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 (VA) and the Department of Defense (DOD) guidelines are based on the best information available at the time of publication. The guidelines 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 (CPG) 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 providers consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every health care professional using these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DOD policies. Further, inclusion of recommendations for specific testing, therapeutic interventions, or both within these guidelines does not guarantee coverage of civilian sector care.

Version 3.0 – 2025

Prepared by

The Primary Care Management of Asthma Work Group

With support from

Office of Quality and Patient Safety, Veterans Health Administration

And

Clinical Quality Improvement Program, Defense Health Agency

Version 3.0 – 2025

Based on evidence reviewed through May 2024

Table of Contents

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 Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration and Military Health System," by facilitating the development of clinical practice guidelines (CPGs) for the VA and DOD populations.(1) Development and update of VA/DOD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and wellbeing.

In 2019, the VA and DOD published a CPG for the Primary Care Management of Asthma[1], (2019 Asthma CPG), which was based on evidence reviewed through July 2018. Since the release of that CPG, the evidence based on asthma has expanded. Consequently, a recommendation to update the 2019 Asthma CPG was initiated in 2024. This updated CPG's use of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach reflects a more rigorous application of the methodology than previous iterations.(2) Therefore, the strength of some recommendations might have been modified because of the confidence in the quality of the supporting evidence (see Evidence Quality and Recommendation Strength).

This CPG provides an evidence-based framework for evaluating and managing care for children aged five years and older, and adults who have asthma treated in a VA/DOD ambulatory care setting.

Successful implementation of this CPG will

- Assess the patient's condition and determine, in collaboration with the patient, the best treatment method;
- Optimize human health outcomes and improve quality of life;
- Minimize preventable complications and morbidity;
- Emphasize the use of Patient-Centered Care (PCC) or Family-Centered Care (FCC), especially when caring for children.

II. Background

A. Description of Asthma

Respiratory illnesses, including asthma, are a common medical problem frequently managed by primary care providers. Asthma usually presents in the primary care setting with symptoms of wheezing, coughing, shortness of breath, chest tightness, difficulty sleeping, fatigue, or feeling

[1] See the 2019 VA/DOD Clinical Practice Guideline for the Primary Care Management of Asthma. Available at: https://www.healthquality.va.gov/

weak. 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. Additionally, other respiratory diseases can co-exist with asthma, such as Chronic Obstructive Pulmonary Disease (COPD) which may confuse diagnosis or treatment plans. 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. Standard therapy applied by the primary care provider is appropriate for the vast majority of patients. This CPG will only focus on the treatment and management of asthma.

CPGs attempt to reduce inappropriate practice variability by providing recommendations based on scientific evidence. The use of a standardized approach across patients can reveal when this approach will require more nuanced care or subspecialty consultation. Clinical research and the application of that research to individual patients has changed greatly as new drugs and therapies have been developed. CPGs thus 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 a limited group of controller therapies to that specific severity level. The goal in that 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, maintaining that control, thus reducing the risk of exacerbations and drug therapy related side effects. The expansion of therapy options has necessitated the primary care provider to monitor symptom relief with a plan of when to step therapy up or down over time to achieve 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) between the provider and the patient/family and are periodically reviewed over time.

B. Classification of Asthma Severity and Control

Asthma severity is commonly classified as mild, moderate, or severe. The GINA (Global Initiative for Asthma) guidelines were updated in 2024 (3) and shifted the paradigm for asthma classification from symptom burden on initial evaluation to therapy required for adequate control of symptoms. However, the assumption remains that the prescribed treatment is appropriate for the patient's needs. Asthma is classified as an Ambulatory Care Sensitive Condition (ACSC). Therefore, it is paramount these patients are treated adequately in the primary care setting to prevent asthma exacerbations and costly hospitalizations.

This CPG did not determine if applying a particular classification system for asthma severity led to improved outcomes. We recognize that this classification system is widely used by clinicians, researchers, and other guideline developers and provides a common reference for communication. Table C-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 2019 VA/DOD Asthma CPG. The Algorithm within this CPG refers to Appendix C for the initial management of newly diagnosed patients. Decision points in the algorithm are determined by the CPG's key recommendations and by current standards of care.

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 C-2 was carried forward from the 2019 VA/DOD Asthma CPG. The Algorithm within this CPG refers to Appendix C 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 2022 National Health Interview Survey, over 20 million adults (comprised of 13 million white people, 3 million black people, and 4.5 million Hispanic/Mexican people) and 5 million children (comprised of 2 million white children, 1 million Hispanic children, and almost 1 million black children) had a diagnosis of asthma in the United States (U.S.). The prevalence of asthma is ten times more common in females than males.(4) According to the 2021 National Hospital Ambulatory Medical Care Survey(5), over 9% of all ER visits are from asthma, and the 2020 National Ambulatory Medical Care Survey of Community Health Centers shows that 10% of visits to community health centers were from asthma, where asthma was at least one of the diagnoses.(6)

According to the 2015 National Ambulatory Medical Care Survey, over 6% of all office-based provider visits included asthma as a diagnosis.(7) The morbidity caused by chronic asthma impacts society. Uncontrolled asthma may lead to activity limitation. According to Medical Costs and Productivity Loss Due to Mild, Moderate, and Severe Asthma in the United States, in 2013, children lost 13.8 million days of school, and adults lost 14.2 million days of work in 2008. In 2007, the estimated cost of asthma from loss of productivity was $3.8 billion along with $50.3 billion in direct medical costs and $29 billion in asthma-related mortality.(8)

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 2022, states the following with respect to asthma and disqualification for service: (9)

- History of airway hyper responsiveness including asthma, reactive airway disease, exercise-induced bronchospasm or asthmatic bronchitis, after the 13th birthday.
    - Symptoms suggestive of airway hyper responsiveness 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 hyper responsiveness after the 13th birthday.

Additional information can be found in Appendix E.

