potatoes, or shrimp if they cause asthma symptoms.
- Cold air: Cover your nose and mouth with a scarf on cold or windy days.
- Other medicines: Tell your doctor about all the medicines you take. Include cold medicines, aspirin, vitamins and other supplements, and nonselective beta-blockers (including those in eye drops).

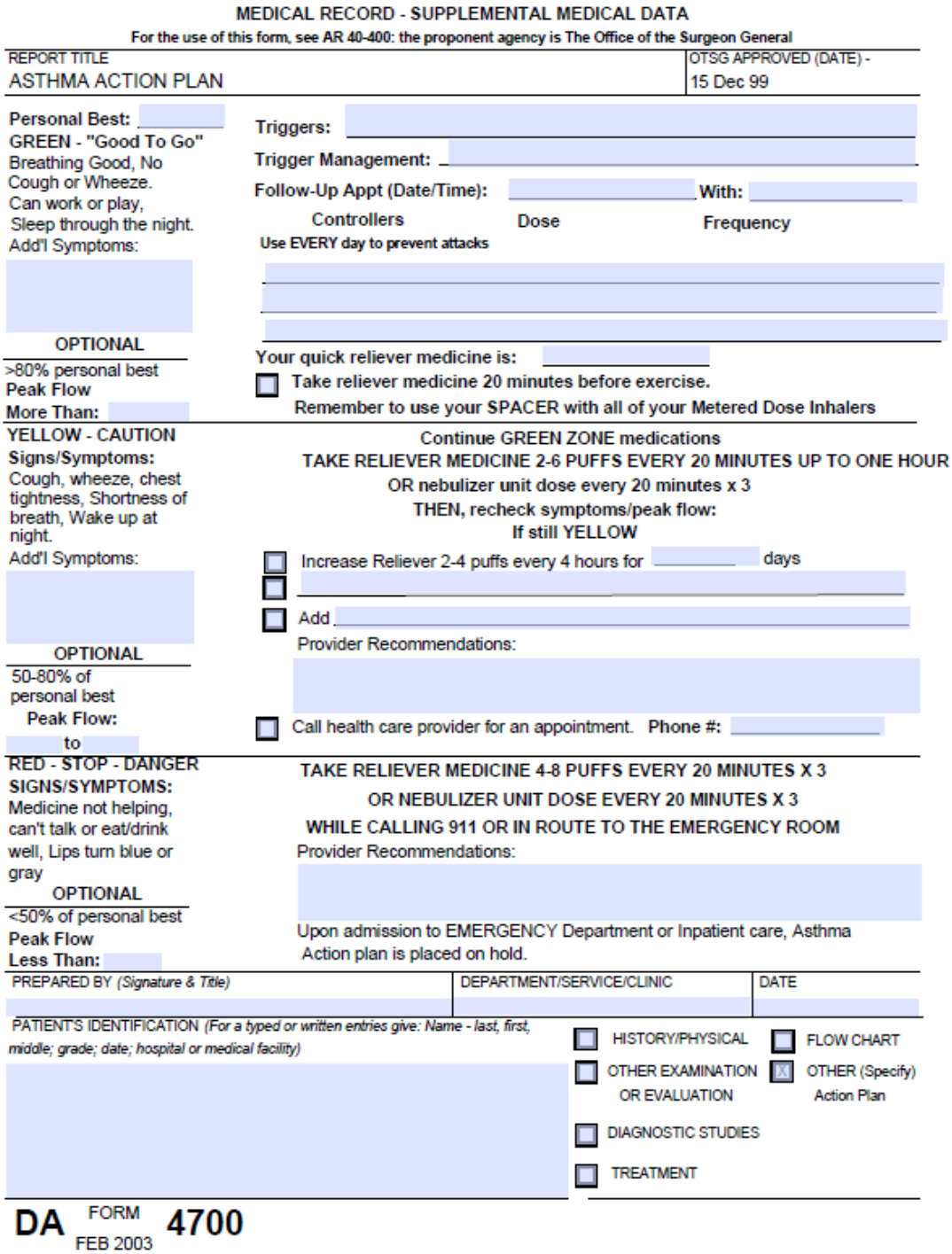
U.S. Department of Health and Human Services
National Institutes of Health

National Heart Lung and Blood Institute

For More Information, go to: www.nhlbi.nih.gov

NIH Publication No. 07-5251
April 2007

B. Department of Defense Asthma Action Plan Example Template[149]



MEDICAL RECORD - SUPPLEMENTAL MEDICAL DATA

For the use of this form, see AR 40-400: the proponent agency is The Office of the Surgeon General

REPORT TITLE	OTSG APPROVED (DATE) -
ASTHMA ACTION PLAN	15 Dec 99

Personal Best: _____

GREEN - "Good To Go"
Breathing Good, No Cough or Wheeze.
Can work or play,
Sleep through the night.
Add'l Symptoms:

OPTIONAL
>80% personal best
Peak Flow
More Than:

Triggers:
Trigger Management:
Follow-Up Appt (Date/Time): **With:**

Controllers	Dose	Frequency
Use EVERY day to prevent attacks		

Your quick reliever medicine is:

☐ **Take reliever medicine 20 minutes before exercise.**
Remember to use your SPACER with all of your Metered Dose Inhalers

YELLOW - CAUTION
Signs/Symptoms:
Cough, wheeze, chest tightness, Shortness of breath, Wake up at night.
Add'l Symptoms:

OPTIONAL
50-80% of personal best
Peak Flow:
to

Continue GREEN ZONE medications
TAKE RELIEVER MEDICINE 2-6 PUFFS EVERY 20 MINUTES UP TO ONE HOUR
OR nebulizer unit dose every 20 minutes x 3
THEN, recheck symptoms/peak flow:
If still YELLOW

☐ Increase Reliever 2-4 puffs every 4 hours for _____ days
☐
☐ Add
Provider Recommendations:

☐ Call health care provider for an appointment. **Phone #:**

RED - STOP - DANGER
SIGNS/SYMPTOMS:
Medicine not helping, can't talk or eat/drink well, Lips turn blue or gray

OPTIONAL
<50% of personal best
Peak Flow
Less Than:

TAKE RELIEVER MEDICINE 4-8 PUFFS EVERY 20 MINUTES X 3
OR NEBULIZER UNIT DOSE EVERY 20 MINUTES X 3
WHILE CALLING 911 OR IN ROUTE TO THE EMERGENCY ROOM
Provider Recommendations:

Upon admission to EMERGENCY Department or Inpatient care, Asthma Action plan is placed on hold.

PREPARED BY *(Signature & Title)*	DEPARTMENT/SERVICE/CLINIC	DATE

PATIENT'S IDENTIFICATION *(For a typed or written entries give: Name - last, first, middle; grade; date; hospital or medical facility)*

☐ HISTORY/PHYSICAL ☐ FLOW CHART
☐ OTHER EXAMINATION OR EVALUATION ☒ OTHER (Specify) Action Plan
☐ DIAGNOSTIC STUDIES
☐ TREATMENT

DA FORM FEB 2003 **4700**

Appendix F: Additional Information on Pharmacotherapy

A. Considerations Regarding Biological Agents

The Work Group determined that patients for which biological agents are being considered should be referred from primary to specialty care. These medications are out of the scope of this CPG, as they are not intended to be used in primary care. Thus, primary care practitioners should consult a pulmonologist or allergist prior to offering biologic agents (including omalizumab, mepolizumab, benralizumab, reslizumab, dupilumab) approved for treatment of asthma. Biologic agents targeting immunoglobulin E (IgE) (omalizumab), interleukin-5 (mepolizumab, reslizumab, benralizumab), and interleukin-4 (dupilumab) are used as add-on therapy for moderate-to-severe asthma that is inadequately controlled (e.g., remains symptomatic, asthma exacerbations) with ICS and other controller medications. Compared to placebo, these agents have reduced exacerbations and showed modest improvement in patient symptoms and quality of life. A steroid-sparing effect has been demonstrated in studies in patients who were receiving maintenance oral steroids. Omalizumab is for moderate-to-severe persistent asthma in patients six years of age and older with sensitivity to a perennial aeroallergen and elevated serum IgE. Mepolizumab, reslizumab, and benralizumab are for patients with severe asthma who have an eosinophilic phenotype. Mepolizumab and benralizumab are approved for those who are 12 years and older and reslizumab is approved for those 18 years and older. Dupilumab is for moderate-to-severe asthma in patients 12 years of age and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.[150-154]

B. Considerations Regarding Theophylline

The Work Group determined that patients for which theophylline is being considered should be referred from primary to specialty care. This medication is out of the scope of this CPG, as it is not intended to be used in primary care. Theophylline is considered a mild-to-moderate bronchodilator and may have mild anti-inflammatory effects. LABA or LTRA are preferred as add-on therapy to ICS. Theophylline is associated with significant food and medication interactions and adverse reactions including insomnia, anxiety, nausea, vomiting, tremor, arrhythmias, delirium, seizures, and death. Patients on theophylline should be maintained at a serum level of 5-15 mcg/ml with routine monitoring of serum level. Theophylline might be considered as a non-preferred alternative when other options cannot be used or have been unsuccessful.[111,155]

C. Additional Information on Drugs Used in Treatment of Asthma

Table F-1. Drugs Used in Treatment of Asthma

Drug Class[a]	Place in Therapy	Clinical Considerations[b]
SABA ▪ Albuterol (MDI/Neb SOLN) ▪ Levalbuterol (MDI/Neb SOLN)	Short-acting agents are used for acute relief of bronchospasm, intermittent asthma, and prevention of exercise-induced bronchospasm	▪ May cause palpitations, chest pain, rapid heart rate, increased blood pressure, tremor, nervousness ▪ Decreases in potassium levels or hyperglycemia have occurred ▪ Frequent use of SABA (>2 days/week) may indicate uncontrolled asthma and the need to intensify drug therapy regimen
ICS ▪ Beclomethasone (MDI) ▪ Budesonide (DPI/Neb SOLN) ▪ Ciclesonide (MDI) ▪ Fluticasone (MDI/DPI) ▪ Mometasone (MDI/DPI)	Considered first line agents for maintenance treatment of asthma	▪ Local adverse effects include oral candidiasis, dysphonia, and reflex cough/bronchospasm. Advise patients to rinse mouth and spit after use of ICS ▪ Prolonged use may slow growth rate in children and adolescents ▪ Higher doses have been associated with adrenal suppression, glaucoma, cataracts, skin thinning, bruising, osteoporosis
LABA ▪ Salmeterol (DPI) ▪ Olodaterol (SMI)[c] ▪ Indacaterol (DPI)[c] ▪ Formoterol (Neb SOLN)[c] ▪ Arformoterol (Neb SOLN)[c]	Preferred add-on agents to inhaled corticosteroids	▪ May cause palpitations, chest pain, rapid heart rate, increased blood pressure, tremor, nervousness ▪ Decreases in potassium levels or hyperglycemia have occurred ▪ Because of the risk of asthma-related death and hospitalization, use of a LABA for the treatment of asthma without concomitant use of a long-term asthma control medication, such as an ICS, is contraindicated
Combination ICS/LABA ▪ Budesonide/formoterol (MDI) ▪ Fluticasone/salmeterol (MDI/DPI) ▪ Mometasone/formoterol (MDI) ▪ Fluticasone/vilanterol (DPI)	Fixed-dose combination ICS/LABA is preferred over using both drugs as separate inhalers to encourage adherence to therapy	See comments for ICS and beta agonists

Drug Class[a]	Place in Therapy	Clinical Considerations[b]
Leukotriene Modifiers ▪ Montelukast (tablets, chewable tablet, oral granules) ▪ Zafirlukast tablets ▪ Zileuton (immediate-release and extended-release tablets)	▪ Monotherapy may be considered as an alternative (not preferred) to ICS for mild persistent asthma ▪ May be used as an alternative (not preferred) to a LABA for add on therapy to ICS ▪ Montelukast may be used for prevention of exercise-induced bronchospasm (zafirlukast and zileuton are not FDA approved)	▪ Neuropsychiatric events (e.g., suicidal ideation, depression, agitation, aggression, anxiousness, irritability, restlessness, dream abnormalities, hallucinations, and insomnia) have been reported. ▪ Rare cases of systemic eosinophilia, eosinophilic pneumonia, or clinical features of vasculitis consistent with eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss) have occurred with montelukast and zafirlukast and may be associated with the reduction of oral steroid therapy. ▪ Serious hepatic adverse events have been reported with zafirlukast. Use in patients with hepatic impairment, including hepatic cirrhosis is contraindicated. ▪ Zileuton may result in increased hepatic transaminases and liver injury. Zileuton is contraindicated in patients with active liver disease or persistent serum alanine aminotransferase elevations of 3 or more times the upper limit of normal ▪ Zileuton is not indicated in children <12 years ▪ Montelukast chewable tablets contain phenylaniline ▪ Do not abruptly substitute leukotriene modifiers for inhaled or oral corticosteroids; reduce steroids gradually
Long-acting anticholinergics (LAMA) ▪ Tiotropium (SMI/DPI) Note: Tiotropium is the only LAMA approved for asthma. Only the SMI is approved for use in asthma in patients ≥6 years.	▪ May be considered as an alternative for add-on to ICS if unable to use LABAs ▪ May be used as add-on for those who remain symptomatic despite maximal therapy with ICS/LABA (recommend referral to specialist)	▪ Maximum benefits may take up to 4-8 weeks of dosing ▪ May cause dizziness and blurred vision ▪ Caution patient to avoid getting product in eyes; temporary blurred vision may result ▪ Use with caution in patients with narrow angle glaucoma, prostatic hyperplasia, or bladder neck obstruction as these conditions may worsen ▪ Use with caution in patients with moderate to severe renal impairment (CrCl ≤60 mL/minute); monitor patient for anticholinergic adverse events. ▪ Contraindicated in patients who have had hypersensitivity to ipratropium

[a] Refer to product package insert or other established resources for dosing recommendations and age specific use.

[b] Table is not intended to be inclusive of all clinical considerations but rather to highlight some of the key points.

[c] Approved for maintenance therapy for COPD; at present, they are not approved for use in asthma.

Abbreviations: COPD: chronic obstructive pulmonary disease; CrCl: creatinine clearance; DPI: dry powder inhaler; FDA: U.S. Food and Drug Administration; ICS: inhaled corticosteroid; LABA: long-acting beta agonist; LAMA: long-acting muscarinic antagonist; MDI: metered dose inhaler; mL: milliliter; SABA: short-acting beta agonist; SMI: soft mist inhaler; Neb SOLN: nebulizer solution

Table F-2. Inhaled Steroids[a, b]

Inhaled Steroid Strengths	Usual dosing interval	FDA-approved ages	Comparative Dose (mcg/day)				Highest recommended dose per product labeling (mcg/day)
			Ages	Low Dose	Medium Dose	High Dose	
Beclomethasone MDI (*QVAR REDIHALER*) 40, 80 mcg	Twice daily	≥4 years	≥ 12 years 4-11 years	80-240 80-160	>240-480 >160-320	>480 >320	640 160
Budesonide DPI (*PULMICORT FLEXHALER*) 90, 180 mcg	Twice daily	≥6 years	≥18 years 6-17 years	180-540 180-360	>540-1170 >360-720	>1200 >800	1440 720
Ciclesonide MDI (*ALVESCO*) 80, 160 mcg	Twice daily	≥12 years[c]	≥12 years	80-160	>160-320	>320	640
Fluticasone propionate MDI (*FLOVENT HFA*) 44, 110, 220 mcg	Twice daily	≥4 years	≥12 years 4-11 years	88-264 88-176	>264-440 >176-352	>440 >352	1760 176
Fluticasone propionate DPI (*FLOVENT DISKUS*) 50, 100, 250 mcg	Twice daily	≥4 years	≥12 years 4-11 years	100-300 100-200	>300-500 >200-400	>500 >400	2000 200
Fluticasone propionate DPI (*ARMONAIR RESPICLICK*) 55, 113, 232 mcg	Twice daily	≥12 years	≥12 years	110	226	464	464
Fluticasone furoate DPI (*ARNUITY ELLIPTA*) 50,100, 200 mcg	Once daily	≥5 years	≥12 years[d]	100	N/A	200	200 (≥12 years) 50 (5-11 years)
Mometasone DPI (*ASMANEX TWISTHALER*) 110, 220 mcg	Once or twice daily	≥4 years	≥12 years[e]	110-220	>220-440	>440	880 (≥12 years) 110 (4-11 years)
Mometasone HFA (*ASMANEX HFA*) 100, 200 mcg	Twice daily	≥12 years	≥12 years	100-200	>200-400	>400	800

[a] Comparative daily dose adapted from guidance from National Heart, Lung, and Blood Institute [147] and Global Initiative for Asthma [49]

[b] For dosing recommendations, refer to the manufacturer's product package insert.

[c] Although ciclesonide is not approved for children <12 years of age, there are clinical data using ciclesonide once daily in this population.

[d] The dose of fluticasone furoate (*ARNUITY*) dry powder inhaler for children aged 5-11 years is 50 mcg daily.

[e] The dose of mometasone dry powder inhaler for childresn aged 4-11 years is 110 mcg daily.

Abbreviations: DPI: dry powder inhaler; FDA: U.S. Food and Drug Administration; HFA: hydrofluoroalkane; mcg: microgram; MDI: metered dose inhaler; N/A: not applicable

Appendix G: Patient Focus Group Methods and Findings

A. Methods

In March 2018, the VA and the DoD commenced the effort to update the VA/DoD Asthma CPG. As part of the effort to update this CPG, VA and DoD Leadership held a patient focus group. The focus group was held on June 22, 2018 at Womack Army Medical Center in Fort Bragg, NC. The aim of the focus group was to further understand the perspective of patients receiving treatment for asthma and who are covered and/or receiving their care through the VA and/or DoD healthcare systems, as these patients are most affected by the recommendations put forth in the CPG. The focus group delved into the patients' perspectives on a set of topics related to management of asthma, including their priorities, challenges they have experienced, the information they received regarding their care, as well as the impact of their care on their lives.