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).(10) 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 primary care providers in the diagnosis and management of asthma.

III. Scope of This Guideline

This CPG is based on published clinical evidence and related information available through May 15, 2024. It is intended to provide general guidance on best evidence-based practices (see Appendix A for additional information on the evidence review methodology). Although the CPG is intended to improve the quality of care and clinical outcomes (see Introduction), it is not intended to define a standard of care (i.e., mandated or strictly required care).

A. Guideline Audience

This CPG is intended for use by primary care providers and others on the healthcare team involved in the care of service members, Veterans, or their family members with asthma.

B. Guideline Population

This CPG is designed to assist providers in managing patients with asthma, not including any co-occurring conditions such as COPD. Moreover, the patient population of interest for this CPG is children aged 5 years and older and adults with asthma treated in a VA/DOD ambulatory care setting. It includes Veterans as well as Active, Guard and Reserve service members and their adult beneficiaries.

IV. Highlighted Features of This Guideline

A. Highlights in This Guideline Update

The current document is an update to the 2019 VA/DOD Asthma CPG. The following significant updates make it important that providers review this version of the CPG:

- Updated Algorithm;
- Added 6 new recommendations, reviewed and replaced 4 recommendations, reviewed and amended 3 recommendations, carried over 6 recommendations not changed, and carried over 1 recommendation amended from the 2019 VA/DOD Asthma CPG.

This CPG also provides expanded recommendations on research needed to strengthen future guidelines.

The 2025 VA/DOD Clinical Practice Guideline for the Management of Asthma (VA/DOD Asthma CPG) was developed with the active engagement of a multidisciplinary team of clinicians whose expertise and broad perspectives helped create a document that addresses clinically relevant topics related to the diagnosis and treatment of Asthma in the primary and ambulatory care setting. This CPG includes many updates from the 2019 VA/DOD Asthma CPG. The Work Group developed 12 key questions (KQ) to guide evidence synthesis. In drafting its recommendations, the Work Group considered the strength of evidence, the balance of desired outcomes with potential harms, the potential for variation in patient values and preferences, and considerations such as resource use and equity.

Some of the recommendations are new-added or new-replaced, and the strength of the evidence recommendation is noted:

- We suggest identifying known risk factors (e.g., deployment, smoking) for developing asthma and asthma-associated conditions (e.g., depression, anxiety disorders). (Weak for)
- There is insufficient evidence to recommend for or against offering any particular patient-oriented technology to augment usual care for asthma. (Neither for nor against)
- For patients (ages 12 and over) with asthma, we suggest inhaled corticosteroids combined with a rapid-onset long-acting beta agonist (e.g., formoterol), for control and relief of asthma. (Weak for)
- In patients with uncontrolled asthma on inhaled corticosteroids and long-acting beta agonists using short-acting beta agonists for relief, we suggest inhaled corticosteroids and rapid-onset long-acting beta agonists as both controller and reliever. (Weak for)
- For patients with asthma (ages 12 and over) not controlled by medium or high dose inhaled corticosteroids and long-acting beta agonists, we suggest adding a long-acting muscarinic antagonist (LAMA). (Weak for)

- In patients with exercise-induced bronchoconstriction, we suggest pre-exertional short-acting beta agonists. (Weak for)
- We suggest offering the treatment of gastroesophageal reflux disease in patients with gastroesophageal reflux disease and asthma for improving asthma control and lung function. (Weak for)
- We suggest weight loss in adults with asthma and obesity to improve asthma control. (Weak for)
- We suggest against the use of indoor air filtration devices such as high efficiency particulate air and nitric oxide filters, for asthma control. (Weak against)
- For patients with asthma, there is insufficient evidence to recommend for or against offering telemedicine as an alternative to in-person treatment. (Neither for nor against)

Finally, the 2025 VA/DOD Asthma CPG applied rigorous criteria for reviewing evidence compared with prior versions of this CPG. The GRADE methodology carefully defines how data will be interpreted. It applies rating criteria that assign strength of evidence to critical outcomes, which might result in some recommendations being excluded or downgraded (see Evidence Quality and Recommendation Strength). However, these methods protect the integrity of the Asthma CPG and ensure the recommendation statements are true to the underlying and available evidence.

B. Components of This Guideline

This CPG provides clinical practice recommendations for the care of patients with asthma (see Recommendations). In addition, the Algorithm incorporates the recommendations in the context of the flow of patient care. This CPG also includes Research Priorities which list areas the Work Group identified as needing additional research. To accompany this CPG, the Work Group also developed toolkit materials for providers and patients, including a provider summary, a patient summary, and a quick reference guide, which can be found at: https://www.healthquality.va.gov/index.asp.

C. Demographic Terminology in this Guideline

The demographic terms used in this guideline are derived from the published literature sources included in the systematic review and evidence base. The Work Group used terms such as Black rather than African American and White rather than Caucasian to avoid presumptions about ancestry and to improve clarity and consistency. In order to most accurately present the research evidence on which this CPG is based, the Work Group made every effort to use the same terminology as reported in the published literature base of systematic reviews (SR), clinical trials, and other studies. Consequently, usage of demographic terms in this CPG may vary and appear inconsistent.

V. Guideline Development Team

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, Defense Health Agency, identified the following four providers to serve as Champions (i.e., leaders) of this CPG's Work Group: Amir Sharafkhaneh, MD, PhD and William C. "Claibe" Yarbrough, MD from VA; and Kimberly Fabyan, MD and Jonathan Schroeder, MD, FAAP from DOD. The Work Group comprised individuals with the following areas of expertise: pulmonology, respiratory therapy, pharmacy, nursing, primary care, social work, and medical management. Table 1 lists the Work Group and Guideline Development Team members.

This CPG Work Group, led by the Champions, was tasked with

- Determining the scope of the CPG;
- Crafting clinically relevant key questions (KQ) to guide the systematic evidence review.
- Identifying discussion topics for the patient focus group and considering the patient perspective;
- Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence; and
- Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation.