Participants for the focus group were recruited by VA and DoD Leadership as well as by the Asthma CPG Champions. Selection of patient focus group participants was not designed to obtain a representative sample of VA and DoD patients. However, recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the guideline development process. Patients were not incentivized for their participation or reimbursed for travel expenses.

The Asthma CPG Champions and Work Group, with support from Lewin, developed a set of questions to help guide the focus group. The focus group facilitator led the discussion using the previously prepared questions as a general guide to elicit the most important information from the patients regarding their experiences and views about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all of the listed questions were addressed.

B. Patient Focus Group Findings

a. Ensure that patient history and symptoms are taken into account when assessing pulmonary issues. Once a patient is diagnosed with asthma, help the patient understand his or her triggers.

- In some cases, patients indicated that they had experienced asthma symptoms repeatedly before receiving a diagnosis of asthma.
- Patients seemed to find it helpful to understand their triggers, as they were better able to prepare for and control their asthma symptoms.

b. For every patient, establish and maintain an asthma action plan in conjunction with the patient. Leverage multiple types of clinical expertise (e.g., pulmonologists, clinical pharmacists) when educating the patient on their condition, their asthma action plan, and treatment adherence.

- Participants agreed that an asthma action plan should be provided to every patient, regardless of his or her experience with asthma and previous knowledge regarding the condition and its treatment.

- The majority of patients stated they did not recall having received education regarding asthma or its treatment, and the participants thought that patients would benefit from improved education, such as in a group class.

c. Work with the patient to identify an effective treatment for asthma, considering co-occurring conditions. Be mindful that different patients may respond to medications differently.

- While all patients used a rescue inhaler, only some used maintenance medications.
- Some participants adhered to the medication schedule prescribed by their provider. However, some others had difficulty adhering to their medication schedules.
- Participants sometimes needed to change medications due to, for example, side effects, perceived loss of efficacy, and changes in the formulary. In most cases, these changes were favorable; however, in some cases, the participants needed to change to a less effective medication due to access limitations.
- Many patients had co-occurring conditions in addition to asthma; therefore, it was important that they understood the tradeoffs between their asthma medications and treatment(s) for their other conditions and the best options for their particular situation.

d. Be mindful that, in some cases, diagnosis of asthma or the inability to achieve control of asthma symptoms may affect an active duty Service Member differently than a civilian.

- The active duty Service Member needed to achieve specific goals on physical training tests and be able to complete certain tasks in order to avoid occupational consequences, such as a medical board.
- Although the active duty Service Member who participated in the focus group indicated his colleagues were supportive of him and understood his condition, the focus group participants indicated that the situation for other active duty Service Members may be different (i.e., less understanding).

e. Ensure that various types of clinicians are engaged as appropriate (e.g., specialists provide pulmonary expertise as needed based on patient condition, clinical pharmacists provide education). Leverage telehealth, mobile applications, and other information technology to the extent that it is available and helpful for the patient.

- Participants thought it was most helpful when their providers were explicit regarding their treatment. They indicated that a provider other than their primary care provider or their pulmonologist (e.g., a clinical pharmacist) could provide education regarding asthma and its treatment.
- Although they were skeptical of the usefulness of telehealth to diagnose and assess asthma, participants thought telehealth would be useful to be able to accomplish some healthcare activities, particularly for patients who lived farther away from their healthcare facility.

f. Acknowledge the seriousness of asthma and its impact on the life of the patient. Discuss the patient's goals for asthma treatment and help each patient work toward those goals.

- Participants expressed concern that, in some cases, providers and other members of the community do not regard asthma as a serious condition.
- Throughout the focus group, participants mentioned goals for their treatment and indicated that providers could help them achieve these goals by providing clear education and information regarding their treatment.

Appendix H: Evidence Table

Table H-1. Evidence Table[a,b,c,d]

Recommendation	2009 Grade	Evidence	Strength of Recommendation	Recommendation Category
1. We suggest spirometry if there is a need to confirm a clinical diagnosis of asthma.	None, None, None, C	[21,22]	Weak for	Reviewed, New-replaced
2. In primary care, we suggest against whole-body plethysmography as part of the diagnostic evaluation of asthma.	None, C, None, B	[23]	Weak against	Reviewed, New-replaced
3. There is insufficient evidence to recommend for or against the routine use of bronchodilator response testing to exclude the initial diagnosis of asthma in the absence of airway obstruction.	B	[21,24]	Neither for nor against	Reviewed, New-replaced
4. If bronchoprovocation testing is considered, we suggest methacholine challenge testing.	C, None	[25-30]	Weak for	Reviewed, New-replaced
5. We recommend against offering computed tomography scan to diagnose asthma in patients with persistent airflow obstruction post-bronchodilator.	Not applicable	[31] **Additional References:** [32-34]	Strong against	Reviewed, New-added

[a] 2010 Grade column: The 2009 VA/DoD Asthma CPG used the USPSTF evidence grading system. Inclusion of more than one 2009 Grade indicates that more than one 2009 CPG recommendation is covered under the 2019 recommendation. The strength of recommendations were rated as follows: A- a strong recommendation that the clinicians provide the intervention to eligible patients; B- a recommendation that clinicians provide (the service) to eligible patients; C- no recommendation for or against the routine provision of the intervention is made; D- recommendation is made against routinely providing the intervention; I- the conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. "None" indicates that the 2009 VA/DoD Asthma CPG recommendation was not graded. "Not applicable" indicates that the 2019 Asthma CPG recommendation was a new recommendation, and therefore does not have an associated 2009 Grade.

[b] Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference needed to be identified through the 2018 evidence review or included in the evidence base for the 2009 VA/DoD Asthma CPG. The second set of references in the evidence column (called "Additional References") includes references that provide additional information related to the recommendation, but which were not systematically identified through a literature review. These references were not included in the evidence base for the recommendation and therefore did not influence the strength and direction of the recommendation.

[c] Strength of Recommendation column: Refer to the Grading Recommendations section for more information on how the strength of the recommendation was determined using GRADE methodology.

[d] Strength of Recommendation column: Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

Recommendation	2009 Grade	Evidence	Strength of Recommendation	Recommendation Category
6. In adults and children with asthma, we suggest identifying known risk factors of asthma-related outcomes including overweight/obesity, atopy, secondhand smoke exposure in children, and history of lower respiratory infection.	None, None, C, B, C, None, C, A, B, B	[6,35-46] **Additional References:** [47-50]	Weak for	Reviewed, New-replaced
7. In adults with asthma, we suggest identifying known risk factors of asthma-related outcomes including depression, current smokers, and Operation Iraqi Freedom/Operation Enduring Freedom combat deployment.	None, None, C, B, C, None, C, A, B, B	[6,35-46] **Additional References:** [47-50]	Weak for	Reviewed, New-replaced
8. We suggest offering a written asthma action plan to improve asthma-related quality of life.	None, A, B, A, A, None	[51,54,55] **Additional References:** [52,53]	Weak for	Reviewed, New-replaced
9. We suggest offering asthma education.	B	[56-72]	Weak for	Reviewed, New-replaced
10. There is insufficient evidence to recommend one particular asthma education program or education component(s) over others.	B	[57-64,66-72]	Neither for nor against	Reviewed, New-replaced
11. There is insufficient evidence to recommend for or against patient-oriented technologies (e.g., mobile apps, web based, or telemedicine) as a means to reduce the number or severity of asthma-related exacerbations.	B, B	[73-86]	Neither for nor against	Reviewed, New-replaced
12. For patients with persistent asthma, we recommend inhaled corticosteroids as initial controller medication.	None, None, None, None, A, A	[87-95]	Strong for	Reviewed, Amended
13. Among patients with moderate-to-severe persistent asthma and significant symptom burden, we suggest offering a combination of inhaled corticosteroid and long-acting beta agonist as initial controller treatment.	None, None	[89,96-108]	Weak for	Reviewed, New-replaced

Recommendation	2009 Grade	Evidence	Strength of Recommendation	Recommendation Category
14. For patients with asthma not controlled by inhaled corticosteroids alone, we suggest adding long-acting beta agonists as a step-up treatment over increasing inhaled corticosteroids alone or adding long-acting muscarinic antagonists or leukotriene receptor antagonists.	None, None. A, A, A, B, A, A, A	[98,100-106,110,111] **Additional References:** [109]	Weak for	Reviewed, New-replaced
15. In patients with controlled asthma on a stable medication regimen, we suggest either stepping down (not discontinuing) inhaled corticosteroids dose or discontinuing long-acting beta agonists.	None, None	[112-117]	Weak for	Reviewed, New-replaced
16. We suggest short-acting beta agonists or leukotriene receptor antagonists for prevention of exercise-induced bronchospasm.	A, C, C	[119,120]	Weak for	Not reviewed, Amended
17. We suggest a multidisciplinary treatment approach to improve asthma-related quality of life, asthma control, and treatment adherence.	None	[121-132]	Weak for	Reviewed, New-replaced
18. We suggest patients with asthma participate in regular exercise to improve quality of life and asthma control.	B	[118,134,135] **Additional References:** [133]	Weak for	Reviewed, Amended
19. We suggest offering cognitive behavioral therapy as a means of improving asthma-related quality of life and self-reported asthma control for adult patients with persistent asthma.	Not applicable	[122] **Additional References** [136]	Weak for	Reviewed, New-added
20. We suggest against utilizing spirometry for routine monitoring of patients with stable asthma.	A, None, None, None	[21,137]	Weak against	Reviewed, New-replaced
21. There is insufficient evidence to recommend for or against routine use of fractional exhaled nitric oxide in monitoring patients in primary care settings to improve asthma-related clinical outcomes.	None	[44,139,140] **Additional References:** [138]	Neither for nor against	Reviewed, New-replaced
22. We suggest leveraging electronic health record capabilities such as trackers and reminders in the care of patients with asthma.	Not applicable	[71,75,141-143]	Weak for	Reviewed, New-added

Appendix I: 2009 Recommendation Categorization Table

Table I-1. 2010 Recommendation Categorization Table[a,b,c,d,e]

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
2.1	1	17	During the diagnostic evaluation a thorough history should be performed to include focus on the following elements (see Appendix B-1 for expanded details of the history): A. Characterization of symptoms related to airway obstruction or airway hyper-responsiveness to include cough, wheezing, shortness of breath, chest tightness, and sputum production B. In children, cough may be the only presenting symptom, while wheezing may not be present in some patients with asthma C. The pattern of symptoms should be characterized to include onset, duration, frequency, diurnal variation, and seasonality D. Precipitating and aggravating factors (including occupational exposure) E. Prior diagnosis, prior symptoms, prior exacerbations, and prior therapies F. Review of all current medications including over-the-counter and supplements G. Family and social history.	N/A	Reviewed, Deleted	--
2.1	2	18	In children, a thorough birth history must also be obtained. Important factors in a birth history would include evidence of maternal smoking, prematurity, chronic lung disease, bronchopulmonary dysplasia, and postnatal smoke exposure.	N/A	Reviewed, Deleted	--

[a] 2009 Location column: The first three columns indicate the location of each recommendation within the 2009 VA/DoD Asthma CPG.
[b] 2009 Recommendation Text column: This column contains the wording of each recommendation from the 2009 VA/DoD Asthma CPG.
[c] 2010 Grade column: The 2009 VA/DoD Asthma CPG used the U.S. Preventive Services Task Force (USPSTF) evidence grading system: http://www.uspreventiveservicestaskforce.org. The strength of recommendations were rated as follows: A- a strong recommendation that the clinicians provide the intervention to eligible patients; B- a recommendation that clinicians provide (the service) to eligible patients; C- no recommendation for or against the routine provision of the intervention is made; D- recommendation is made against routinely providing the intervention; I- the conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. "N/A" indicates there was no grade assigned to the recommendation in the 2009 VA/DoD Asthma CPG.
[d] Recommendation Category column: This column indicates the way in which each 2009 VA/DoD Asthma CPG recommendation was updated.
[e] 2019 Recommendation column: For recommendations that were carried forward to the 2019 VA/DoD Asthma CPG, this column indicates the new recommendation(s) to which they correspond.

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
2.1	3	18	Careful review of systems for any condition which can mimic asthma, such as pulmonary emboli, congestive heart failure, congenital heart disease, viral syndromes, or hypersensitivity pneumonitis.	N/A	Reviewed, Deleted	--
2.1	4	18	During the diagnostic evaluation, a thorough physical examination should be performed, emphasizing findings in the following areas (see Appendix B-2 for expanded details of the physical exam): A. Upper respiratory tract, including presence of increased nasal secretions, mucosal swelling, or nasal polyps B. Chest, including wheezing during normal breathing or prolonged forced exhalation, hyperexpansion of the thorax, use of accessory muscles, or chest deformity C. Skin, including the presence of atopic dermatitis or eczema D. Absence of the above findings does not exclude the diagnosis of asthma and the examination should include findings that may support alternative diagnoses (see Appendix B-2) E. Consider cardiac evaluation of all murmurs or evidence of cardiovascular disease before initiating, or concurrent with initiating, asthma therapy.	N/A	Reviewed, Deleted	--
2.2	1	19	In the pediatric and adolescent patients, a chest radiograph should be considered during the initial treatment period to rule out other diagnoses.	N/A	Not reviewed, Deleted	--
2.2	2	19	In the adult patient with new symptoms suggestive of asthma, a chest radiograph should always be obtained during the initial evaluation.	N/A	Not reviewed, Deleted	--
2.3	1	19	Alternative diagnoses should be considered in all patients, and in particular those over age 30 and under age two with new symptoms suggestive of asthma. (see Tables 2 and 3)	N/A	Not reviewed, Deleted	--
2.3	2	19	A significant history of smoking exceeding 20 pack years makes the diagnosis of COPD more likely than asthma.	N/A	Reviewed, New-replaced	Recommendation 6 Recommendation 7
2.3	3	20	Absence of airway obstruction on initial spirometry should prompt consideration for alternative diagnoses and additional testing.	N/A	Reviewed, New-replaced	Recommendation 1
2.3	4	20	Abnormalities found on Chest X-Ray (CXR) screening should prompt referral to a specialist for further evaluation.	N/A	Not reviewed, Deleted	--
2.3	5	20	When there is no clear response to initial therapy, other significant causes of airway obstruction must be considered.	N/A	Not reviewed, Deleted	--

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
2.3.1	1	23	The presence of restrictive indices on spirometry (reduction in both FEV1 and FVC) should prompt the clinician to perform full pulmonary function testing to include lung volumes and diffusing capacity.	N/A	Not reviewed, Deleted	--
2.3.1	2	23	In those patients with confirmed restriction on full pulmonary function testing, referral to specialty care is indicated.	N/A	Not reviewed, Deleted	--
2.3.1	3	23	In those patients with normal spirometry and significant pulmonary symptoms, consideration should also be given to full pulmonary function testing to exclude mild reductions in vital capacity or diffusing capacity.	N/A	Not reviewed, Deleted	--
2.3.1	4	23	Careful review of the flow volume loop should be performed on all spirometric exams to look for the presence of truncated or flattened loops suggestive of possible upper airway obstruction.	N/A	Not reviewed, Deleted	--
2.3.2	1	24	Spirometry should be performed in accordance with published standards and documented in the medical record. In general, there is no minimum age for spirometry, but patients under age 5 may not be able to perform breathing maneuvers correctly.	A	Not reviewed, Deleted	--
2.3.2	2	24	A diagnosis of expiratory airflow limitation can be made in accordance with validated reference values (such as National Health and Nutrition Examination Survey (NHANES) III as recommended by the ATS/ERS guidelines).	N/A	Not reviewed, Deleted	--
2.3.2	3	24	The presence of obstruction should be based on a forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) value less than the fifth percentile and not on the percent reduction of the FEV1. (Healthcare providers not trained in the interpretation of spirometry should have the results reviewed by a specialist.)	B	Not reviewed, Deleted	--
2.3.2	4	24	If airway obstruction is present or there is suspicion of asthma, spirometry should be repeated post-bronchodilators to establish the presence and degree of reversibility of the FEV1.	B	Reviewed, New-replaced	Recommendation 3
2.3.2	5	24	A 10-12 percent increase in the FEV1 (and > 200 ml in adults) may be considered significant airway reversibility.	C	Reviewed, New-replaced	Recommendation 4
2.3.3	1	26	Refer patients to a pulmonary function laboratory capable of performing bronchoprovocation testing in accordance with American Thoracic Society (ATS) standards.	N/A	Reviewed, New-replaced	Recommendation 4

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
2.3.3	2	26	The preferred method for bronchoprovocation testing is histamine or methacholine challenge testing. Other established methods are less commonly available such as cold air or eucapnic hyperventilation.	N/A	Reviewed, New-replaced	Recommendation 2
2.3.3	3	26	Exercise challenge testing is a less sensitive test for detecting the presence of airway hyperreactivity and may be considered for symptoms primarily associated with exertion.	N/A	Not reviewed, Deleted	--
2.3.4	1	27	Biomarkers such as nitric oxide are not currently validated clinical indicators of asthma severity or control and should not be used in the primary care setting as a means of diagnosis or evaluating response to therapy.	N/A	Reviewed, New-replaced	Recommendation 21
2.3.4	2	27	Biomarker evaluation is best performed in specialty clinics where such testing is frequently conducted and interpreted.	N/A	Not reviewed, Deleted	--
2.3.5	1	28	Consider allergy testing in patients with asthma with symptoms suggesting significant co-morbid allergic rhinoconjunctivitis or if recommended by specialty referral.	N/A	Not reviewed, Deleted	--
2.3.5	2	28	Allergy testing may be useful in the diagnostic evaluation of asthma to: A. Identify atopy and co-morbid allergic rhinoconjunctivitis as risk factors for the development of asthma B. Identify precipitating factors and/or triggers related to asthma symptoms and worsening co-morbid allergic rhinoconjunctivitis C. Allergy testing in children is less sensitive.	B	Not reviewed, Deleted	--

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
2.4	1	29	Patients who are under consideration for an asthma diagnosis by their primary care provider should be referred to a subspecialist (Allergist / Immunologist, Pulmonologist, Gastroenterologist, Otolaryngologist) if any of the following are present: A. Findings NOT consistent with typical asthma diagnosis that should prompt referral to specialty: • Poor growth / failure-to-thrive (especially in infants and children) • Cyanosis at feeding (infants and children) • Vomiting at feeding (infants and children) • Clubbing • Stridor / upper airway wheeze • Hemoptysis • Any significant chest radiograph abnormality • Lymphadenopathy • Persistent oxygen requirement • Chest pain • Pneumothorax • Recurrent bacterial pneumonia • Monophonic or unilateral wheeze • Recurrent bronchitis (only for adults) • History of anaphylaxis • Chronic productive cough or irreversible airway obstruction on spirometry in the absence of a diagnosis of COPD B. Signs and symptoms are atypical, or there are problems in differential diagnosis such that the primary care provider is uncertain of making an asthma diagnosis C. Patient requires confirmation of a history that suggests that an occupational or environmental inhalant or ingested substance is provoking or contributing to asthma.	C	Not reviewed, Deleted	--
2.4	2	30	Patients who have significant psychiatric, substance abuse, psychosocial, or family problems that interfere with their asthma therapy may need referral to an appropriate mental health professional for counseling or treatment.	B	Not reviewed, Deleted	--

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
2.4	3	30	Patient/parent requests for consultation with subspecialist.	N/A	Not reviewed, Deleted	--
3.1	1	31	Patients with asthma should be questioned about the frequency of heartburn symptoms, effectiveness of previous treatments, and the presence of symptoms such as nocturnal cough or wheezing, morning hoarseness, or sore throat even in the absence of heartburn.	B	Not reviewed, Deleted	--
3.1	2	31	Parents of children under age 5 should be questioned about irritability after feeds, regurgitation while supine, or complaints of chest pain that may be a manifestation of GERD.	B	Not reviewed, Deleted	--
3.1	3	31	Treatment should include specific food avoidance (especially caffeine and alcohol), avoidance of food and drink 3 hours before bedtime, elevation of head of bed, and appropriate pharmacologic therapy.	C	Not reviewed, Deleted	--
3.2	1	32	Patients with asthma should undergo an assessment for allergic rhinitis or sinusitis that is either seasonal or year-round in variation. This assessment should include a history of seasonal variations, specific triggers, diurnal variation, and changes in the workplace.	B	Not reviewed, Deleted	--
3.2	2	32	Physical examination of all patients with asthma should include evaluation for the presence of conjunctival inflammation, nasal mucosal inflammation, nasal discharge, polyps, and post nasal drip.	B	Not reviewed, Deleted	--
3.2	3	32	Consideration for allergy testing should be given to patients with asthma who have allergic rhinitis and who experience year-round symptoms or difficulty controlling asthma.	B	Not reviewed, Deleted	--
3.2	4	32	Adequate treatment of allergic rhinitis or sinusitis should be undertaken in an effort to improve asthma outcomes. Treatment may include allergen avoidance, medications, immunotherapy, or surgical therapy.	B	Not reviewed, Deleted	--
3.3	1	33	Weight loss should be highly encouraged in patients with asthma who are overweight or obese to improve pulmonary mechanics, decrease exacerbations, and reduce the use of steroids, especially in children who are more likely to have asthma persistence.	C	Not reviewed, Deleted	--
3.4	1	34	Overweight patients with asthma should be questioned about their sleep habits and hygiene and in particular a history of loud snoring, excessive daytime somnolence, and witnessed apneas.	N/A	Not reviewed, Deleted	--

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
3.4	2	34	Patients with excessive daytime somnolence or witnessed apneas should be referred for sleep testing (polysomnography).	B	Not reviewed, Deleted	--
3.4	3	34	Patients with unstable uncontrolled asthma and sleep apnea should be treated with continuous positive airway pressure (CPAP). Weight loss, dental appliances, and evaluation for surgery may be considered in selected patients.	C	Not reviewed, Deleted	--
4	1	35	Current impairment and risk of exacerbations should be assessed in the initial evaluation of asthma to classify severity (see Table 5).	N/A	Not reviewed, Deleted	--
4	2	35	A history of asthma symptoms, nighttime awakenings, need for SABA for relief of symptoms and interference with activities should be used to assess current impairment.	N/A	Not reviewed, Deleted	--
4	3	36	The frequency and severity of asthma exacerbations should be used in assessing the domain of risk. Lung function and psychosocial factors may also help predict risk.	N/A	Not reviewed, Deleted	--
4	4	36	Spirometry should be used in the initial assessment of all patients who are capable of performing an adequate expiratory maneuver. Lung function is a measure of impairment but may also predict risk.	N/A	Not reviewed, Deleted	--
4	5	36	Classification of severity of the disease should be based on initial assessment of the patient who is not on long-term control therapy.	N/A	Reviewed, Amended	Recommendation 13
5.1	1	38	Patient and parent education on asthma self-management should begin at diagnosis and be reviewed regularly.	N/A	Not reviewed, Deleted	--
5.1	2	38	Patients and parents should be familiar with, and receive education from, the entire healthcare team: physicians, nurses, pharmacists, respiratory therapists, etc.	N/A	Reviewed, New-replaced	Recommendation 17
5.1	3	38	Communication with the patient/parents should focus on patient-centered goals of treatment; at every visit, reinforce self-management of asthma.	N/A	Not reviewed, Deleted	--
5.1	4	38	Written asthma action plans, developed jointly between patient and provider, should focus on daily management and techniques to manage exacerbations for all patients with asthma.	N/A	Reviewed, New-replaced	Recommendation 8
5.2	1	39	Patients with persistent asthma should be evaluated for possible allergen and environmental triggers that can be avoided (see Section 9 – Environmental Control), including outdoor activity if levels of air pollution are high.	N/A	Not reviewed, Deleted	--

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
5.2	2	39	Patients should be advised to avoid non-selective beta-blocker therapy.	B	Not reviewed, Deleted	--
5.2	3	39	Encourage avoidance of sulfite-containing foods or other foods determined by history to trigger exacerbations.	B	Not reviewed, Deleted	--
5.2	4	39	NSAID and aspirin use in patients with nasal polyps, severe persistent asthma, or known NSAID/ASA sensitivity should be strictly avoided.	B	Not reviewed, Deleted	--
5.2	5	39	All patients with asthma who are older than 6 months of age should receive inactivated flu vaccine to decrease the risk of complications from infection with influenza. Patient or parents should be counseled that the vaccination will not decrease the frequency or severity of exacerbations during the flu season.	A	Not reviewed, Deleted	--
5.2	6	39	Pneumococcal polysaccharide vaccine should be administered to adults with chronic persistent asthma.	B	Not reviewed, Deleted	--
5.3	1	40	Patients who do not respond to typical asthma therapy should be reevaluated for the presence of unmanaged co-morbid conditions.	N/A	Not reviewed, Deleted	--
5.3	2	40	Identify and treat conditions such as allergic rhinitis, sinusitis, gastro-esophageal reflux, obstructive sleep apnea, obesity, substance abuse, depression, or other mental health disorders to ensure optimal control of asthma.	N/A	Reviewed, New-replaced	Recommendation 6 Recommendation 7
5.4	1	41	Patients diagnosed with persistent asthma require treatment with an inhaled corticosteroid to reduce inflammation. Additional long-term control medications such as long-acting beta agonists (LABAs) or leukotriene inhibitors may be added based on initial asthma severity and subsequent assessment of control to relieve bronchospasm. Patients must never be treated solely with long-acting beta2-agonists.	N/A	Reviewed, Amended	Recommendation 13
5.4	2	41	Short-Acting Beta Agonists (SABAs) should be used for relief of acute asthma symptoms. An asthma action plan is needed to guide home use of SABAs. Two to six puffs of SABA may be used in accordance with the asthma action plan. Patients who do not experience relief after 3 doses in a one hour period OR who need a dose more frequently than every 4 hours, should seek medical care.	N/A	Not reviewed, Deleted	--
5.4	3	42	To ensure adequate medication delivery, an appropriate inhaler device should be used. Device selection must include consideration of the patient's developmental age and ability to perform proper technique (see Table 8 Comparison of Inhaler Devices).	N/A	Not reviewed, Deleted	--

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
5.4	4	42	A large volume spacer such as the Aerochamber should be used in patients who have difficulty using metered-dose inhalers.	N/A	Not reviewed, Deleted	--
5.5	1	43	Patients and their caregivers should be educated regarding the essential and basic facts about asthma that includes: A. What defines well-controlled asthma B. Roles of medications C. Appropriate technique in using inhaler devices D. Self-monitoring (either symptom or peak flow-based) E. Identification of triggers and environmental exposure control measures F. When and how to handle signs and symptoms of worsening asthma G. When and where to seek care.	B	Reviewed, New-replaced	Recommendation 10
5.5	2	43	Asthma self-management education should be incorporated into all points of contact with the patient and his/her caregivers.	B	Reviewed, New-replaced	Recommendation 11
5.6	1	44	Patients should be encouraged to continue regular exercise and activities of daily living.	A	Reviewed, Amended	--
5.6	2	44	Ensure family members, teachers, coaches, and school nurses are aware of the basic principles of asthma symptom recognition and management for acute exacerbation.	N/A	Not reviewed, Deleted	--
5.6	3	44	All patients should have a written asthma action plan that includes instructions for recognition of worsening conditions along with actions to take at home/work/school/daycare.	A	Reviewed, New-replaced	Recommendation 8

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
5.6	4	44	Patients should be educated about the instructions included in the action plan. A. Education regarding exercise-induced asthma: • Explain that pharmacologic therapies and other strategies may improve exercise tolerance and decrease the occurrence of exercise-related symptoms • Use SABA 20 minutes prior to planned exertion; if symptoms appear during activity, a repeated dose of SABA may be offered as addressed in the written asthma action plan • Extend warm-up periods prior to exercise B. Education regarding occupational asthma • Obtaining serial peak flow values both at work and away from work may suggest a relationship between work and asthma • Patients with occupation-related asthma may require referral to an occupational health specialist	A,B	Not reviewed, Deleted	--
5.6	5	45	Managing asthma during school/day care activities: A. The asthma action plan for children should be provided to the school and/or daycare B. Establish a partnership with schools and/or daycare centers to provide education programs for staff and/or peers C. Use of medication: • Controller medication: ▪ If possible, schedule controller medications to be given at home and not at school or daycare ▪ If patient adherence is questionable, medication may need to be given at school to ensure compliance during the school year ▪ When daily controller medication is required at school/daycare, the ability of school/daycare personnel to administer the medication should be determined • Rescue medication: ▪ Rescue medications should be available at school/daycare ▪ For school-age children, determine availability of rescue medication; some school systems do not allow children to personally carry any medication ▪ For daycare or young school-age children, the ability of the staff to administer medication should be determined.	C,B,N/A	Reviewed, Deleted	--

2009 Location			2009 Recommendation Text	2009 Grade	Recommendation Category	2019 Recommendation
Section	Number	Page				
5.7	1	46	Asthma care should be provided in an environment that is culturally and ethnically sensitive and at an educational level appropriate to the patient and caregivers.	A	Reviewed, Deleted	--
5.7	2	46	Socio-economic barriers to patient adherence to asthma care should be identified with the patient and caregivers, and addressed by education or appropriate referrals.	B	Reviewed, Deleted	--
5.7	3	46	Psychiatric disorders, to include chronic stress or depression, should be identified and patients referred as appropriate.	B	Not reviewed, Deleted	--
6.1	1	48	Patients with a new diagnosis of asthma, regardless of initial severity, should be seen frequently until they are on an effective regimen and demonstrate sufficient understanding of their disease management. Thereafter, patients with intermittent and mild persistent asthma should be seen at least every 6 months. Those asthma patients with more labile or persistent symptoms should have more frequent follow up.	B	Not reviewed, Deleted	--
6.1	2	48	Every patient with asthma should be taught to recognize their asthma symptoms, and a written asthma action plan, developed in partnership with the patient, should detail the daily management (medications and environmental control strategies), and how to recognize and handle worsening asthma. The action plan is particularly recommended for patients who have moderate or severe asthma, a history of severe exacerbations, or poorly controlled asthma. The written plan can be either symptom or peak flow-based; evidence shows similar benefits for each.	B	Reviewed, New-replaced	Recommendation 8
6.1	3	48	Periodic pulmonary function tests or spirometry to assess asthma control should be performed: A. At the initial evaluation B. After treatment and stabilization C. If symptoms worsen D. If change of medication is considered.	A	Reviewed, New-replaced	Recommendation 20
6.1	4	48	Periodic spirometry should be considered in patients with controlled symptoms to assess changes in airways function.	N/A	Reviewed, New-replaced	Recommendation 20
6.1	5	48	Providers should consider giving patients a peak flow device and including peak flow values in written action plans for adults. Peak flow devices would be especially useful in patients with moderate-severe asthma, poor perceivers of symptoms, and those with frequent asthma exacerbations. Peak flow devices may help the patient and provider assess changes in therapy and detect changes in disease state.	N/A	Not reviewed, Replaced	Recommendation 20

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6.1	6	48	Self-assessment tools should be considered in monitoring patients with asthma. Examples include: A. Asthma Control Test (ACT) scores used for assessment of symptoms over the past 4 weeks B. Quality of life monitors to determine a patient's satisfaction with asthma control and care.	B	Not reviewed, Deleted	--
6.1	7	48	Patient adherence and inhaler technique should be evaluated at every asthma visit.	N/A	Not reviewed, Deleted	--
6.1	8	48	Adherent patients with poorly controlled asthma or intolerance of medications should be referred to a specialist.	N/A	Not reviewed, Deleted	--
6.2	1	50	Ongoing monitoring is essential to maintain control of asthma. Patients should be monitored at 2-6 week intervals after initial evaluation and treatment to re-evaluate their response and current symptoms.	N/A	Reviewed, Deleted	--
6.2	2	50	Regular follow-up contacts at 1 to 6-month intervals, depending on level of control, are recommended to ensure that control is maintained. A closer follow-up and objective measurement of airway obstruction should be obtained whenever the patient's asthma medication regimen is changed.	N/A	Reviewed, Deleted	--
6.2	3	50	When adjusting medications: (see Table 7): A. If asthma is not controlled on current regimen, a 'step up' in therapy is indicated after assuring that the patient has good adherence and technique with the medication B. If asthma is partially controlled, the provider should consider 'stepping up' the patient's medication until control is achieved C. If the patient is able to maintain control of asthma symptoms for at least 3-6 months on their medicine regimen, a 'step down' or decrease in their asthma control medication may be considered.	N/A	Reviewed, New-replaced	Recommendation 14 Recommendation 15
7	1	52	Stable asthma patients with persistent mild, moderate, or severe asthma should be seen for a visit every 6 months unless symptoms warrant sooner follow-up.	N/A	Reviewed, Deleted	--
7	2	52	Stable asthma patients with persistent mild, moderate, or severe asthma should receive spirometry at initial evaluation, after treatment and stabilization, if they experience worsening of symptoms, and at least every 1-2 years.	N/A	Reviewed, New-replaced	Recommendation 20

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7	3	52	Aspects of the follow-up visit should include: A. An interim focused history, review of signs and symptoms, and physical exam B. Obtaining history of acute exacerbations C. Assessing the impact of co-morbid conditions affecting asthma control D. Identifying new environmental triggers E. Reviewing spirometry and peak flow monitoring F. Assessing adherence to treatment, spacer use or MDI technique G. Assessing indications for step-down or step-up therapy H. Reviewing and updating patient education and written Action Plans I. Preventive health maintenance, including smoking status of patients and family members J. Scheduling the next follow-up visit.	N/A	Reviewed, Deleted	--

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7.1	1	53	Patients may benefit from referral for assistance in asthma management in the following circumstances: A. Patient has had a life-threatening asthma exacerbation B. Patient is not meeting the goals of asthma therapy after 3–6 months of treatment. An earlier referral or consultation is appropriate if the primary care provider concludes that the patient is unresponsive to therapy C. Patient requires step 4 care or higher (step 3 for children 0–4 years of age). Consider referral if patient requires step 3 care (step 2 for children 0–4 years of age) D. Patient required more than two bursts of oral corticosteroids in 1 year or had an exacerbation requiring hospitalization E. Other conditions that complicate asthma or its diagnosis (e.g., recurrent sinusitis, nasal polyps, aspergillosis, severe rhinitis, VCD, GERD, COPD) that do not respond to appropriate management F. Additional diagnostic testing is indicated (e.g., allergy skin testing, rhinoscopy, complete pulmonary function studies, bronchoscopy) G. Patient is being considered for immunotherapy or specialized medication such as omalizumab H. Patient requires additional education and guidance on complications of therapy, problems with adherence, or allergen avoidance (Asthma Educator) I. Patient / parent requests consultation with a subspecialist.	N/A	Not reviewed, Deleted	--
8.1	1	54	Always prescribe an inhaled short-acting bronchodilator for use as needed for intermittent symptoms.	N/A	Not reviewed, Deleted	--
8.1	2	54	Always prescribe an anti-inflammatory controller medication for use in persistent asthma.	N/A	Reviewed, Amended	Recommendation 13
8.1	3	54	Inhaled corticosteroids are the preferred anti-inflammatory controller.	N/A	Reviewed, Amended	Recommendation 13
8.1	4	55	Alternative anti-inflammatory controllers include anti-leukotriene, and cromolyn sodium medications.	N/A	Reviewed, Deleted	--
8.1	5	55	Consider prescribing a long-acting bronchodilator controller medication for use in persistent asthma in addition to an anti-inflammatory controller.	N/A	Reviewed, New-replaced	Recommendation 13
8.1	6	55	The preferred long-acting bronchodilator controller is an inhaled long-acting beta2-agonist.	N/A	Reviewed, New-replaced	Recommendation 13