The Sigma Team, Sigma Health Consulting, and Duty First Consulting were contracted by VA to help develop this CPG.

Table 1. Guideline Work Group and Guideline Development Team

Organization	Names*
Department of Veterans Affairs	**Amir Sharafkhaneh, MD, PhD (Champion)**
	William C. "Claibe" Yarbrough, MD (Champion)
	Donald Curran, MD
	Katherine Richards, MD
	Mary H. Gollings, LCSW
	LaToya Huff, RT
	Christina Nguyen, RT
	Kimberly Schnacky, PharmD
	Elizabeth Rees Atayde, RN, MSN, FNP, CCM-R
Department of Defense	**Kimberly D. Fabyan, MD (Champion)**
	Jonathan C. Schroeder, MD (Champion)
	Lan-Anh Ngo, MD
	Daniel A. Steigelman, MD
	Brian D. Nibbelink, PharmD

Organization	Names*
	William C. Wilson, RRT
	Jane E. Jacknewitz-Woolard, DNP, CRNP-BC, AE-C
	Juhyun Cho, FNP-BC
	Deona J. Eickhoff, MBA, BSN, RN, CCM
VA Evidence Based Practice, Office of Quality and Patient Safety Veterans Health Administration	James Sall, PhD, FNP-BC
	René M. Sutton, BS, HCA, FAC-COR II
	Jennifer Ballard-Hernandez, DNP, RN, FNP-BC
	Sarah Davis-Arnold, MSN, RN, NPD-BC, RCIS, EBP-C
	Lisa M. Wayman, PhD, RN, EBP-C
	Kelley Ern
Clinical Quality Improvement Program Defense Health Agency	Isabella M. Alvarez, MA, BSN, RN
	Lynn M. Young, BSN, RN, CIC
	Gwen Holland, MSN, RN
Sigma Health Consulting, LLC	Frances Murphy, MD, MPH
	James Smirniotopoulos, MD
	Will Wester, MLIS
	Erin Gardner, MPH, PMP
	James Reston, MPH, PhD
	Joann Fontanarosa, PhD
	Samantha Speed-Gangitano, MPH
	Jennifer Falgione, MPH
	Ruth Bekele, MPP
	Annie Tran, MPH
	Sophie Roberts
	Susan Connor
	Dan Sztubinski
Duty First Consulting	Kate Johnson, BS
	Anita Ramanathan, BA

* Additional contributor contact information is available in Appendix J

VI. Summary of Guideline Development Methodology

The methodology used in developing this CPG follows the Guideline for Guidelines, an internal document of the VA/DOD EBPWG updated in January 2019 that outlines procedures for developing and submitting VA/DOD CPGs.(11) The Guideline for Guidelines is available at http://www.healthquality.va.gov/policy/index.asp. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and

strength, management of potential conflicts of interest [COI], interdisciplinary stakeholder involvement, use of SR (systematic review) and external review).(12) Appendix A provides a detailed description of the CPG development methodology.

A. Evidence Quality and Recommendation Strength

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (see Determining Recommendation Strength and Direction).(13)

1. Balance of desirable and undesirable outcomes
2. Confidence in the quality of the evidence
3. Patient or provider values and preferences
4. 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 (*Strong or Weak*). 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 incorporates the four domains.(13) A Strong recommendation generally indicates High or Moderate confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, insufficient evidence exists on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The way this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for an intervention that might be in common practice although it is unsupported by clinical evidence and particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text as shown in Table 2.

Table 2. Strength and Direction of Recommendations and General Corresponding Text

Recommendation Strength and Direction	General Corresponding Text
Strong for	We recommend . . .
Weak for	We suggest …
Neither for nor against	There is insufficient evidence to recommend for or against . . .
Weak against	We suggest against . . .
Strong against	We recommend against . . .

That a recommendation's strength (i.e., Strong versus Weak) is distinct from its clinical importance (e.g., a Weak recommendation is evidence based and still important to clinical care) is important to note. The strength of each recommendation is shown in Recommendations.

This CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations; the determination of the strength of the recommendation is more directly linked to the confidence in the quality of the evidence on outcomes that are critical to clinical decision making. The confidence in the quality of the evidence is assessed using an objective, systematic approach independent of the clinical topic of interest. Therefore, recommendations on topics for which designing and conducting rigorous studies might be inherently more difficult (e.g., randomized controlled trials [RCT]) are typically supported by lower quality evidence and, in turn, Weak recommendations. Recommendations on topics for which rigorous studies can be designed and conducted might more often be Strong recommendations. Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2,14) This stricter standard provides a consistent approach to determining recommendation strengths. For additional information on GRADE or CPG methodology, see Appendix A.

B. Categorization of Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, staying current typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations.(15) For example, the United States Preventive Services Task Force (USPSTF) has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every five years for either an update or reaffirmation.(16)

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England).(17,18) Table 3 lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified, and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The 2025 CPG recommendation categories can be found in Recommendations. Appendix A outlines the 2019 VA/DOD Asthma CPG's recommendation categories.

Table 3. Recommendation Categories and Definitions[a]

Evidence Reviewed	Recommendation Category	Definition
Reviewed[b]	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[c]	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

[a] Adapted from the NICE guideline manual (2012)(17) and Garcia, et al. (2014)(18)
[b] The topic of this recommendation was covered in the evidence review carried out as part of the development of the current CPG.
[c] The topic of this recommendation was not covered in the evidence review carried out as part of the development of the current CPG.
Abbreviation: CPG: clinical practice guideline.