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8.1	7	55	Alternative controller medications include oral theophylline, oral beta2-agonists, and anti-IgE antibody injections.	N/A	Reviewed, New-replaced	Recommendation 15
8.1	8	55	The dosage of inhaled corticosteroids and added use of combination controller therapy is determined by the degree of initial and ongoing impairment and risk.	N/A	Reviewed, Deleted	--
8.1	9	55	Step-care includes both stepping up and stepping down the dosage and use of combination controller therapy. Stepping down therapy may be considered after a minimum period of stability (3-6 months).	N/A	Reviewed, New-replaced	Recommendation 15
8.2.1	1	55	All patients should have a SABA as needed for acute relief of symptoms.	A	Not reviewed, Deleted	--
8.2.1	2	55	SABAs should not be used on a scheduled basis for maintenance therapy.	N/A	Not reviewed, Deleted	--
8.2.1	3	55	Providers should evaluate frequency of SABA use. Use of SABA more than 2 days/week for symptom control, increasing use, or lack of expected response may indicate inadequate asthma control and the need to intensify maintenance drug therapy.	N/A	Not reviewed, Deleted	--
8.2.1	4	55	Clinical efficacy and safety are comparable between racemic and non-racemic agents; therefore, the least costly agent may be selected.	N/A	Not reviewed, Deleted	--
8.2.2	1	56	ICS should be used as first-line therapy to control persistent asthma.	A	Reviewed, Amended	Recommendation 12
8.2.2	2	56	ICS initial dosing should be based on the asthma severity.	N/A	Reviewed, Deleted	--
8.2.2	3	56	ICS should be integrated into a step care approach.	A	Reviewed, Amended	Recommendation 12
8.2.2	4	56	ICS treatment should be monitored for adverse effects and the patient/parent should be counseled regarding management adverse effects.	N/A	Not reviewed, Deleted	--
8.2.2	5	56	ICS delivery via nebulization should be administered using specific nebulizer equipment.	N/A	Not reviewed, Deleted	--
8.2.2	1	57	LABAs are not recommended for treatment of acute symptoms or exacerbations.	I	Not reviewed, Deleted	--
8.2.2	2	57	LABAs must NOT to be used as monotherapy for maintenance treatment of asthma.	D	Reviewed, Deleted	--
8.2.2	3	57	LABAs are the preferred agents for add-on therapy to ICS.	A	Reviewed, New-replaced	Recommendation 14

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8.2.2	4	57	LABAs should be integrated into a step care approach: A. For patients who are not adequately controlled on low-dose ICS, consider increasing the dose of ICS or adding a LABA. Strong preference should be given to increasing the dose of inhaled corticosteroid due to safety concerns, while recognizing that efficacy is greater with the addition of a LABA. B. For patients who are not adequately controlled on moderate/high-dose ICS, the addition of a LABA is preferred to further increasing the ICS dose. C. Combining a LABA + ICS is preferred to combining a LABA + leukotriene receptor antagonist (LTRA) for greater efficacy.	A	Reviewed, New-replaced	Recommendation 14
8.2.2	5	57	Patient/parent counseling and monitoring for LABA adverse effects should be performed.	N/A	Not reviewed, Deleted	--
8.2.2	1	57	Monotherapy with leukotriene modifiers may be considered as an alternative (not preferred) to ICS for mild persistent asthma.	A	Reviewed, Deleted	--
8.2.2	2	58	Leukotriene modifiers may be used as an alternative (not preferred) to LABA for add-on therapy to ICS.	A	Reviewed, New-replaced	Recommendation 14
8.2.2	3	58	Zileuton is NOT recommended for use in children < 12 years of age, and is discouraged from use in adults due to safety concerns (liver toxicity).	D	Not reviewed, Deleted	--
8.2.2	4	58	Leukotriene modifiers should be integrated into a step care approach.	B	Reviewed, New-replaced	Recommendation 14
8.2.2	1	60	Cromolyn may be considered as an alternative for mild persistent asthma when other preferred options have not been successful.	A	Not reviewed, Deleted	--
8.2.2	2	60	Consult a specialist if the use of cromolyn is being considered.	I	Not reviewed, Deleted	--
8.2.2	1	61	Theophylline may be considered as an alternative for maintenance of mild persistent asthma when other preferred options have not been successful. Consult a specialist if maintenance therapy with theophylline is being considered.	N/A	Reviewed, Deleted	--
8.2.2	2	61	Theophylline may be considered as an adjunctive therapy with ICS for maintenance of moderate or persistent asthma.	N/A	Reviewed, Deleted	--
8.2.2	3	61	Patients on theophylline should be maintained at a serum level of 5-15 mcg/ml with routine monitoring of serum level.	N/A	Not reviewed, Deleted	--

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8.2.2	1	61	Omalizumab may be considered, in consultation with a specialist, as adjunctive therapy for severe persistent asthma (step 5 or 6) in patients with sensitivity to relevant allergens.	I	Not reviewed, Deleted	--
8.2.2	1	62	Consult a specialist if maintenance therapy with an oral corticosteroid is being considered.	N/A	Not reviewed, Deleted	--
8.2.3	1	62	Combination ICS with LABA is preferred over ICS and LTRA, or zileuton or theophylline for the treatment of moderate persistent asthma.	A	Reviewed, New-replaced	Recommendation 14
8.2.3	2	62	Combination of low-dose ICS with LABA may be considered equivalent to medium dose ICS for the treatment of moderate persistent asthma.	C	Not reviewed, Deleted	--
8.2.3	3	62	Combination of high-dose ICS with LABA is the preferred therapy for severe persistent asthma.	A	Reviewed, New-replaced	Recommendation 14
8.2.3	4	62	Addition of LABA is preferred to further increasing the ICS dose for patients who are not adequately controlled on medium-dose ICS.	A	Reviewed, New-replaced	Recommendation 14
8.3	1	64	Metered Dose Inhalers with Valved Holding Chambers are as effective as nebulizer therapy for delivery of aerosolized medications (quick relief) in the adult and pediatric patient.	B	Not reviewed, Deleted	--
9.1	1	65	For all patients with asthma at any level of severity: A. Use the patient's medical history to identify allergen exposures that may trigger the patient's asthma B. Use the patient's history to assess sensitivity to seasonal allergens C. Educate the patient and consider measures to reduce exposure to the identified inhaled allergen(s).	B	Not reviewed, Deleted	--
9.1	2	65	For patients with persistent asthma and indoor-related symptoms, the investigation of the potential role of allergens should be considered: A. Allergy testing should be performed to reliably determine sensitivity to common inhalant allergens to which the patient is exposed (skin testing or serum-specific IgE [i.e., RAST] testing) B. The patient's history should be used to assess the significance of positive allergen-specific IgE tests C. Educate the patient and consider measures to reduce exposure to the identified allergens.	C	Not reviewed, Deleted	--

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9.1	3	65	A comprehensive approach to inhaled allergen avoidance in sensitized patients should be employed rather than implementing a single specific environmental avoidance strategy or regimen.	C	Reviewed, New-replaced	Recommendation 6 Recommendation 7
9.1	4	65	Consider allergen immunotherapy when there is clear evidence of a relationship between symptoms and exposure to an allergen to which the patient is sensitive.	B	Reviewed, New-replaced	Recommendation 6 Recommendation 7
9.2	1	67	Patients who have asthma at any level of severity should: A. Avoid exposure to environmental tobacco smoke and other respiratory irritants, including smoke from wood-burning stoves and fireplaces and, if possible, substances with strong odors B. Avoid exertion outdoors when levels of air pollution are high.	C	Reviewed, New-replaced	Recommendation 6 Recommendation 7
9.2	2	67	There is insufficient evidence to recommend any specific environmental strategies to prevent the development of asthma.	N/A	Reviewed, New-replaced	Recommendation 6 Recommendation 7
9.3	1	67	Patients who have asthma and are employed, particularly those who have new-onset disease, should be queried about possible occupational exposures that may include allergens, irritants, or other exposures.	C	Reviewed, New-replaced	Recommendation 6 Recommendation 7
9.3	2	67	Specialist care management over a period of time, or co-management with the primary care provider, should be considered when history suggests that an occupational or environmental inhalant or ingested substance is provoking or contributing to asthma. Treatment or intervention may be required in the work environment.	N/A	Not reviewed, Deleted	--
10.1	1	69	All patients should be asked about tobacco use and should have their tobacco use status documented on a regular basis.	A	Reviewed, New-replaced	Recommendation 6 Recommendation 7
10.1	2	69	All providers should strongly advise every patient who smokes to quit. (See the VA/DoD Clinical Practice Guideline for Tobacco Use.)	A	Not reviewed, Deleted	--
10.1	3	69	Asthma patients and their families and/or caregivers should be instructed to avoid ETS.	A	Not reviewed, Deleted	--
10.1	4	69	All pregnant patients should be instructed not to smoke and to avoid exposure to ETS.	A	Not reviewed, Deleted	--
10.2	1	70	Advise patients who have asthma symptoms associated with consuming foods to which they are sensitized and/or foods high in sulfites (e.g., processed potatoes, shrimp, dried fruit, beer or wine) to avoid these products.	C	Not reviewed, Deleted	--

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10.3	1	71	Advise patients with asthma who are overweight or obese that excess body weight may have negative effects on asthma control and that weight loss may be associated with improvement of symptoms.	B	Reviewed, New-replaced	Recommendation 6 Recommendation 7
10.3	2	71	Encourage all patients with asthma to attain and maintain healthy body weight (see the VA/DoD Guidelines for Overweight and Obesity).	B	Reviewed, New-replaced	Recommendation 6 Recommendation 7
10.4	1	72	In the process of interviewing the patient and reconciling medications, query every patient for the use of complementary and alternative medicine (CAM).	I	Not reviewed, Deleted	--
10.4	2	72	Discourage patients and caregivers from substituting alternative therapies for evidence-based conventional asthma management by providing evidence-based information.	D	Not reviewed, Deleted	--
11.1	1	73	Assess patient and/or family for educational needs as well as for preferences and/or barriers to learning, which may include limited medical and/or English literacy, physical, developmental, emotional or psychological challenges as well as specific cultural and/or spiritual beliefs.	A	Not reviewed, Deleted	--
11.1	2	73	Provide asthma self-management education at all points of care where health professionals interact with patients and their families. [A] Education may be effective at other points of care such as pharmacies, hospitals, schools, and emergency departments.	B	Reviewed, New-replaced	Recommendation 11
11.1	3	73	Teach and review core asthma education and self-management concepts at every visit with return demonstration when appropriate.	B	Not reviewed, Deleted	--
11.1	4	73	Encourage a varied diet that is consistent with the Dietary Guidelines for Americans.	B	Reviewed, Deleted	--
11.1	5	73	Encourage asthma patients to participate in regular exercise to maintain general health and improve pulmonary conditioning.	B	Reviewed, Amended	Recommendation 18
11.2	1	75	Utilize a variety of educational strategies to include frequent appointments with asthma educators, individualized case management, and/or patient age-appropriate standard curriculums.	B	Reviewed, New-replaced	Recommendation 9
11.2	2	75	Consider utilizing interactive, multi-media resources in providing asthma education.	B	Reviewed, New-replaced	Recommendation 11

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11.2	3	75	Consider providing information on web-based comprehensive education sites that may include journaling, bulletin boards, support systems, electronic symptom questionnaires, and/or quality of life surveys to track and reinforce patient self-monitoring and management skills.	B	Reviewed, New-replaced	Recommendation 11
11.3	1	76	Ensure optimal self-management by providing education on self-monitoring, use of a written asthma action plan and regular medical review.	A	Reviewed, New-replaced	Recommendation 8
11.3	2	76	Develop asthma action plans that include instructions for daily management and recognition of worsening conditions along with actions to take at home (monitoring and medication adjustment) based on symptoms or peak expiratory flow (PEF) measurements and symptoms as appropriate.	A	Reviewed, New-replaced	Recommendation 8
12.1	1	79	Patients are considered high risk for complications from an acute exacerbation in the following situations: A. Previous severe exacerbation (e.g., intubation or ICU admission for asthma) B. Two or more hospitalizations or greater than three Emergency Department visits in the past year C. Use of greater than two canisters of short-acting beta-agonist per month D. Difficulty perceiving airway obstruction or the severity of worsening asthma E. Recent use of oral glucocorticoids for exacerbation F. Major psychosocial problems or psychiatric disease (including illicit drug use) G. Co-morbidities such as cardiovascular disease or other chronic lung disease H. History of non-compliance with asthma medication plan.	C	Not reviewed, Deleted	--
12.1	2	79	Patients in respiratory failure, or at imminent risk of respiratory failure, should be treated very aggressively and transported immediately to the emergency department. Treatment using continuous nebulized bronchodilators (albuterol or levoalbuterol) and/or systemic bronchodilators (subcutaneous epinephrine or terbutaline) should be initiated in the office setting pending transport	N/A	Not reviewed, Deleted	--
12.2	1	80	The severity of acute exacerbation should be determined by assessing specific characteristics of the symptoms, signs, and by objective measurement of SAO2 and PaCO2 (see Table 11).	N/A	Not reviewed, Deleted	--
12.3	1	82	Early treatment of exacerbations is best; patients (or parents) should be able to recognize early indicators of an exacerbation to include cough and/or worsening peak expiratory flow.	N/A	Not reviewed, Deleted	--

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12.3	2	82	All patients should be provided with – and instructed on how to use – a written asthma action plan that includes an individualized daily management plan and instructions on recognizing and handling worsening asthma. It should also include self-adjustment of medications in response to acute symptoms or changes in peak flow measures in the event of an exacerbation.	N/A	Reviewed, New-replaced	Recommendation 8
12.3	3	82	Initial adjustments in medication should include an increase in frequency of SABA. [For mild –moderate AE, up to 3 treatments within an hour (i.e., to 2-6 puffs per treatment); for severe AE, 4-8 puffs and seek medical care.]	B	Not reviewed, Deleted	--
12.3	4	82	Addition of a short course of oral systemic corticosteroids may be considered for 4-7 days following frequent use of SABA.	A	Not reviewed, Deleted	--
12.3	5	82	The dose of inhaled corticosteroids should NOT be doubled and patients should contact their healthcare provider before instituting a course of oral systemic corticosteroids.	D	Not reviewed, Deleted	--
12.3	6	82	Patients should be advised to withdraw from any environmental allergens or irritants that may contribute to the exacerbation.	N/A	Not reviewed, Deleted	--
12.3	7	82	Response to treatment should be monitored and communicated to the provider to determine if an office visit or referral to the emergency department is warranted.	N/A	Not reviewed, Deleted	--
12.4	1	83	A brief history and physical examination pertinent to the exacerbation should be conducted concurrently with the prompt initiation of therapy.	N/A	Not reviewed, Deleted	--
12.4	2	83	The history should include: A. Severity and duration of symptoms, including exercise limitation and sleep disturbance B. All current medications, including dose (and device) prescribed, dose usually taken, dose taken in response to the deterioration, and the patient's response (or lack thereof) to this therapy C. Time of onset and cause of the present exacerbation D. Risk factors for asthma-related death.	N/A	Not reviewed, Deleted	--
12.4	3	83	The physical examination should assess exacerbation severity by evaluating pulse rate, respiratory rate, use of accessory muscles, the patient's ability to complete a sentence, and other signs.	N/A	Not reviewed, Deleted	--

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12.4	4	83	Any complicating factors should be identified (e.g., pneumonia, atelectasis, pneumothorax, or pneumomediastinum).	N/A	Not reviewed, Deleted	--
12.4	5	84	Without unduly delaying treatment, a baseline PEF or FEV1 measurement should be made before treatment is initiated.	N/A	Not reviewed, Deleted	--
12.4	6	84	Subsequent measurements should be made at intervals until a clear response to treatment has occurred.	N/A	Not reviewed, Deleted	--
12.4	7	84	Oxygen saturation should be closely monitored, preferably by pulse oximetry. This is especially useful in children because objective measurements of lung function may be difficult. Oxygen saturation in children should normally be greater than 95%, and oxygen saturation less than 92% is a good predictor of the need for hospitalization	C	Not reviewed, Deleted	--
12.4	8	84	A chest X-ray (CXR) is not routinely required unless there are signs of infection such as fever or cough productive of purulent sputum. A patient presenting for the first time with signs and symptoms of asthma may require a CXR to rule out other causes of airway hyperreactivity. Additionally, if the clinician suspects secondary complications such as pneumothorax based on history and physical examination, a CXR should be obtained.	N/A	Not reviewed, Deleted	--
12.5	1	84	Patients discharged from the emergency department should contact the primary care provider within 1-2 days and schedule a follow-up visit as considered appropriate by the provider.	N/A	Not reviewed, Deleted	--
12.5	2	84	An acute exacerbation episode may indicate a lack of control of the patient's chronic asthma. A step-up adjustment of the patient's routine care and/or a consultation with a specialist may be considered.	N/A	Not reviewed, Deleted	--
13.1	1	85	All patients with asthma should have a regular exercise program and be asked about any limitations to exercise.	N/A	Not reviewed, Deleted	--
13.1	2	85	Bronchoprovocation testing (exercise spirometry) should be considered if the patient notes increased symptoms suggestive of EIB during or immediately following exercise.	C	Reviewed, New-replaced	Recommendation 2
13.1	3	85	Primary treatment is a warm-up period prior to exercise and pretreatment with short-acting beta-agonists is recommended.	A	Not reviewed, Amended	Recommendation 16

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13.1	4	85	Alternative treatments include LTRAs, which can attenuate EIB in up to 50 percent of patients.	C	Not reviewed, Deleted	--
13.1	5	85	Cromolyn sodium or nedocromil taken shortly before exercise is an alternative treatment, but it is not as effective as SABAs.	C	Not reviewed, Deleted	--
13.1	6	85	Consideration for increasing controller medications may be indicated to control or alleviate increased asthma symptoms during exercise.	N/A	Not reviewed, Deleted	--
13.2	1	86	The patient's history should focus on the correlation of symptoms (dyspnea, wheezing, cough, or chest tightness) with exertion during or immediately after prolonged exercise such as running.	N/A	Not reviewed, Deleted	--
13.2	2	86	Normal baseline resting spirometry (no evidence of obstruction or restriction with a normal flow volume loop) should prompt referral for bronchoprovocation testing.	N/A	Reviewed, New-replaced	Recommendation 1
13.2	3	87	The preferred method for bronchoprovocation testing is histamine and methacholine challenge testing or eucapneic hyperventilation as other methods are less sensitive for detecting airway hyperreactivity.	N/A	Reviewed, New-replaced	Recommendation 1 Recommendation 2
13.3	1	87	Methacholine or histamine challenge testing is indicated to establish the presence of airway hyperreactivity in patients with exertional symptoms (cough, wheezing, dyspnea, chest tightness) and normal resting spirometry.	C	Reviewed, New-replaced	Recommendation 1
13.3	2	87	Exercise challenge testing is indicated to establish the diagnosis of exercise-induced bronchospasm (or exercise-induced asthma) in known patients with asthma who exhibit exertional symptoms.	B	Reviewed, New-replaced	Recommendation 2
13.3	3	87	Eucapneic hyperventilation or cold air testing are equivalent to methacholine or histamine challenge testing but should be used in laboratories experienced in these techniques.	B	Reviewed, Deleted	--
13.4	1	88	The initial treatment regimen should consist of a warm-up period (gradual increase in exercise) and short-acting beta-agonist use 15-20 minutes prior to exercise.	C	Not reviewed, Amended	Recommendation 16
13.4	2	89	The use of LTRA or inhaled cromolyn prior to exercise may be considered.	C	Not reviewed, Amended	Recommendation 16
13.4	3	89	Lack of symptomatic improvement to inhaled beta-agonists or continued poor exercise tolerance should prompt referral for further evaluation by a specialist.	N/A	Not reviewed, Deleted	--

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14	1	90	Active duty service members should be diagnosed with asthma or exercise-induced bronchospasm on the basis of the following criteria: A. Chronic symptoms of cough, dyspnea, or wheezing B. Associated decrease in tolerance of exercise and/or running C. Normal chest radiograph (should be obtained in all active duty patients) D. Demonstration of persistent airway hyperreactivity • Baseline spirometry with reversible airflow obstruction post-bronchodilator • OR, Reactive bronchoprovocation testing or lower dose of methacholine (preferred method of bronchoprovocation testing).	N/A	Not reviewed, Deleted	--
14	2	90	Guidelines for deploying or redeploying service members with asthma to/from a theater of operations: A. In general, service members should be able to perform all required duties, wear protective gear, and have stable disease not requiring frequent treatments or oral corticosteroids B. Failure to meet these criteria should prompt consideration for redeployment C. See Appendix C – DoD Service-Specific Regulation Concerning Asthma D. Army; AR 40-501, Section 5–14. Medical fitness standards for deployment and certain geographical areas: • "Asthma. See paragraph 3–27a for profile guidance and for MEB/PEB processing criteria. If it is determined that the Soldier can be returned to duty, the Soldier should not deploy if he/she cannot wear protective gear, has experienced recent emergency room visits, or requires repetitive use of oral corticosteroids." E. Navy, Air Force, Coast Guard – No specific regulatory guidance.	N/A	Not reviewed, Deleted	--

Appendix J: Participant List

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Appendix K: Literature Review Search Terms and Strategy

A. Embase.com syntax

Question	Set #	Concept	Strategy
Questions 1, 2 – Diagnosis	#1	Population (adults and children with asthma; fixed obstruction)	('asthma'/mj OR asthma*:ti,ab OR wheez*:ti,ab OR ((asthma* NEXT/3 (sever* OR chronic*)):ti,ab) OR 'bronchus hyperreactivity':ti,ab OR bronchial hyperreactivity:ti,ab OR ((asthma*:ti OR wheez*:ti OR respirat*:ti OR breath*:ti) AND (symptom*:ti OR exacerbat*:ti OR severe:ti OR severity:ti))) OR ('fixed obstruction':ti,ab OR 'airway obstruction'/exp OR 'airway obstruction':ti,ab OR (airway NEXT/2 obstruction) OR (fixed NEXT/2 obstruction))
	#2	Diagnosis	'asthma'/exp/dm_di OR (asthma AND diagnos*):ti
	#3		'differential diagnosis'/exp OR 'diagnostic procedure'/exp
	#4		diagnostic:ti OR diagnostics:ti OR diagnose*:ti OR diagnosis:ti OR evaluate*:ti OR evaluation:ti OR measure*:ti OR assess*:ti OR determine:ti OR determination:ti OR distinguish:ti OR differentia*:ti OR predict*:ti,ab
	#5	Diagnostic tests	spirometry:ti,ab OR 'impulse oscillometry':ti,ab OR oscillometry:ti,ab OR ios:ti,ab OR (respiratory NEXT/2 function) OR (breath NEXT/2 test*) OR (forced NEXT/2 volume) OR exhalation:ti,ab OR 'exhaled nitric oxide':ti,ab OR 'fractional exhaled nitric oxide':ti,ab OR feno:ti,ab OR xray:ti,ab OR 'x ray':ti,ab OR scan*:ti,ab OR imaging:ti,ab OR 'forced expiratory volume'/exp OR 'exhaled nitric oxide'/exp OR 'lung function test'/exp OR 'oscillometry'/exp
	#6	Sensitivity/specificity	'sensitivity and specificity'/exp OR 'predictive value' OR 'predictive accuracy' OR 'diagnostic accuracy'/exp OR 'diagnostic test accuracy study'/exp OR 'clinical assessment'/exp OR 'receiver operating characteristic'/exp OR accuracy:ti,ab OR accurate:ti,ab OR sensitivity:ti,ab OR specificity:ti,ab OR validity:ti,ab OR reliability:ti,ab
	#7	Specialist/referral	('patient referral'/exp AND 'asthma'/exp/dm_di) OR ((Special*.ti,ab OR refer*.ti,ab OR pulmonology*:ti,ab OR cardiolog*:ti,ab) AND (diagnostic:ti OR diagnostics:ti OR diagnose*:ti OR diagnosis:ti OR evaluate*:ti OR evaluation:ti OR measure*:ti OR assess*:ti OR determine:ti OR determination:ti OR distinguish:ti OR differentia*:ti OR predict*:ti,ab) AND asthma:ti.)
	#8	Combine sets	#2 OR (#1 AND (#3 OR #4) AND #5)
	#9		#6 AND #8
	#10		#8 OR #9
	#11	Study types	'clinical trial'/exp OR 'prospective study'/exp OR 'retrospective study'/exp OR 'major clinical study'/exp OR 'cohort analysis'/exp OR 'controlled clinical trial'/exp OR 'diagnostic accuracy study'/exp OR 'randomized controlled trial'/exp OR 'randomized controlled trial'/de OR random*:ab,ti OR nct* OR controlled:ti OR review:ti OR 'controlled clinical trial'/exp OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR 'meta analysis'/de OR 'systematic review'/de OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab
	#12	Combine	#10 AND #11
	#13	Apply Limits	See Search Limits at the end of the table

Question	Set #	Concept	Strategy
Questions 3 – Risk Factors	#1	Population (adults and children with asthma)	'asthma'/mj OR asthma*:ti,ab OR wheez*:ti,ab OR ((asthma* NEXT/3 (sever* OR chronic*)):ti,ab) OR 'bronchus hyperreactivity':ti,ab OR bronchial hyperreactivity:ti,ab
	#2	Comorbidities/risk factors	(Risk factor/exp OR risk*:ti) OR comorbidity/exp OR ((comorbid* or co-morbid* or stress* or smoke or smoking or GERD or reflux or (gastro* NEXT3 reflux) or apnea or vaping or second-hand or secondhand or emotion* or stress or (respiratory NEXT2 infection*) or trigger* or risk*):ti,ab.
	#3	Exposures/hazards	'environmental exposure'/exp OR 'occupational exposure'/exp OR 'occupational hazard'/exp OR (occupation* NEXT/2 exposure) OR (environment* NEXT/2 exposure)
	#4		'dangerous goods'/exp OR ((hazard* OR risk* OR trigger*:ti,ab.) AND (environment*:ti,ab OR occupation*:ti,ab)) OR ('occupational exposure'/exp OR 'occupational safety'/exp OR 'work environment'/exp) AND (hazard*:ti,ab OR risk*:ti,ab OR trigger*:ti,ab) OR ((gas* OR fuel* OR desert* OR military) AND asthma:ti)
	#5	Exacerbate/onset	'disease exacerbation'/exp OR 'disease onset'/exp OR exacerbat*:ti,ab OR onset:ti,ab
	#6	Combine	#1 AND (#2 OR #3 OR #4) AND #5
	#7	Study types	'cohort analysis'/exp OR 'controlled clinical trial'/exp OR 'observational study'/exp OR 'case control study'/exp) OR ('randomized controlled trial'/exp OR 'randomized controlled trial'/de OR random*:ab,ti OR nct* OR controlled:ti OR review:ti OR 'controlled clinical trial'/exp OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR 'meta analysis'/de OR 'systematic review'/de OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
	#8	Combine	#6 AND #7
	#9	Apply Limits	See Search Limits at the end of the table
Question 4, 5, 6, 7 – Pharma	#1	Population (adults and children with asthma)	'asthma'/mj OR asthma*:ti,ab OR wheez*:ti,ab OR ((asthma* NEXT/3 (sever* OR chronic*)):ti,ab) OR 'bronchus hyperreactivity':ti,ab OR bronchial hyperreactivity:ti,ab OR 'asthma'/exp/dm_dm,dm_h
	#2	Focused intervention (drug classes and generic/brand names)	('steroid'/exp AND 'inhalational drug administration'/exp) OR 'Inhaled steroids' OR beclomethasone OR QVAR OR Budesonide OR Pulmicort OR ciclesonide OR Alvesco OR Flunisolide OR Aerospan OR Fluticasone OR Flovent OR Armonair OR Arnuity OR Mometasone OR Asmanex OR ('Inhaled steroids' AND 'long-acting beta agonists' OR (Budesonide AND Formoterol) OR Symbicort OR (Fluticasone AND Salmeterol) OR Advair OR AirDuo OR (Fluticasone AND vilanterol) OR "Breo Ellipta" OR (Mometasone AND formoterol) OR Dulera) OR 'short acting beta agonist'/exp OR 'Short-acting beta agonists' OR albuterol OR Ventolin OR Pro-Air OR Proventil OR Levalbuterol OR Xopenex OR 'Long-acting anticholinergic' OR Tiotropium OR Spiriva OR 'cholinergic receptor blocking agent'/exp OR 'Leukotriene receptor antagonist' OR Montelukast OR Singulair OR Zafirlukast OR Accolate OR Zileuton OR Zyflon OR 'leukotriene'/exp/dd_ae,dd_ad,dd_cb,dd_dt OR 'corticosteroid'/exp/dd_ae,dd_ad,dd_cb,dd_dt OR 'beta adrenergic receptor stimulating agent'/exp/dd_ae,dd_ad,dd_cb,dd_dt
	#3	Broad intervention (drug therapy)	(asthma/mj AND ('drug therapy'/exp OR 'combination drug therapy'/exp OR 'drug therapy'/lnk OR (pharmacotherap* OR medicine* OR medicat* OR (drug* NEAR/2 (therap* OR treat OR treatment*))):ti) OR (Asthma/mj OR asthma:ti) AND (pharmacotherap*:ti OR medicine*:ti OR medicat*:ti OR ((drug* NEAR/2 (therap* OR treat OR treatment*)):ti))

Question	Set #	Concept	Strategy
Question 4, 5, 6, 7 – Pharma (continued)	#4	Combine sets	(#1 AND #2) OR #3
	#5	Stepped dosage	#1 AND ((dose:ti.ab OR dosage:ti,ab OR 'drug dose'/exp AND ('asthma'/mj OR asthma*:ti,ab)) AND ('step up':ti,ab OR 'step down':ti,ab OR stepped:ti,ab OR stepwise:ti,ab OR increase*:ti,ab OR decrease*:ti,ab))
	#6	Study types	'clinical trial'/exp OR 'prospective study'/exp OR 'retrospective study'/exp OR 'major clinical study'/exp OR 'cohort analysis'/exp OR 'controlled clinical trial'/exp OR 'diagnostic accuracy study'/exp OR 'randomized controlled trial'/exp OR 'randomized controlled trial'/de OR random*:ab,ti OR nct* OR controlled:ti OR review:ti OR 'controlled clinical trial'/exp OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR 'meta analysis'/de OR 'systematic review'/de OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab
	#7		('comparative study'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'double blind procedure'/de OR 'drug dose comparison'/de OR 'major clinical study'/de OR 'meta analysis'/de OR 'multicenter study'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)
	#8	Combine	(#4 OR #5) AND (#6 OR #7)
	#9	Apply Limits	See Search Limits at the end of the table
Question 8 – Interdisciplinary/Integrative Treatment	#1	Population (adults and children with asthma)	'asthma'/mj OR asthma*:ti,ab OR wheez*:ti,ab OR ((asthma* NEXT/3 (sever* OR chronic*)):ti,ab) OR 'bronchus hyperreactivity':ti,ab OR bronchial hyperreactivity:ti,ab
	#2	Broad intervention (Integrated/ Interdisciplinary)	'interdisciplinary communication'/exp OR 'integrated programs'/exp OR 'integrated health care system'/exp OR 'integrative medicine'/exp OR 'collaborative care'/exp OR group:ti,ab OR collaborat*:ti,ab OR coordinat*:ti,ab OR integrat*:ti,ab OR interdisciplin*:ti,ab OR multidiscipline:ti,ab OR 'multi disciplin*':ti,ab OR crossdisciplin*:ti,ab OR team*:ti,ab OR 'team based':ti,ab
	#3	Healthcare team	healthcare:ti,ab OR doctor*:ti OR physician*:ti OR nurse*:ti OR practitioner*:ti OR specialist*:ti OR clinical:ti OR medical:ti OR clinician*:ti OR pharma*:ti,ab OR therap*:ti OR counsel*:ti OR dietitian:ti OR 'health care personnel' OR 'licensed practical nurse' OR 'pharmacist' OR 'physician assistant' OR 'medical staff' OR 'dietitian' OR 'occupational therapist' OR 'physiotherapist' OR 'pulmonologist' OR 'medical specialist'
	#4	Team-based decision making	'shared decision making'/exp OR ((decision*:ti,ab OR diagnos*:ti,ab OR treat*:ti,ab OR therap*:ti,ab OR plan*:ti,ab) AND (share*:ti OR group*:ti OR collaborat*:ti OR interdisciplin*:ti OR team*:ti))
	#5		('asthma'/exp OR asthma:ti) AND (group:ti OR team*:ti OR integrat*:ti OR interdisciplinary:ti OR collaborat*:ti)
	#6	Focused intervention (alternative therapies)	'psychotherapy' OR psychotherapy*:ti OR 'psychotherapist' OR 'paramedical profession' OR 'counselor' OR 'counseling' OR counsel*:ti OR educat*:ti OR 'behavior therapy' OR 'physiotherapy' OR therapist*:ti OR 'kinesiotherapy' OR exercise*:ti
	#7	Focused intervention (lifestyle modifications)	(lifestyle:ti OR life*:ti OR behavior*:ti OR health*:ti) AND (change*:ti OR modify:ti OR modification*:ti) OR 'lifestyle modification' OR 'behavior change'/exp OR 'behavior changes' OR ((behavior OR behavior OR lifestyle OR health) NEXT/3 (modif* OR change* OR improve*))
	#8	Behavior health	bhop OR 'behavior health optimization' OR 'behavioral health optimization'
	#9	Patient centered home	'patient centered medical home' AND ('asthma'/exp OR asthma*:ti)

Question	Set #	Concept	Strategy
Question 8 – Interdisciplinary/Integrative Treatment (continued)	#10	Outcomes	'treatment outcome'/exp OR 'disease management'/exp OR 'disease control'/exp OR outcome*:ti,ab OR manage*:ti,ab OR control*:ti,ab OR 'chronic disease prevention and control'/exp OR treat* OR manage* OR improve* OR decline* OR deteriorat* OR reduc* OR impact* OR effect* OR fewer OR short* OR result* OR change* OR experience* OR sever* OR increase* OR decrease* OR adhere* OR comply OR compliance OR control* OR utiliz*
	#11	Combine	#1 AND #2 AND (#3 OR #6)
	#12		(#1 AND #4) OR #5
	#13		(#1 AND #7) OR #8 OR #9
	#14		#11 OR #12 OR #13
	#15	Outcomes	'treatment outcome'/exp OR 'disease management'/exp OR 'disease control'/exp OR outcome*:ti,ab OR manage*:ti,ab OR control*:ti,ab OR 'chronic disease prevention and control'/exp OR treat* OR manage* OR improve* OR decline* OR deteriorat* OR reduc* OR impact* OR effect* OR fewer OR short* OR result* OR change* OR experience* OR sever* OR increase* OR decrease* OR adhere* OR comply OR compliance OR control* OR utiliz*
	#16	Combine	#14 AND #15
	#17	Study types	#16 AND ('randomized controlled trial'/exp OR 'randomized controlled trial'/de OR random*:ab,ti OR nct* OR controlled:ti OR review:ti OR 'controlled clinical trial'/exp OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR 'meta analysis'/de OR 'systematic review'/de OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab))
	#18	Apply Limits	See Search Limits at the end of the table
Question 9 – Self-management	#1	Population (adults and children with asthma)	'asthma'/mj OR asthma*:ti,ab OR wheez*:ti,ab OR ((asthma* NEXT/3 (sever* OR chronic*)):ti,ab) OR 'bronchus hyperreactivity':ti,ab OR bronchial hyperreactivity:ti,ab
	#2	Self-management	('self care'/exp OR 'self management support'/exp OR 'self manag*':ti,ab OR 'self care':ti,ab OR 'self manage*':ti,ab) OR ((goal setting/exp or motivation/exp or (goal or goals):ti,ab.) and (patient* or caregiver*):ti,ab. and (educat* or manage* or self-manage* or action* or plan*):ti,ab) OR (action NEXT/3 plan*)
	#3	Education/Attitude	'patient participation'/exp OR 'patient education'/exp OR 'consumer health information'/exp OR 'health literacy'/exp OR 'attitude to health'/exp OR ((patient*:ti OR caregiver*:ti) AND (attitude*:ti,ab OR educat*:ti,ab OR goals:ti,ab OR practices:ti,ab OR knowledge:ti,ab OR adherence:ti,ab OR compliance:ti,ab))
	#4		((patient* OR caregiver*) NEXT/3 (participation OR motivat* OR educat*)):ti
	#5	Combine	#1 AND (#2 OR #3 OR #4)
	#6	Study types	#5 AND ('randomized controlled trial'/exp OR 'randomized controlled trial'/de OR random*:ab,ti OR nct* OR controlled:ti OR review:ti OR 'controlled clinical trial'/exp OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR 'meta analysis'/de OR 'systematic review'/de OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab))
	#7	Apply Limits	See Search Limits at the end of the table