C. Management of Potential or Actual Conflicts of Interest

Management of COIs for the CPGs is conducted as described in the Guideline for Guidelines.(11) Further, the Guideline for Guidelines refers to details in the VHA Handbook 1004.07 Financial Relationships between VHA Health Care Professionals and Industry (November 2014, issued by the VHA National Center for Ethics in Health Care)(19) as well as to disclosure statements (i.e., standard disclosure form completed at least twice by CPG Work Group members and the guideline development team).(11) The disclosure form includes inquiries regarding relevant financial and intellectual interests or other relationships with, for example, manufacturers of commercial products, providers of commercial services, or other commercial interests. The

disclosure form also includes inquiries regarding any other relationships or activities that could be perceived to have influenced, or that give the appearance of potentially influencing, a respondent's contributions to the CPG. In addition, instances of potential or actual COIs among the CPG Work Group and the guideline development team were subject to random web-based identification via standard electronic means (e.g., Centers for Medicare and Medicaid Services Open Payments, ProPublica).

D. Patient Perspective

When developing a CPG, consideration should be given to patient perspectives and experiences, which often vary from those of providers.(14) Focus groups can be used to help collect qualitative data on patient perspectives and experiences. VA and DOD Leadership arranged a virtual patient focus group on March 20, 2024. The focus group aimed to gain insights into patient perspectives of individuals who received care in the VA and DOD healthcare systems for asthma and incorporate these insights into the CPG, as appropriate. Topics discussed included the patients' priorities, challenges they have experienced, information they have received regarding their care, and impacts of their care on their lives and their family members' lives.

The patient focus group was comprised of a convenience sample of seven participants, which included three women and four men. Participants were mixed in terms of receiving care from VA or DOD, as well as all three women being caregivers for children with asthma. The time of diagnosis of asthma ranged from childhood to midlife, and a few of the participants also had co-occurring conditions present such as COPD and other health changes that impacted their lung health. The Work Group acknowledges this convenience sample is not representative of all individuals with asthma within the VA and DOD healthcare systems and, thus, findings are not generalizable and do not comprise evidence. For more information on the patient focus group methods and findings, see Appendix B. Patient focus group participants were provided the opportunity to review the final draft of this CPG and provide additional feedback.

E. External Peer Review

The Work Group drafted, reviewed, and edited this CPG using an iterative process. For more information, see Drafting and Finalizing the Guideline. Once the Work Group members completed a near-final draft, they identified experts from VA and DOD health care systems and outside organizations generally viewed as experts in the respective field to review it. The draft was sent to those experts for a 14-business-day review and comment period. The Work Group considered all feedback from the peer reviewers and modified the CPG where justified, in accordance with the evidence. Detailed information on the external peer review can be provided by the VA Office of Quality and Patient Safety.

F. Implementation

This CPG and algorithm are designed for adaptation by individual health care providers with respect to unique patient considerations and preferences, local needs, and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the care of patients with asthma. The Work Group submits suggested performance metrics for VA and DOD to use when assessing the implementation of this CPG. Robust implementation is identified in VA

and DOD internal implementation plans and policies. Additionally, implementation would entail wide dissemination through publication in medical literature, online access, educational programs, and, ideally, electronic medical record programming in the form of clinical decision support tools at the point of care.

VII. Approach to Care in the Department of Veterans Affairs and the Department of Defense

A. 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.(20-22) Improved patient-clinician communication and a PCC approach conveys openness and supports disclosure of current and future concerns. This can be included as part of VA's Whole Health system.

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 Asthma Action Plan (AAP) (see Appendix F for example), and any steps that need to be taken and any decisions that need to be made and should involve the individual in decision making regarding management of their asthma.

An Asthma Action Plan is a written tool that is jointly created by medical provider, patient, and/or caregiver. It is important that the AAP is individualized with clear instructions for patient and/or caregivers to prevent asthma from worsening. The AAP should include guidance on:

- Signs of asthma episode
- Patient specific reliever (how much to use and when to use)
- When to call healthcare provider
- When to go to the emergency department (ED)

Providers should choose the appropriate AAP for the patient's language and age to increase understanding of instructions and adherence. There are some examples of AAP ready for immediate printing or copy (Appendix F,(23)). There are also web sites with AAP in various languages for different age groups:

- Create an Asthma Action Plan | American Lung Association
- My Asthma Action Plan (lung.org)
- My Asthma Action Plan for Home and School (lung.org)
- School or Child Care Asthma/Allergy Action Plan March 2024 (aafa.org)
- Asthma Action Plan April 2018 (aafa.org)

- CDC Asthma Action Plan
- Asthma Action Plan (nih.gov)
- SMART Asthma Action Plan (allergyasthmanetwork.org)

B. 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.(24) 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.

C. Patients with 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. This approach might entail reference to other VA/DOD CPGs.[2]

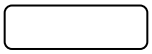
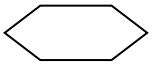
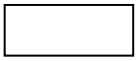
[2] The VA/DOD Clinical Practice Guidelines are available at: https://www.healthquality.va.gov/