Question	Set #	Concept	Strategy
Question 10 – Disease Classification/Severity/Monitoring	#1	Population (adults and children with asthma)	'asthma'/mj OR asthma*:ti,ab OR wheez*:ti,ab OR ((asthma* NEXT/3 (sever* OR chronic*)):ti,ab) OR 'bronchus hyperreactivity':ti,ab OR bronchial hyperreactivity:ti,ab
	#2	Disease severity	'disease severity assessment'/exp OR 'disease severity'/exp OR ((disease:ti OR condition:ti) AND (severity:ti OR severe:ti OR progression:ti))
	#3	Disease classification	'disease classification'/exp OR ((disease:ti OR condition:ti) AND classif*:ti,ab))
	#4	Disease monitoring	('monitoring'/exp monitor*:ti,ab OR assess*:ti,ab) AND (tool*:ti,ab OR test*:ti,ab OR spirometry:ti,ab OR 'exhaled nitric oxide':ti,ab)
	#5		'monitoring'/exp AND 'disease severity'/exp AND 'asthma'/mj
	#6		('asthma'/mj AND ('disease severity assessment'/exp OR 'disease severity'/exp OR ((disease:ti OR condition:ti) AND (severity:ti OR severe:ti OR progression:ti)) AND ((classify OR classification OR assess OR assessment OR severity OR progress*)) OR (asthma*:ti AND (classify:ti OR classification:ti)) OR (asthma*:ti AND sever*:ti AND (monitor:ti OR assess*:ti OR test*:ti,ab OR evaluat*:ti))
	#7	Combine	(#1 AND (#2 OR #3 OR #4)) OR #5 OR #6
	#8	Study types	#7 AND ('randomized controlled trial'/exp OR 'randomized controlled trial'/de OR random*:ab,ti OR nct* OR controlled:ti OR review:ti OR 'controlled clinical trial'/exp OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR 'meta analysis'/de OR 'systematic review'/de OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab))
	#9	Apply Limits	See Search Limits at the end of the table
Question 11, 12 – Technology-based Tools/Interventions	#1	Population (adults and children with asthma)	'asthma'/mj OR asthma*:ti,ab OR wheez*:ti,ab OR ((asthma* NEXT/3 (sever* OR chronic*)):ti,ab) OR 'bronchus hyperreactivity':ti,ab OR bronchial hyperreactivity:ti,ab
	#2	Interventions (provider)	'teleconsultation'/exp OR 'telenursing'/exp OR 'telementoring'/exp OR 'telemedicine'/exp OR telemedicine:ti,ab OR telehealth*:ti,ab OR telenurs*:ti,ab OR 'tele medicin*':ti,ab OR 'tele health*':ti,ab OR 'tele nurs*':ti,ab OR ehealth:ti,ab OR 'e health':ti,ab OR (remote NEXT/2 consult*) OR telephone:ti,ab
	#3		'Electronic Health Record'/exp OR 'electronic medical record'/exp OR 'electronic patient record'/exp OR 'medical informatics'/exp OR 'medical information system'/exp OR 'medical decision making'/exp OR 'decision support system'/exp OR 'clinical decision support system'/exp OR 'computer assisted diagnosis'/exp OR 'information processing'/exp OR 'computerized provider order entry'/exp OR 'hospital information system'/exp
	#4		'shared decision*' OR 'decision aid*' OR (decision* NEXT/2 model*) OR (decision* NEXT/2 support*) OR ('decision making' AND computer*) OR (medical AND informatics) OR ((care or health-care or healthcare or 'health care') and (transition* or coordination or coordinate)) OR ((clinical OR clinician* OR doctor* OR medical* OR nurse* OR physician* OR practitioner*) NEXT/3 decision*) OR 'shared decision making'/exp OR 'medical decision making'/exp OR 'decision making'/exp OR 'expert system'/exp OR 'expert judgement'/exp
	#5	Combine	#1 AND (#2 OR #3 OR #4)

Question	Set #	Concept	Strategy
Question 11, 12 – Technology-based Tools/Interventions (continued)	#6	Interventions (patient)	Telephone:ti,ab OR telephoning:ti,ab OR phone*:ti,ab OR OR phoning:ti,ab OR telemedicine:ti,ab OR telehealth*:ti,ab OR telenurs*:ti,ab OR 'tele medicin*':ti,ab OR 'tele health*':ti,ab OR 'tele nurs*':ti,ab OR ehealth:ti,ab OR 'e health':ti,ab OR remote:ti,ab OR 'telemedicine' OR 'telemonitoring' OR 'teleconsultation' OR 'telenursing' OR 'telehealth' OR 'telephone' OR 'telephone counseling' OR 'telemonitoring'
	#7		'mobile phone' OR 'cell phone use' OR 'technology' OR 'electronic device' OR 'internet' OR 'online monitoring' OR 'social media' OR 'website' OR 'personal digital assistant' OR 'iphone' OR 'smartphone' OR 'tablet computer'
	#8		pda:ti,ab OR 'personal digital assistant':ti,ab OR 'smart phone':ti,ab OR smartphone:ti,ab OR 'cell* phone':ti,ab OR 'smart watch':ti,ab OR 'smartwatch':ti,ab OR android*:ti,ab OR 'hand held':ti,ab OR iphone*:ti,ab OR ipad*:ti,ab OR tablet:ti,ab OR 'i phone*':ti,ab OR 'i pad*':ti,ab OR blackberry:ti,ab OR webbased:ti,ab OR 'web based':ti,ab OR computer*:ti,ab OR internet*:ti,ab OR laptop:ti,ab OR text*:ti,ab OR web*:ti,ab OR internet*:ti,ab OR mobile*:ti,ab OR apps:ti,ab OR applications:ti,ab OR technolog*:ti,ab OR messaging:ti,ab OR ((text* NEXT/2 message*):ti,ab) OR 'short message service':ti,ab OR twitter:ti,ab OR tweet:ti,ab OR facebook:ti,ab OR 'instant message*':ti,ab OR 'social media':ti,ab
	#9		(mobile OR wireless OR bluetooth) NEXT/2 (health* OR device OR phone OR internet OR application* OR app OR apps OR notification* OR alert* OR reminder*)
	#10	Combine	#1 AND (#6 OR #7 OR #8 OR #9)
	#11		#5 OR #10
	#12	Study types	#11 AND ('randomized controlled trial'/exp OR 'randomized controlled trial'/de OR random*:ab,ti OR nct* OR controlled:ti OR review:ti OR 'controlled clinical trial'/exp OR [cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR 'meta analysis'/de OR 'systematic review'/de OR ((systematic* NEAR/2 review*):ab,ti) OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab))
	#13	Apply Limits	See Search Limits at the end of the table
Search Limits Applied to Each Search		Limit to humans and newly added publications	AND (english language AND humans AND yr="2008 - 2018")
		Exclude conference publications, books, letters, editorials,case studies, etc..	NOT (abstract:nc OR annual:nc OR book/de OR 'case report'/de OR 'case study'/de OR conference:nc OR 'conference abstract':it OR 'conference paper'/de OR 'conference paper':it OR 'conference proceeding':pt OR 'conference review':it OR congress:nc OR editorial/de OR editorial:it OR erratum/de OR letter:it OR note/de OR note:it OR meeting:nc OR sessions:nc OR 'short survey'/de OR symposium:nc) .
		Limit to meta-analyses and systematic reviews	AND ('research synthesis' OR 'systematic review'/exp OR 'systematic review' OR 'meta analysis'/exp OR 'meta analysis' OR Cochrane OR ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim)
		Limit to randomized controlled trials	AND ('randomized controlled trial'/exp OR 'randomization'/de OR 'double blind procedure'/de OR 'single blind procedure'/de OR 'placebo'/de OR 'crossover procedure'/de OR placebo* OR random*:de,ti OR crossover* OR 'cross over' OR ((singl* OR doubl* OR tripl* OR trebl*) NEAR/3 (blind* OR mask* OR sham*)) OR 'latin square' OR isrtcn* OR actrn* OR (nct* NOT nct))

B. MEDLINE syntax

Question	Set #	Concept	Strategy
Questions 1, 2 – Diagnosis	#1	Population (children and adults with suspicion of asthma or fixed obstruction)	Exp asthma/ OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Broad Diagnosis	(diagnosis differential/ OR exp differential diagnosis/ OR diagnostic tests/ OR "diagnostic techniques and procedures"/) OR Exp Diagnosis/ OR diagnos*.mp. OR assess*.mp. or predict*.mp. or evaluat*.mp. OR measure*.ti,ab. OR exp medical diagnosis/ or exp diagnosis/ or exp prognosis/ or exp measurement/ or exp diagnostic criteria/ OR exp asthma/di, dg
	#3		((symptom* OR severe OR severity OR exacerbat*).ti,ab.) AND (Exp Diagnosis/ OR diagnos*.mp. OR differentia* OR assess*.ti,ab. OR predict*.ti,ab. OR evaluat*.ti,ab. OR diagnostic accuracy.ti,ab.)
	#4	Combine	#2 OR #3
	#5	Tests used to diagnose asthma	*Oscillometry/ OR *Respiratory Function Tests/ OR *Breath tests/mt OR Forced Expiratory Volume/ OR exhalation/ OR *Nitric oxide/me,an OR Spirometry.mp. OR impulse oscillometry.ti,ab OR oscillometry.ti,ab OR IOS.ti,ab OR (respiratory adj2 function) OR (breath adj2 test*) OR (forced adj3 volume) OR exhalation.ti,ab OR exhaled nitric oxide.mp. OR fractional exhaled nitric oxide.mp. OR FENO.mp. OR test*.ti,ab OR xray.ti,ab OR x-ray.ti,ab OR scan*.ti,ab OR imaging.ti,ab OR (spirometry and (bronchodilator* or methacholine)).mp.
	#6	Combine	#1 AND #4 AND #5
	#7	Fixed obstruction	(Exp asthma/di AND exp Airway Obstruction/) OR 'airway obstruction'/di OR ((exp Airway obstruction/ or 'fixed airflow obstruction' or 'fixed obstruction') AND (diagnosis differential/ OR exp differential diagnosis/ OR diagnostic tests/)) OR (((fixed adj obstruction) OR (airway adj obstruction)) AND (diagnos*.ti,ab. OR differentia*.ti,ab. OR assess*.ti. OR predict*.ti. OR evaluat*.ti. OR diagnostic accuracy.ti,ab.))
	#8	Combine	#5 AND (exp Airway obstruction/ or 'fixed airflow obstruction' or 'fixed obstruction')
	#9	Combine	#6 OR #7 OR #8
	#10	Specialist/Referral	((Special*.ti,ab OR refer*.ti,ab) AND asthma.ti,ab AND diagnos*.ti,ab) OR Exp Asthma/ AND referral and consultation/
	#11	Combine	#6 AND #10
	#12	Sensitivity/specificity	#9 AND (Sensitivity.mp. and specificity/) or Predictive value of tests/ or accuracy.tw. or accurate.mp. or sensitivity.mp. or specificity.mp. or validity.mp. or reliability.mp. or exp "sensitivity and specificity"/
	#13	Combine	#11 OR #12
	#14	Study types	#14 AND (clinical trials/ and random*.ti). OR random sampling/ OR Exp randomized controlled trial/ or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.mp. or random*.ti,ab. or crossover*.mp. or 'cross over'.mp. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).mp. or 'latin square'.mp. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. OR 'diagnostic cohort'.mp. OR 'diagnostic accuracy'.mp.

Question	Set #	Concept	Strategy
Questions 1, 2 – Diagnosis (continued)	#15		#14 AND systematic review/ or meta analysis/ or metaanalysis/ OR ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).mp. or ("critical review" or "evidence based").ti. OR search*.ab. OR (systematic review or meta-analysis).ti,ab. Or (clinical study or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or observational study or randomized controlled trial).pt.
	#16	Combine	#14 OR #15
	#17	Apply limits	See Search Limits at the end of the table
Questions 3 – Risk Factors	#1	Population (children and adults with asthma)	Exp asthma/ OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Comorbidities/risk factors	Exp comorbidity/ OR ((comorbid* or co-morbid* or stress* or smoke or smoking or GERD or reflux or (gastro* adj3 reflux) or apnea or vaping or second-hand or secondhand or emotion* or stress or (respiratory adj2 infection*) or trigger* or risk*).ti,ab.
	#3	Exposures/hazards	exp environmental exposure/ or exp occupational exposure/ OR (occupation* adj2 exposure*).mp. OR (environment* adj2 exposure).mp. OR exp hazardous materials/ or ((hazard* or risk* or trigger*) and (environment* or occupation*)).ti,ab. OR (occupational exposure/ or occupational safety/ or working conditions/) AND (hazard* OR risk* OR trigger*).ti,ab. OR ((gas* OR fuel* OR desert* OR military) AND asthma:ti)
	#4	Combine	#1 AND (#2 OR #3)
	#5	Study types	#4 AND (comparative study or controlled clinical trial or observational study).pt. OR (exp case-control studies/ or exp cohort studies/) OR ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.) OR (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.)
	#5	Apply Limits	See Search Limits at the end of the table
Question 4, 5, 6, 7 – Pharmacotherapy	#1	Population (children and adults with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Focused intervention (drug classes and generic/brand names)	Budesonide, Formoterol Fumarate Drug Combination/ad, ae, tu or ((budesonide adj formoterol) or symicort).mp. OR ((fluticase adj salmeterol) or advair or airduo or ((fluticase adj vilanterol) or breo*)).mp. or fluticasone-salmeterol drug combination/ OR ((mometasone adj formoterol) or dulera).mp. or Mometasone Furoate, Formoterol Fumarate Drug Combination/

Question	Set #	Concept	Strategy
Question 4, 5, 6, 7 – Pharmacotherapy (continued)	#3		('long-acting beta agonist*' or 'laba' or ('short-acting beta agonist*' or 'saba')).ti,ab. OR Adrenergic beta-Agonists/ad, ae, tu
	#4		Steroids/ad, ae, tu or steroid*.ti. or corticosteroid*.ti. OR ('inhaled steroids' or Beclomethasone or QVAR or Budesonide or Pulmicort or Ciclesonide or Alvesco or Flunisolide or Aerospan or Fluticasone or Flovent or Armonair or Arnuity or Mometasone or Asmanex).mp
	#5		Beclomethasone/ad, ae, tu or budesonide/ad, ae, tu or fluticasone/ad, ae, tu or mometason furoate/ad, ae, tu
	#6		Anti-Asthmatic Agents/ad, ae, tu
	#7		'long-acting anticholinergic'.ti,ab. OR (tiotropium or spiriva).ti,ab. OR albuterol/ or albuterol.ti,ab. or ventolin.ti,ab. or pro-air.ti,ab. or proventil.ti,ab. or levalbuteral.ti,ab. or xopenex.ti,ab. OR (albuterol or Ventolin or Pro-Air or Proventil or Levalbuterol or Xopenex).mp OR (Montelukast or Singulair or Zafirlukast or Accolate or Zileuton or Zyflo).mp
	#8		Leukotriene receptor antagonist.ti,ab. OR Leukotriene Antagonists/ad, ae, tu or *Leukotrienes/ or leukotriene*.ti,ab.
	#9	Combine	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
	#10	Broad intervention (drug therapy)	(exp "Nebulizers and Vaporizers"/ and *asthma/dt) OR (administration, inhalation/ and asthma/dt) OR asthma/de, dt OR (((inhaled or inhalation) adj3 (corticosteroid* or steroid*)) and asthma*).ti,ab.
	#11		(asthma* and (drug* or prescription* or prescribed or pharma* or medicine* or medicat*)).ti,ab. OR (Asthma/ or asthma.it,ab or asthma.mp.) and exp drug therapy/)
	#12	Combine	#10 OR #11
	#13	Combine sets	#1 AND (#9 OR #12)
	#14	Stepped dosage	#13 AND (step-up OR step-down OR step up OR step down OR stepwise OR stepped OR increase* OR decrease*).ti,ab. AND (dose OR dosage).ti,ab.
	#15	Combine	#13 OR #14
	#16		#15 AND ((clinical trials/ and random*.ti). OR random sampling/ OR Exp randomized controlled trial/ or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.mp. or random*.ti,ab. or crossover*.mp. or 'cross over'.mp. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).mp. or 'latin square'.mp. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp.)
	#17		#15 AND (("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review").mp. or (pooled or pooling or search*).ab. or ("critical review" or "evidence based").ti.) OR (systematic review/ or meta analysis/ or metaanalysis/) OR (systematic review or meta-analysis).ti,ab. OR (systematic review or meta-analysis).ti,ab. or (comparative study or controlled clinical trial or evaluation studies or meta analysis or randomized controlled trial).pt.)
	#18	Combine	#16 OR #17
	#19	Apply limits	See Search Limits at the end of the table