VIII. Algorithm

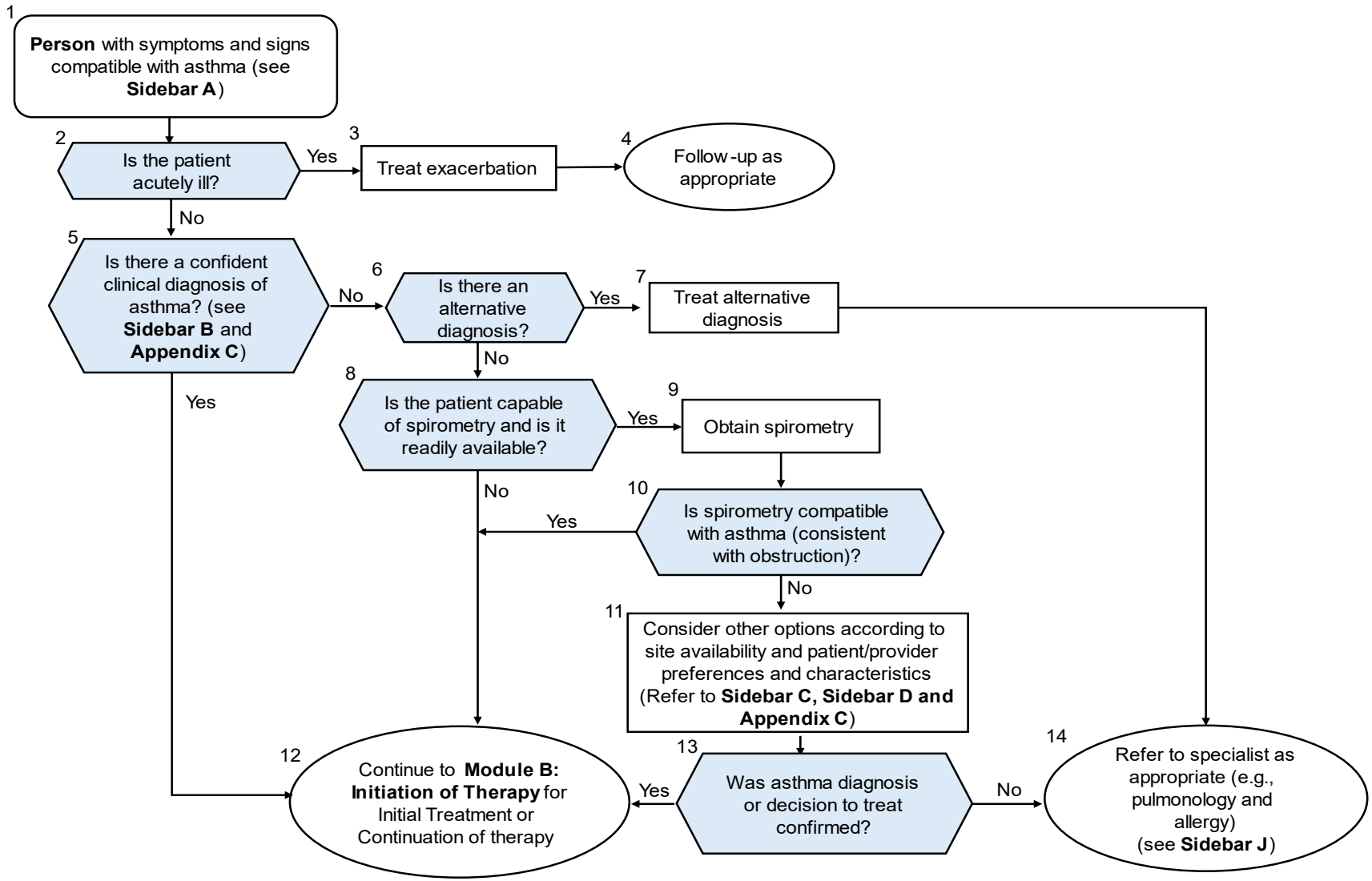
This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in the primary care management of asthma. This algorithm format represents a simplified flow of the management of patients with asthma and helps foster efficient decision making by providers. It includes:

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

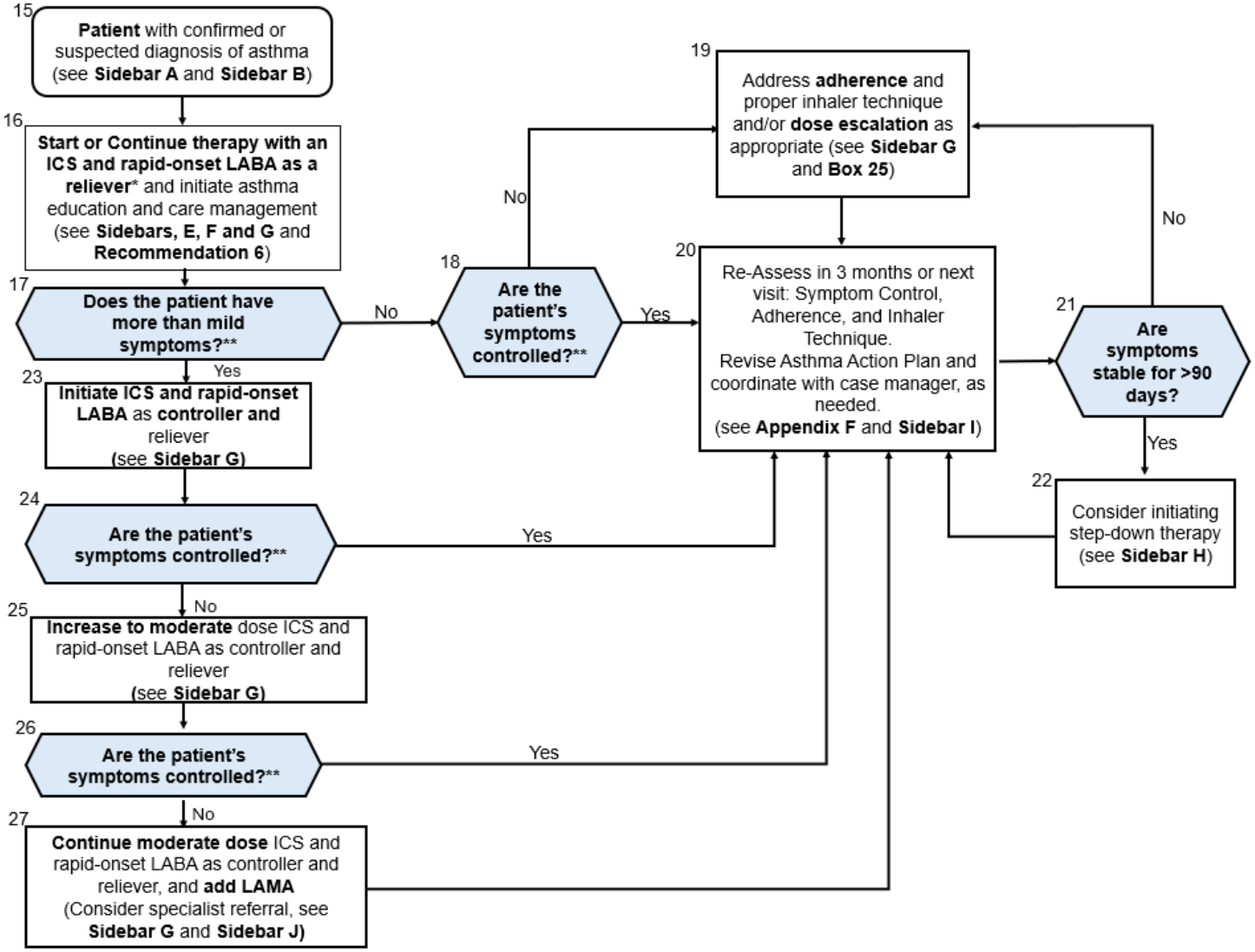
The algorithm is a step-by-step decision tree. Standardized symbols are used to display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.(25) Sidebars A-J provide more detailed information to assist in defining and interpreting elements in the boxes.

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 algorithm.

Module A. Assessment and Diagnosis of Asthma



Module B. Initiation of Therapy



Abbreviations: LABA: Long-acting beta agonist; ICS: inhaled corticosteroid; LAMA: long-acting muscarinic receptor
*Use lowest effective dose of ICS or intermittent therapy to reduce side effects

**At every visit address patient's adherence and proper inhaler technique

Sidebar A: Asthma Symptoms

- **Adult:** Daytime or nighttime chronic recurring cough, wheeze, chest tightness, and shortness of breath
- **Child:** Daytime or nighttime prolonged (more than 2 weeks) or recurring cough, wheeze, chest tightness, shortness of breath and other associated non-respiratory symptoms including irritability and being fatigued or tired

Sidebar B: Assessment

- Symptoms (see Sidebar A)
- Pattern (exercise, diurnal vs. nocturnal symptoms)
- Precipitating triggers (exercise, allergens, cold air, laughter)
- Aggravating factors/risk factors (see **Recommendations 1 and 2**)
  - Adults and children: Overweight/obesity, atopy, secondhand smoke exposure in children, history of lower respiratory infection
  - Adults: Depression, current smokers, OIF/OEF deployment
  - Occupational exposure
- Medical history including allergic rhinitis or eczema and physical exam (Appendix D)
- Comorbidities
- Effects of symptoms on quality of life, sleep, and performance (work or school)
- Response to treatment
- If not previously done, suggest radiograph if other diagnoses are being considered
- Review CBC for eosinophil count
- Assess patient/caregiver educational needs (health literacy, knowledge, skills, confidence, preferences for education methods, modalities)
- Utilize the ACT to assess asthma control

Abbreviations: ACT: Asthma Control Test; CBC: complete cell blood count; OIF/OEF: Operation Iraqi Freedom/Operation Enduring Freedom

Sidebar C: Alternative Evaluation for Asthma

Asthma is a clinical diagnosis, though diagnostic studies and response to treatment may be supportive of the diagnosis. In situations in which routine spirometry does not demonstrate obstruction yet there remains a clinical suspicion for asthma, any of the following options should be offered dependent upon site availability and patient/provider preferences:

- Spirometry with bronchodilator testing (if not previously performed)
- Bronchoprovocation testing
    - May be required for some service members or in some situations in the DOD
    - Methacholine is the preferred agent for bronchoprovocation
    - Bronchoprovocation should not be ordered for children; refer to specialist only
- Trial of treatment (See Module B)
- Specialist Referral (Pulmonary or Allergy and Immunology)

Abbreviations: DOD: Department of Defense

Sidebar D: Lung Function Testing

- **Spirometry:** initial test for use when obstructive or restrictive ventilatory disease are suspected
- Use bronchodilators testing to assess for reversibility if obstruction is noted on spirometry
- **Bronchoprovocation** should be considered when reactive airways disease/asthma is suspected despite baseline spirometry inconsistent with the diagnosis. Methacholine is a reasonable first line bronchoprovocative test. It may be required for some DOD personnel. However, due to administrative and logistical concerns related to MCT, patients requiring bronchoprovocation testing should be referred to specialist for evaluation
- Bronchoprovocation should not be ordered for children; refer to specialist only
- Exercise challenge test considered for patients with symptoms only with exercise
- **Full PFT** (spirometry, plethysmography, and SB DLCO measurement): plethysmography allows for a confirmation of a restrictive ventilatory defect. SB DLCO measurement is used to assess for abnormal alveolar gas exchange

Abbreviations: DOD: Department of Defense; MCT: Marine Combat Training; PFT: pulmonary function testing; SB DLCO: single breath diffusing capacity of the lung for carbon monoxide

Sidebar E: Asthma Education and Self-Management Support

Patients and caregivers should be informed of the diagnosis of asthma. Their current understanding of asthma and treatment adherence should be assessed, they should be provided evidence-based education and materials/resources, and they should be given the opportunity to ask questions so they can fully understand their asthma. Consistent follow-up should ensure the patient and caregiver are confident in their ability to self-manage their asthma and take a more active role in the management of their asthma with their healthcare team. Asthma education should include:

- Basic pathophysiology of asthma
- Typical asthma symptoms (see Sidebar A)
- How to identify well-controlled asthma
- Asthma patterns (exercise, nocturnal symptoms, and seasonal allergens) and risk factors (see **Recommendations 1 and 2**)
- Asthma exacerbations and precipitating triggers
- Goals of treatment and use of Asthma Action Plan
- Medication use (e.g., what it does, how to use it, potential side effects, and rationale for why each medication was selected) including assessment of device technique
- How to recognize loss of asthma control and 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 3**)
- Consider a team approach to asthma management (dietician, pulmonologist, behavioral health provider, disease manager, health coach, etc.)
- Lifestyle changes and psychosocial considerations (see Sidebar F)