Question	Set #	Concept	Strategy
Question 8 – Interdisciplinary/Integrative Treatment	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Broad intervention (Integrated/ Interdisciplinary)	Delivery of Health Care, Integrated/ or (integrat* adj2 (care or healthcare or treat*)).ti. OR (interdisciplinary or inter-disciplinary or team-oriented or team* or alternat* or complement* or compliment*).ti. OR ((home adj2 (service or services or care or healthcare or visit?)).ti,ab. or home care services/ or home nursing/ or ((visit* or home*) adj3 (nurse* or aid*)).ti,ab.
	#3	Focused intervention (alternative therapies or lifestyle modifications)	(psychotherap* or 'allied health' or counsel* or therapist* or holistic or complement* or compliment* or educator or behavior* or behaviour* or physiotherapist* or physical therapist* or exercise therap* or ((patient* or caregiver) and (educat* or motivat* or participat*))).ti,ab. or ((lifestyle or life* or behavior* or behaviour* or health*) and (change* or modify or modification*)).ti. OR exp psychotherapy/ or exp behavior therapy/ or psychotherapy, brief/ or psychotherapy, multiple/ or psychotherapy, psychodynamic/ or psychotherapy, rational-emotive/ or behavior change/
	#4	Combine	#1 AND (#2 OR #3)
	#5	Healthcare team	health personnel/ or exp allied health personnel/ or home health aides/ or licensed practical nurses/ or nurses' aides/ or pharmacy technicians/ or physician assistants/ or medical staff/ or nurses/ or nursing staff/ or nutritionists/ or occupational therapists/ or personnel, hospital/ or pharmacists/ or physicians/ OR ((nurse* or aide* or pharma* or pharmacist or 'pharmacy tech*' or therapist* or counselor* or doctor* or physician* or clinician).mp. and ((disease management/ or patient care planning/ or (care adj2 team* or chronic disease management.ti,ab. or disease adj2 management or chronic adj2 management))
	#6	Team-based decision making	((patient care planning/ or interdisciplinary communication/) and (disease management/ or asthma/)) OR ((decision making/ or group decision making/) and (disease management/ or asthma/)) OR (((shared decision* or decision*) adj support*) or ((clinical or clinician* or doctor* or medical or nurse or nurses or nursing or physician* or practitioner*) adj3 decision*)).mp
	#7	Combine	#1 AND (#5 OR #6)
	#8	Behavior health	BHOP.ti,ab. or behavior* health optimization.mp. or (behavior and optimization).ti,ab.
	#9	Patient centered home	(PCMH or 'patient?centered medical home').ti,ab. or 'patient centered medical home'.mp.
	#10	Combine	#1 AND (#8 OR #9)
	#11	Combine	#4 OR #7 OR #10
	#12	Study types	#11 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)

Question	Set #	Concept	Strategy
Question 8 – Interdisciplinary/Integrative Treatment (continued)	#13		#11 AND ((clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#14		#11 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#15	Combine	#12 OR #13 OR #14
	#16	Apply limits	See Search Limits at the end of the table
Question 9 – Self-management	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Self-management	exp knowledge level/ and (self-manage* or 'action plan').ti,ab. OR (self-care or self-manag* or 'self care' or 'self manage*').ti,ab. or self-management support/ or self care/exp OR ((goal setting/ or (goal or goals).ti,ab.) and (patient* or caregiver*).ti,ab. and (educat* or manage* or self-manage* or action* or plan*).ti,ab.)
	#3	Education/Attitude	Patient Participation/ or consumer participation/ or Patient Education as Topic/ or consumer health information/ or health literacy/ or health knowledge/ OR Attitude to Health/ or ((patient* or caregiver*) and (attitude* or educat* or goals or practices or knowledge or adherence or compliance)).ti,ab.
	#4		((patient* OR caregiver*) NEXT/3 (participation OR motivat* OR educat*)):ti
	#5	Combine	#2 OR #3 OR #4
	#6	Combine	#1 AND #5
	#7	Study types	#6 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#8		#6 AND ((clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#9		#6 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#10	Combine	#7 OR #8 OR #9
	#11	Apply limits	See Search Limits at the end of the table

Question	Set #	Concept	Strategy
Question 10 – Disease Classification/Severity/Monitoring	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Disease severity/classification/ monitoring	Disease course/ OR disease progression/ OR ((Disease OR condition).ti,ab. AND (course* OR progression OR severity OR classify OR classification).ti.) OR Severity (disorders)/ OR severity of illness index/
	#3		(course* OR progression* OR severity).ti,ab. AND (classify OR classification OR monitor* OR assess*).ti.
	#4		((monitor OR monitoring OR assess OR assessment).ti,ab. AND (tool* OR test* OR spirometry OR exhaled nitric oxide).ti,ab.)
	#5	Combine	#1 AND (#2 OR #3 OR #4)
	#6	Study types	#5 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#7		#5 AND ((clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#8		#5 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#9	Combine	#6 OR #7 OR #8
	#10	Apply limits	See Search Limits at the end of the table
Question 11, 12 – Technology-based Interventions/Tools	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Interventions (provider)	exp Telemedicine/ or telenursing/ or remote consultation/ OR ((telemedicine or telehealth$ or telenurs$ or tele-medicin$ or tele-health$ or tele-nurs$ or ehealth or e-health or remote consult$) adj10 chronic).ti,ab. or telephone.ti. OR exp Electronic Health Records/ OR medical informatics/ or health information exchange/ or decision making, computer-assisted/ or "information storage and retrieval"/ or information systems/ OR ((care or health-care or healthcare or 'health care') and (transition* or coordination or coordinate)).ti,ab.
	#3		Decision Support Systems, Clinical/ or Decision Making, Computer-Assisted/ or Medical Informatics Applications/ or exp decision support techniques/ OR ((shared decision$ or decision aid? or (decision$ adj2 model$) or (decision$ adj support?) or (decision making adj2 computer$) or informatics).ti,ab.
	#4		((clinical or clinician* or doctor* or medical* or nurse* physician* or practitioner*) adj3 decision making).ti,ab. OR exp Group Decision Making/ or exp Decision Making/ or exp Decision Support Systems/ or Computer Applications/ or decision support.mp. or exp Expert Systems/

Question	Set #	Concept	Strategy
Question 11, 12 – Technology-based Interventions/Tools (continued)	#5	Combine	#2 OR #3 OR #4
	#6	Interventions (patient)	exp telemedicine/ or exp telenursing/ or exp remote consultation/ OR ((telemedicine or telehealth$ or telenurs$ or tele-medicin$ or tele-health$ or tele-nurs$ or ehealth or e-health or remote consult$) adj10 chronic).ti,ab. or telephone.ti.)
	#7		exp cellular phones/ or exp mobile devices/ or exp technology/ or exp electronic communication/ or exp self-management/ OR (PDA or 'personal digital assistant' or 'smart phone' or 'cell phone' or smart-watch or 'smart watch' or android* or hand-held? or Iphone? or ipad? or i-phone? or i-pad? or blackberry or personal digital assistant? or webbased or computeri?ed or laptop).ti,ab. OR ((mobile or wireless or bluetooth) adj2 (health* or device or phone or internet or application or app or notification)).ti,ab.
	#8		exp internet/ or exp computer applications/ or exp exp electronic learning/ or exp online therapy/ or exp social media/ or exp websites/ or exp digital computers/ or exp computer software/ OR (text* or web* or internet* or mobile* or apps or applications or technolog* or messaging or (text* adj2 message*) or 'short message service' or twitter or tweet or facebook or 'instant message*' or 'social media').ti,ab.
	#9	Combine	#6 OR #7 OR #8
	#10	Combine	#1 AND (#5 OR #9)
	#11	Study type	#10 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#12		#10 AND (clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#13		#10 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#14	Combine	#11 OR #12 OR #13
	#15	Apply limits	See Search Limits at the end of the table
Search Limits Applied to Each Search		Limit to humans and newly added publications	AND (english language AND humans AND yr="2008 - 2018")
		Exclude conference publications, books, letters, editorials, case studies, etc.	NOT ((("column/opinion" OR "comment/reply" OR dissertation OR editorial OR letter OR book).dt. OR book.pt.) OR (letter/ or editorial/ OR news/ OR comment/ OR case report OR case reports/ OR note/ OR conference paper/) OR (letter OR editorial OR news OR comment OR case reports OR conference abstract* OR book or case reports or clinical conference or consensus development conference or consensus development conference nih or dissertation abstract or editorial or government publications or technical report).pt.)

C. PyscINFO syntax

Question	Set #	Concept	Strategy
Questions 1,2 – Diagnosis	#1	Population (children and adults with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Diagnosis	((symptom* OR severe OR severity OR exacerbat*).ti,ab.) AND (Exp Diagnosis/ OR diagnos*.mp. OR differentia*.ti,ab. OR assess*.ti,ab. OR predict*.ti,ab. OR evaluat*.ti,ab. OR measure*.ti,ab.)
	#3		exp Medical Diagnosis/ OR exp Diagnosis/ OR exp differential diagnosis/ OR exp misdiagnosis/ OR exp diagnostic criteria/ OR exp prognosis/ OR exp "severity (disorders)"/ OR (diagnos*.ti,ab. OR differentia*.ti,ab. OR assess*.ti. OR predict*.ti. OR evaluat*.ti. OR diagnostic accuracy.ti,ab.)
	#4	Combine	#2 OR #3
	#5	Tests used to diagnose asthma	Spirometry.mp. OR impulse oscillometry.ti,ab OR oscillometry.ti,ab OR IOS.ti,ab OR (respiratory adj2 function) OR (breath adj2 test*) OR (forced adj3 volume) OR exhalation.ti,ab OR exhaled nitric oxide.mp. OR fractional exhaled nitric oxide.mp. OR FENO.mp. OR test*.ti,ab OR xray.ti,ab OR x-ray.ti,ab OR scan*.ti,ab OR imaging.ti,ab OR (spirometry and (bronchodilator* or methacholine)).mp.
	#6	Combine	#1 AND #4 AND #5
	#7	Fixed obstruction	(Exp asthma/ AND 'airway obstruction') OR (('fixed airflow obstruction' or 'fixed obstruction') OR ((fixed adj obstruction) OR (airway adj obstruction))
	#8	Combine	(#4 OR #5) AND #7
	#9	Combine	#6 OR #8
	#10	Specialist/Referral	((Special*.ti,ab OR refer*.ti,ab) AND asthma.ti,ab AND diagnos*.ti,ab) OR (Exp Asthma/ AND exp professional referral/
	#11	Combine	#6 AND #10
	#12	Sensitivity/specificity	#9 AND (Sensitivity.mp. and specificity/) or Predictive value of tests/ or accuracy.tw. or accurate.mp. or sensitivity.mp. or specificity.mp. or validity.mp. or reliability.mp. or exp "sensitivity and specificity"/
	#13	Combine	#11 OR #12
	#14	Study types	#13 AND (exp randomized controlled trial/ or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.mp. or random*:de,ti.mp. or crossover*.mp. or 'cross over'.mp. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).mp. or 'latin square'.mp. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or 'diagnostic cohort'.mp. or 'diagnostic accuracy'.mp.)
	#15		#13 AND Systematic review/ or meta analysis/ or metaanalysis/ OR (systematic review or meta-analysis).ti,ab. or (clinical study or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or observational study or randomized controlled trial).pt. OR ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).mp. or ("critical review" or "evidence based").ti. or search*.ab.
	#16	Combine	#14 OR #15
	#17	Apply limits	See Search Limits at the end of the table

Question	Set #	Concept	Strategy
Question 3 – Risk Factors	#1	Population (children and adults with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Comorbidities/risk factors	Exp comorbidity/ OR ((comorbid* or co-morbid* or stress* or smoke or smoking or GERD or reflux or (gastro* adj3 reflux) or apnea or vaping or second-hand or secondhand or emotion* or stress or (respiratory adj2 infection*) or trigger* or risk*).ti,ab.)
	#3	Exposures/hazards	exp environmental exposure/ or exp occupational exposure/ or (occupation* adj2 exposure*).mp. or (occupation* adj2 hazard*).mp. or (occupation* adj3 toxic*).mp. or (environment* adj2 exposure).mp.OR ((occupational safety/ or working conditions/) and (hazard* or risk* or trigger*).ti,ab.) OR ((gas* OR fuel* OR desert* OR military) AND asthma:ti)
	#4	Combine	#1 AND (#2 OR #3)
	#5	Study types	#4 AND (comparative study or controlled clinical trial or observational study).pt. OR exp case-control studies/ or exp cohort studies/ OR cohort* OR Cohort Analysis/ OR exp longitudinal studies/ OR exp prospective studies/ OR exp retrospective studies/
	#6		#4 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#7		#4 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt. OR (systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.)
	#8	Combine	#5 OR #6 OR #7
	#9	Apply limits	See Search Limits at the end of the table
Questions 4, 5, 6, 7 – Pharma	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Focused intervention (drug classes and generic/brand names)	Budesonide, Formoterol Fumarate Drug Combination/ad, ae, tu or ((budesonide adj formoterol) or symicort).mp. OR ((fluticase adj salmeterol) or advair or airduo or ((fluticase adj vilanterol) or breo*)).mp. or fluticasone-salmeterol drug combination/ OR ((mometasone adj formoterol) or dulera).mp.
	#3		('long-acting beta agonist*' or 'laba' or ('short-acting beta agonist*' or 'saba')).ti,ab.
	#4		Steroids/ad, ae, tu or steroid*.ti. or corticosteroid*.ti. OR ('inhaled steroids' or Beclomethasone or QVAR or Budesonide or Pulmicort or Ciclesonide or Alvesco or Flunisolide or Aerospan or Fluticasone or Flovent or Armonair or Arnuity or Mometasone or Asmanex).mp. OR (((inhaled or inhalation) adj3 (corticosteroid* or steroid*)) and asthma*).ti,ab.
	#5		'long-acting anticholinergic'.ti,ab. OR (tiotropium or spiriva).ti,ab.

Question	Set #	Concept	Strategy
Questions 4, 5, 6, 7 – Pharma (continued)	#6		albuterol/ or (albuterol or Ventolin or Pro-Air or Proventil or Levalbuterol or Xopenex).mp. OR (Montelukast or Singulair or Zafirlukast or Accolate or Zileuton or Zyflo).mp.
	#7		Leukotriene receptor antagonist.ti,ab. OR Leukotriene Antagonists/ad, ae, tu or *Leukotrienes/ or leukotriene*.ti,ab.
	#8	Broad intervention (drug therapy)	(asthma/ or asthma.ti,ab. or asthma.mp.) AND (exp Drug Therapy/ OR (drug* or prescription* or prescribed or pharma* or medicine* or medicat*).ti,ab.)
	#9	Combine sets	#2 OR #3 OR #4 OR #5 OR #6 OR #7
	#10	Stepped dosage	#9 AND ((dose.ti.ab OR dosage.ti,ab OR exp drug dosages/ AND (asthma/ OR asthma*.ti,ab)) AND ('step up'.ti,ab OR 'step down'.ti,ab OR stepped.ti,ab OR stepwise.ti,ab OR increase*.ti,ab OR decrease*.ti,ab))
	#11	Combine	#1 AND (#8 OR #9)
	#12	Study types	#11 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#8		#11 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt. OR (systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.)
	#9	Apply limits	See Search Limits at the end of the table
Question 8 – Interdisciplinary/Integrative Treatment	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Broad intervention (Integrated/ Interdisciplinary)	Delivery of Health Care, Integrated/ or (integrat* adj2 (care or healthcare or treat*)).ti. OR (interdisciplinary or inter-disciplinary or alternat* or complement* or compliment*).ti. OR (home adj2 (service or services or care or healthcare or visit?)).ti,ab. or home care services/ or home nursing/ or ((visit* or home*) adj3 (nurse* or aid*)).ti,ab.
	#3	Focused intervention (alternative therapies or lifestyle modifications)	((psychotherap* or 'allied health' or counsel* or therapist* or holistic or complement* or compliment* or alternative or educator or behavior* or behaviour* or physiotherapist* or physical therapist* or exercise therap* or yoga OR patient* OR caregiver*) and (educat* or motivat* or participat* OR treat* OR therap*)).ti,ab. or ((lifestyle or life* or behavior* or behaviour* or health*) and (change* or modify or modification*)).ti. OR exp psychotherapy/ or exp behavior therapy/ or psychotherapy, brief/ or psychotherapy, multiple/ or psychotherapy, psychodynamic/ or psychotherapy, rational-emotive/ or behavior change/ OR exp alternative Medicine/ OR exp meditation/ or exp mindfulness/ or exp relaxation therapy/ OR exp yoga/ OR exp exercise/ OR exp physical activity/
	#4	Combine	#1 AND (#2 OR #3)