Sidebar F: Care Management

- **Multidisciplinary care management:**
  - Multidisciplinary care management consists of comprehensive assessment and treatment (not necessary to be in the same location) (see **Recommendation 15**)
  - CBT may be considered to reduce anxiety and improve quality of life (see **Recommendation 17**)
  - Triggers for worsening control should be identified for both indoor and outdoor settings, and if possible, steps taken to reduce exposure
  - Psychological comorbidities may affect patient outcome
  - Medical co-occurring conditions should be identified and addressed such as: Gastroesophageal Reflux Disease (GERD), Obstructive Sleep Apnea (OSA), hormonal disorders, rhinitis, along with chronic disorders such as diabetes and depression
- **Lifestyle changes:**
  - Smoking/vaping cessation
  - Regular exercise to help reduce obesity (see **Recommendation 16**)
  - Weight management, choose healthy foods, allergy reducing diet choices
  - Avoidance of triggers especially outdoor seasonal allergies such as dust, tree and grass pollen, and fungus; indoor triggers such as dust mites, mold, scented candles and strong perfumes/odors
  - Ensure patient compliance with medications, allergy testing and treatment, etc.
  - Avoid environmental triggers which may include wood burning fireplaces or stoves in winter, particulate matter (PM) – ozone, vehicle exhaust and others
- **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)
  - Increased anxiety may be experienced during times of asthma trigger exposure and lead to poor asthma control and/or perception of a lower quality of life
  - Family support of patient treatment emotionally, spiritually, and behaviorally
  - Reduce stress response through stress management and reduction techniques, medications, mindfulness, etc.

Abbreviations: CBT: cognitive behavioral therapy

Sidebar G: Steps for Escalation and De-escalation of Asthma

- **Consideration for Step-up Therapy**
  - Low dose ICS + rapid-onset long-acting beta agonist as reliever
  - Low dose ICS + rapid-onset long-acting beta agonist as controller and reliever (see **Recommendation 6**, **Recommendation 7**, and **Recommendation 8**)
  - Moderate dose ICS + rapid-onset long-acting beta agonist as controller and reliever
  - Moderate dose ICS + rapid-onset long-acting beta agonist as controller and reliever + LAMA (see **Recommendation 9**)
    - Consider specialist referral
  - High dose ICS + rapid-onset long-acting beta agonist as controller and reliever + LAMA
    - Consider specialist referral for consideration of advanced treatments (e.g., biologics, PD4 inhibitor, etc.)
- **Additional Consideration for Step-up Therapy**
  - Assess and address inhaler technique whenever step-up therapy is indicated
  - Monitor whether patient is overusing reliever beta agonist medications (e.g., SABA, rapid-onset long-acting beta agonist)
- **Consideration for Step-down Therapy**
  - Patient selection
    - De-escalation of therapy should be avoided in patients who cannot be closely monitored and patients at high risk of severe exacerbations, such as pregnant individuals and those with recent acute illness
  - Use lowest effective dose of ICS or intermittent therapy to reduce side effects. (see **Recommendation 11**, Sidebar H)
    - ICS dose should be reduced gradually with regular reassessment of asthma control
    - ICS should not be discontinued (see **Recommendation 5**) when de-escalating therapy. In cases of mild and well-controlled asthma, low dose ICS + rapid- onset long-acting beta agonist should be continued as reliever therapy
    - Patients should have a written action plan including instructions for recognizing early signs of worsening asthma and steps to take, including medication adjustments and when to seek medical attention
- Refer to Appendix G, Tables G-1 and G-2 for discussion of specific medications

Abbreviations: ICS: inhaled corticosteroid; LAMA: long-acting muscarinic antagonist; PD4: phosphodiesterase-4; SABA: short-acting beta agonist

Sidebar H: Considerations for Stepping Down Therapy

- **Patient Selection for ICS Reduction:**
  - Do not reduce ICS dose in patients who cannot be closely monitored, such as those who are planning to travel or have inconsistent follow-up appointments
  - Avoid stepping down in individuals at high risk of severe exacerbations, such as pregnant individuals or those with recent acute illnesses
- **ICS Reduction Strategy:**
  - Decrease the ICS dose gradually by 25-50% every 3 months
  - The goal is to reach the lowest effective maintenance dose that continues to control asthma symptoms
  - Assess asthma symptoms regularly throughout the tapering process to ensure stable control
- **Discontinuing LABAs:**
  - LABAs can generally be discontinued without a taper, as they do not require a gradual reduction like ICS
- **Action Plan for Symptom Management:**
  - Patients should have a written action plan to monitor for any signs of worsening asthma
- **Action Plan:**
  - Ensure that the patient has a written asthma action plan
  - The action plan should include instructions for recognizing early signs of worsening asthma and steps to take, including medication adjustments and when to seek medical attention
  - Make sure they have access to adequate medication and know what actions to take if symptoms return or worsen after discontinuing LABA or stepping down the ICS
- Refer to Appendix G, Tables G-1 and G-2 for discussion of specific medications

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

Sidebar I: Considerations for Short Term Follow-up

- Recent hospitalization
- Urgent Care (UC)/Emergency Department (ED) visit
- Step medication change
- Recent exacerbation
- Increasing use of rescue inhalers
- Inability to use inhaler correctly

Sidebar J: Considerations for Specialty Referral
■ Life-threatening exacerbation/intubation ■ Multiple hospitalizations or ICU admission ■ Difficulty confirming the diagnosis of asthma ■ Persistent or severely uncontrolled asthma or frequent exacerbations ■ Evidence of, or risk of, significant treatment side effects ■ Suspected occupational asthma ■ Symptoms suggesting complications or a sub-type of asthma (e.g., eosinophilia)

Abbreviations: ICU: intensive care unit

IX. Recommendations

The evidence-based clinical practice recommendations listed in the table below were developed using a systematic approach considering four domains as per the GRADE approach (see Summary of Guideline Development Methodology). These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences, and other implications (e.g., resource use, equity, acceptability).