Question	Set #	Concept	Strategy
Question 8 – Interdisciplinary/Integrative Treatment (continued)	#5	Healthcare team	health personnel/ or exp allied health personnel/ or home health aides/ or licensed practical nurses/ or nurses' aides/ or pharmacy technicians/ or physician assistants/ or medical staff/ or nurses/ or nursing staff/ or nutritionists/ or occupational therapists/ or personnel, hospital/ or pharmacists/ or physicians/ OR ((nurse* or aide* or pharma* or pharmacist or 'pharmacy tech*' or therapist* or counselor* or doctor* or physician* or clinician).mp. and ((disease management/ or patient care planning/ or (care adj2 team* or chronic disease management.ti,ab. or disease adj2 management or chronic adj2 management)))
	#6	Team-based decision making	((patient care planning/ or interdisciplinary communication/) and (disease management/ or asthma/)) OR ((decision making/ or group decision making/) and (disease management/ or asthma/)) OR (((shared decision* or decision*) adj support*) or ((clinical or clinician* or doctor* or medical or nurse or nurses or nursing or physician* or practitioner*) adj3 decision*)).mp OR interdisciplinary or inter-disciplinary or team-oriented or team*
	#7	Combine	#1 AND (#5 OR #6)
	#8	Behavior health	BHOP.ti,ab. or behavior* health optimization.mp. or (behavior and optimization).ti,ab.
	#9	Patient centered home	(PCMH or 'patient?centered medical home').ti,ab. or 'patient centered medical home'.mp.
	#10	Combine	#1 AND (#8 OR #9)
	#11	Combine	#4 OR #7 OR #10
	#12	Study types	#11 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#13		#11 AND ((clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#14		#11 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#15	Combine	#12 OR #13 OR #14
	#16	Apply limits	See Search Limits at the end of the table

Question	Set #	Concept	Strategy
Question 9 – Self-management	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Self-management	(exp knowledge level/ and (self-manage* or 'action plan').ti,ab.) OR (self-care or self-manag* or 'self care' or 'self manage*').ti,ab. or (self-care or self-manag* or 'self care' or 'self manage*').ti,ab. or exp self-management/ or self care/ OR ((goal setting/ or (goal or goals).ti,ab.) and (patient* or caregiver*).ti,ab. and (educat* or manage* or self-manage* or action* or plan*).ti,ab.)
	#3	Education/Attitude	Patient Participation/ or consumer participation/ or Patient Education as Topic/ or consumer health information/ or health literacy/ or health knowledge/ OR attitude to health/ or ((patient* or caregiver*) and (attitude* or educat* or goals or practices or knowledge or adherence or compliance)).ti,ab.
	#4		((patient* OR caregiver*) NEXT/3 (participation OR motivat* OR educat*)).ti
	#5	Combine	#2 OR #3 OR #4
	#6	Combine	#1 AND #5
	#7	Study types	#6 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#8		#6 AND ((clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#9		#6 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#10	Combine	#7 OR #8 OR #9
	#11	Apply limits	See Search Limits at the end of the table

Question	Set #	Concept	Strategy
Question 10 – Disease Classification/Severity/Monitoring	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Disease severity/classification/ monitoring	Disease course/ OR disease progression/ OR ((Disease OR condition).ti,ab. AND (course* OR progression OR severity OR classify OR classification).ti.) OR Severity (disorders)/ OR severity of illness index/
	#3		(course* OR progression* OR severity).ti,ab. AND (classify OR classification OR monitor* OR assess*).ti.
	#4		((monitor OR monitoring OR assess OR assessment).ti,ab. AND (tool* OR test* OR spirometry OR exhaled nitric oxide).ti,ab.)
	#5	Combine	#1 AND (#2 OR #3 OR #4)
	#6	Study types	#5 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#7		#5 AND ((clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#8		#5 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#9	Combine	#6 OR #7 OR #8
	#10	Apply limits	See Search Limits at the end of the table
Questions 11,12 – Technology-based Interventions/Tools	#1	Population (adults and children with asthma)	Exp asthma/ OR asthma.ti. OR (asthmatic* or (asthma adj2 (chronic* or patient*))).ti,ab. OR Bronchial Hyperreactivity/ or bronchial* hyperreactivit*.ti,ab. OR (asthma* or 'fixed airflow obstruction' or 'fixed obstruction' or wheez* or 'lung function').ti,ab. OR (asthma*.ti. and (acute or exacerbat* or progress*)).ti.
	#2	Interventions (provider)	exp Telemedicine/ or telenursing/ or remote consultation/ OR ((telemedicine or telehealth$ or telenurs$ or tele-medicin$ or tele-health$ or tele-nurs$ or ehealth or e-health or remote consult$) adj10 chronic).ti,ab. or telephone.ti. OR exp electronic communication/ OR medical informatics/ or health information exchange/ or decision making, computer-assisted/ or information systems/ OR ((care or health-care or healthcare or 'health care') and (transition* or coordination or coordinate)).ti,ab.
	#3		Decision Support System/ or (exp Decision Making/ AND Computer applications/) or exp decision support systems/ OR ((shared decision$ or decision aid? or (decision$ adj2 model$) or (decision$ adj support?) or (decision making adj2 computer$) or informatics).ti,ab.
	#4		((clinical or clinician* or doctor* or medical* or nurse* physician* or practitioner*) adj3 decision making).ti,ab. OR exp Group Decision Making/ or exp Expert Systems/
	#5	Combine	#2 OR #3 OR #4

Question	Set #	Concept	Strategy
Questions 11,12 – Technology-based Interventions/Tools (continued)	#6	Interventions (patient)	exp telemedicine/ or exp telenursing/ or exp remote consultation/ OR exp online therapy/ OR ((telemedicine or telehealth$ or telenurs$ or tele-medicin$ or tele-health$ or tele-nurs$ or ehealth or e-health or remote consult$) adj10 chronic).ti,ab. or telephone.ti.)
	#7		exp cellular phones/ or exp mobile devices/ or exp technology/ or exp electronic communication/ or exp self-management/ or exp wireless communication/ or (PDA or 'personal digital assistant' or 'smart phone' or 'cell phone' or smart-watch or 'smart watch' or android* or hand-held? or Iphone? or ipad? or i-phone? or i-pad? or blackberry or personal digital assistant? or webbased or computeri?ed or laptop).ti,ab. OR ((mobile or wireless or bluetooth) adj2 (health* or device or phone or internet or application or app or notification)).ti,ab.
	#8		exp internet/ or exp computer applications/ or exp computer mediated communication/ or exp electronic learning/ or exp online therapy/ or exp social media/ or exp websites/ or exp digital computers/ or exp computer software/ OR (text* or web* or internet* or mobile* or apps or applications or technolog* or messaging or (text* adj2 message*) or 'short message service' or twitter or tweet or facebook or 'instant message*' or 'social media').ti,ab.
	#9	Combine	#6 OR #7 OR #8
	#10	Combine	#1 AND (#5 OR #9)
	#11	Study type	#10 AND ('randomized controlled trial'/exp or 'randomization'/de or 'double blind procedure'/de or 'single blind procedure'/de or 'placebo'/de or 'crossover procedure'/de or placebo*.ab. or random*.ti,ab. or crossover*.ab. or 'cross over'.ab. or ((singl* or doubl* or tripl* or trebl*) and (blind* or mask* or sham*)).ab. or 'latin square'.ab. or isrtcn*.mp. or actrn*.mp. or (nct* not nct).mp. or randomized controlled trial.pt.)
	#12		#10 AND (clinical trials/ and random*.ti.) OR random sampling/) OR randomized controlled trial.pt.
	#13		#10 AND (meta analysis/ or ("meta analysis" or "meta analytic" or metaanaly* or "research synthesis" or "systematic review" or pooled or pooling or search*).ti,ab. or ("critical review" or "evidence based").ti. or meta analysis.pt.) OR ((systematic review or meta analysis).mp. or (meta-analysis or systematic* review).ti.) OR (systematic review/ or meta analysis/ or metaanalysis/ or pooled.mp. or meta-analysis.pt. or "systematic review".mp. or search*.ab.)
	#14	Combine	#11 OR #12 OR #13
	#15	Apply limits	See Search Limits at the end of the table
Search Hedges Applied to Each Strategy		Limit to humans and newly added publications	AND (english language AND humans AND yr="2008 - 2018")
		Exclude conference publications, books, letters, editorials, case studies, etc.	NOT ((("column/opinion" OR "comment/reply" OR dissertation OR editorial OR letter OR book).dt. OR book.pt.) OR (letter/ or editorial/ OR news/ OR comment/ OR case report OR case reports/ OR note/ OR conference paper/) OR (letter OR editorial OR news OR comment OR case reports OR clinical conference OR dissertation abstract OR technical report OR government publications OR conference abstract$).pt.

Appendix L: Alternative Text Descriptions of Algorithms

The following outlines narratively describe Module A, Module B, and Module C. An explanation of the purpose of the algorithms and description of the various shapes used within the algorithms can be found in the Algorithm section. The sidebars referenced within these outlines can also be found in the Algorithm section.

A. Module A: Assessment and Diagnosis of Asthma

1. Module A begins with Box 1, in the shape of a rounded rectangle: "Person with chief complaint suggestive of asthma (see Sidebar A)"
2. Box 1 connects to Box 2, in the shape of a rectangle: "Obtain history and physical examination (see Sidebar B)"
3. Box 2 connects to Box 3, in the shape of a hexagon, asks the question: "Is there a confident clinical diagnosis of asthma? (see Sidebar A, Sidebar B, and Appendix B)"
    a. If the answer is "Yes" to Box 3, then Box 4, in the shape of a hexagon, asks the question: "Is patient presenting with acute exacerbation?"
        i. If the answer is "Yes" to Box 4, then Box 5, in the shape of a rectangle: "Treat or refer as clinically indicated; return to beginning of algorithm when clinically stable"
        ii. If the answer is "No" to Box 4, then Box 11, in the shape of an oval: "Diagnose asthma; continue to Module B: Initiation of Therapy for initial treatment (see Appendix B)"
    b. If the answer is "No" to Box 3, then Box 6, in the shape of a hexagon, asks the question: "Is a non-asthma cause of symptoms identified?"
        i. If the answer is "Yes" to Box 6, then Box 7, in the shape of a rectangle: "Treat or refer as clinically indicated"
        ii. If the answer is "No (still suspect asthma)" to Box 6, then Box 8, in the shape of a hexagon, asks the question: "Is the patient capable of spirometry and is it readily available?"
            1. If the answer is "Yes" to Box 8, then Box 9, in the shape of a rectangle: "Obtain spirometry (see Recommendation 1)"
            2. If the answer is "No" to Box 8, then Box 15, in the shape of a rectangle: "Consider trial of therapy (and/or consider specialist referral)"
4. Box 9 connects to Box 10, in the shape of a hexagon, asks the question: "Is spirometry compatible with asthma (consistent with obstruction)?"
    a. If the answer is "Yes" to Box 10, then Box 11, in the shape of an oval: "Diagnose asthma; continue to Module B: Initiation of Therapy for initial treatment (see Appendix B)"
    b. If the answer is "No" to Box 10, then Box 12, in the shape of a rectangle: "Consider the following options based on site availability and patient characteristics: referring for

bronchoprovocation testing (see Sidebar C and Recommendations 3 and 4); trial of therapy; specialist referral"

5. Box 12 connects to Box 13, in the shape of a hexagon, asks the question: "Is bronchoprovocation testing compatible with asthma?"
    a. If the answer is "Yes" to Box 13, then Box 11, in the shape of an oval: "Diagnose asthma; continue to Module B: Initiation of Therapy for initial treatment (see Appendix B)"
    b. If the answer is "No (still suspect asthma)" to Box 13, then Box 14, in the shape of a rectangle, "Refer to specialist"
6. Box 15 connects to Box 16, in the shape of a hexagon, asks the question: "Is trial of therapy effective?"
    a. If the answer is "Yes" to Box 16, then Box 11, in the shape of an oval: "Diagnose asthma; continue to Module B: Initiation of Therapy for initial treatment (see Appendix B)"
    b. If the answer is "No" to Box 16, then Box 14, in the shape of a rectangle: "Refer to specialist"

B. Module B: Initiation of Therapy

1. Module B begins with Box 17, in the shape of a rounded rectangle: "Patient with diagnosed asthma (see Sidebar D and Sidebar E)"
2. Box 17 connects to Box 18, in the shape of a hexagon, asks the question: "Is patient already on controller therapy?"
    a. If the answer is "Yes" to Box 18, then Box 19, in the shape of an oval: "Go to Module C: Follow-up"
    b. If the answer is "No" to Box 18, then Box 20, in the shape of a rectangle: "Assess severity (see Appendix B) and initiate SABA as needed for symptom relief and prevention of exercise-induced symptoms"
3. Box 20 connects to Box 21, in the shape of a hexagon, asks the question: "Is the patient's asthma persistent?"
    a. If the answer is "Yes" to Box 21, then Box 22, in the shape of a hexagon, asks the question: "Does patient have moderate persistent or severe persistent asthma and significant symptom burden? (see Appendix B)"
        i. If the answer is "Yes" to Box 22, then Box 23, in the shape of a rectangle: "Initiate ICS with LABA as initial controller medications (see Recommendation 13)"
        ii. If the answer is "No" to Box 22, then Box 27, in the shape of a rectangle: "Initiate ICS as initial controller medication (see Recommendation 12)"

b. If the answer is "No" to Box 21, then Box 24, in the shape of a hexagon, asks the question: "Is asthma induced only by exercise?"

i. If the answer is "Yes" to Box 24, then Box 25, in the shape of a rectangle: "Continue SABA as needed and consider initiating LTRA for prevention of exercise-induced asthma symptoms (see Recommendation 16)"

ii. If the answer is "No" to Box 24, then Box 26, in the shape of a rectangle: "Continue SABA as needed"

4. Box 23 connects to Box 28, in the shape of an oval: "Go to Module C: Follow-up"
5. Box 25 connects to Box 28, in the shape of an oval: "Go to Module C: Follow-up"
6. Box 26 connects to Box 28, in the shape of an oval: "Go to Module C: Follow-up"
7. Box 27 connects to Box 28, in the shape of an oval: "Go to Module C: Follow-up"

C. Module C: Follow-up

1. Module C begins with Box 29, in the shape of a rounded rectangle: "Patient with asthma on therapy (needs follow-up) (see Sidebar I)"
2. Box 29 connects to Box 30, in the shape of a hexagon, asks the question: "Is patient's asthma (impairment and risk) controlled? (see Appendix B)"

a. If the answer is "Yes" to Box 30, then Box 31, in the shape of a hexagon, asks the question: "Has patient been on current therapy for more than 3 months?"

i. If the answer is "Yes" to Box 31, then Box 32, in the shape of a rectangle: "Consider stepping down by: Decreasing dose of ICS (do not discontinue), or discontinuing LABA or other alternative therapies (see Sidebar F)"

1. Box 32 connects to Box 42, in the shape of a rectangle: "Follow-up (see Sidebar H)"
2. Box 42 connects to Box 30, in the shape of a hexagon, asks the question: "Is patient's asthma (impairment and risk) controlled? (see Appendix B)"

ii. If the answer is "No" to Box 31, then Box 33, in the shape of a rectangle: "Maintain current therapy; reassess once on treatment regimen for 3 months"

1. Box 33 connects to Box 30, in the shape of a hexagon, asks the question: "Is patient's asthma (impairment and risk) controlled? (see Appendix B)"

b. If the answer is "No" to Box 30, then Box 34, in the shape of a hexagon, asks the question: "Is there a problem with patient adherence or technique?"

i. If the answer is "Yes" to Box 34, then Box 35, in the shape of a rectangle: "Address adherence and technique"

ii. Box 35 connects to Box 36. If the answer is "No" to Box 34, then Box 36. Box 36, in the shape of a hexagon, asks the question: "Is there a problem with comorbidity?"

1. If the answer is "Yes" to Box 36, then Box 37, in the shape of a rectangle, "Address comorbidity"

2. Box 37 connects to Box 38. If the answer is "No" to Box 36, then Box 38. Box 38, in the shape of a hexagon, asks the question: "Is there a problem with triggers?"
    a. If the answer is "Yes" to Box 38, then Box 39, in the shape of a rectangle, "Address triggers"
    b. Box 39 connects to Box 40. If the answer is "No" to Box 38, then Box 40. Box 40, in the shape of a rectangle: "Add (see Recommendation 14) or increase medication as indicated (see Sidebar G); reassess diagnosis; consider consultation or referral (see Appendix B and Sidebar I)"
3. Box 40 connects to Box 41, in the shape of a rectangle, "Revisit need for non-pharmacological interventions (see Module B: Initiation of Therapy, Sidebar D, Sidebar E, and Sidebar F)"
4. Box 41 connects to Box 42, in the shape of a rectangle, "Follow-up (see Sidebar H)"
5. Box 42 connects to Box 30, in the shape of a hexagon, asks the question: "Is patient's asthma (impairment and risk) controlled? (see Appendix B)"

Appendix M: Abbreviation List

Abbreviation	Definition
ACQ-6	Asthma Control Questionnaire 6
ACSS	Asthma Control Scoring System
ATS	American Thoracic Society
BMI	body mass index
CBT	cognitive behavioral therapy
COI	conflict of interest
COR	Contracting Officer's Representative
CPG	clinical practice guideline
CT	computed tomography
DoD	Department of Defense
EBPWG	Evidence-Based Practice Work Group
ED	emergency department
EHR	electronic health record
EIB	exercise-induced bronchospasm
FDA	U.S. Food and Drug Administration
FeNO	functional exhaled nitric oxide
FEV1	forced expiratory volume
FVC	forced vital capacity
GERD	gastroesophageal reflux disease
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
ICS	inhaled corticosteroids
IgE	Immunoglobulin E
IOM	Institute of Medicine
KQs	key questions
LABA	long-acting beta agonist
LAMA	long-acting muscarinic antagonists
LTRA	leukotriene receptor antagonists
mL	milliliter
NAM	National Academy of Medicine
Neb SOLN	nebulizer solution
NICE	National Institute for Health and Care Excellence
NPV	negative predictive value
NO	nitric oxide
OIF/OEF	Operation Iraqi Freedom/Operation Enduing Freedom
PAAP	personalized asthma action plan
PCC	patient-centered care
PD	psychologic dysfunction
PEFR	peak expiratory flow rate

Abbreviation	Definition
PPV	positive predictive value
RCT	randomized controlled trial
RR	relative risk
SABA	short acting beta agonist
SDM	shared decision making
SMART	single maintenance and reliever therapy
SOE	strength of evidence
SR	systematic review
USPSTF	U.S. Preventive Services Task Force
VA	Veterans Affairs
WAAP	written-asthma action plan

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