Table 4. Evidence-Based Clinical Practice Recommendations with Strength and Category[a,b]

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Diagnosis and Assessment		1.	We suggest identifying known risk factors (e.g., deployment, smoking) for developing asthma and asthma-associated conditions (e.g., depression, anxiety disorders).	Weak for	Reviewed, New-replaced
		2.	In adults and children with asthma, we suggest identifying known risk factors of asthma-related outcomes including overweight/obesity, atopy, air quality, secondhand smoke exposure in children, and history of lower respiratory infection and screening for presence of anxiety or depression.	Weak for	Not Reviewed, Amended
Treatment and Management	*Asthma Education*	3.	We suggest offering a written asthma action plan to improve asthma control and asthma-related quality of life.	Weak for	Reviewed, Amended
		4.	There is insufficient evidence to recommend for or against offering any particular patient-oriented technology to augment usual care for asthma.	Neither for nor against	Reviewed, New-replaced
	Pharmacotherapy	5.	We recommend inhaled corticosteroids (ICS) for asthma control.	Strong for	Not reviewed, Amended
		6.	For patients (ages 12 and over) with asthma, we suggest inhaled corticosteroids combined with a rapid-onset long-acting beta agonist (e.g., formoterol), for control and relief of asthma.	Weak for	Reviewed, New-replaced
		7.	For patients with uncontrolled asthma on inhaled corticosteroids alone, we recommend the use of both inhaled corticosteroids and rapid-onset long-acting beta agonists (e.g., formoterol) as both controller and reliever.	Strong for	Reviewed, Amended

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Treatment and Management (contd.)		8.	In patients with uncontrolled asthma on inhaled corticosteroids and long-acting beta agonists, who use short-acting beta agonists for relief, we suggest inhaled corticosteroids and rapid-onset long-acting beta agonists (e.g., formoterol) as both controller and reliever.	Weak for	Reviewed, New-added
		9.	For patients with asthma (ages 12 and over) not controlled by medium or high dose inhaled corticosteroids and long-acting beta agonists, we suggest adding a long-acting muscarinic antagonist (LAMA).	Weak for	Reviewed, New-added
		10.	In patients with exercise-induced bronchoconstriction, we suggest pre-exertional short-acting beta agonists.	Weak for	Reviewed, New-replaced
		11.	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	Not reviewed, Not changed
		12.	We suggest offering the treatment of gastroesophageal reflux disease in patients with gastroesophageal reflux disease and asthma for improving asthma control and lung function.	Weak for	Reviewed, New-added
	Non-pharmacotherapy	13.	We suggest weight loss in adults with asthma and obesity to improve asthma control.	Weak for	Reviewed, New-added
		14.	We suggest against the use of indoor air filtration devices such as high efficiency particulate air and nitric oxide filters, for asthma control.	Weak against	Reviewed, New-added
		15.	We suggest a multidisciplinary treatment approach to improve asthma-related quality of life, asthma control, and treatment adherence.	Weak for	Not reviewed, Not changed
		16.	We suggest patients with asthma participate in regular exercise to improve quality of life and asthma control.	Weak for	Not reviewed, Not changed
		17.	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 asthma.	Weak for	Not reviewed, Not changed

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Treatment and Management (contd.)	*Monitoring and Follow-up*	18.	We suggest against utilizing spirometry for routine monitoring of patients with stable asthma.	Weak against	Not reviewed, Not changed
		19.	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	Not reviewed, Not changed
		20.	For patients with asthma, there is insufficient evidence to recommend for or against offering telemedicine as an alternative to in-person treatment.	Neither for nor against	Reviewed, New-added
		21.	We suggest leveraging electronic health record capabilities, such as trackers and reminders, in the care of patients with asthma.	Weak for	Not reviewed, Not changed

[a] For additional information, please refer to Determining Recommendation Strength and Direction
[b] For additional information, please refer to Recommendation Categorization

A. Diagnosis and Assessment

Recommendation

1. We suggest identifying known risk factors (e.g., deployment, smoking) for developing asthma and asthma-associated conditions (e.g., depression, anxiety disorders). **(Weak for | Reviewed, New-replaced)**

Discussion

Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) combat deployment is a risk factor unique to service members and Veterans. Overseas Contingency Operations such as OIF/OEF are linked with increased exposure to hazardous environmental materials including pollutants (e.g., particulate matters [PM], chemical, and biological materials).(26) McClean investigated waste disposal in open-air burn pits, a common practice in OIF/OEF from 2001 to 2009.(26) The systematic review, involving nine articles with a total of 209,423 patients, found no significant difference in the frequency of asthma amongst those with burn pit exposure compared to those not exposed. There was also no significant difference in respiratory system disease risk between deployed and non-deployed personnel.

In terms of air quality index, Williams 2023 (27), reviewed 11 articles in a systematic review on service members and Veterans deployed to Southwest Asia - in particular Kabul, Afghanistan. There was no significant difference in respiratory system disease risk between deployed and non-deployed personnel. Respiratory symptoms including prevalence of wheeze, nocturnal coughing and chronic bronchitis were found to have a significant difference in symptoms reported between

military personnel and non-military controls. However, these symptoms were not specific to asthma. Many of the studies included were limited by bias and lack of adjustment for confounding factors.

In the prior CPG review, Rivera et al. (2018) found a statistically significant association between OIF/OEF combat deployment and incidence of new-onset asthma in adults.(28) The longitudinal cohort study involved 75,770 military participants over 12 years. However, burn-pit exposure was not associated with a greater increase in asthma development risk than non-burn-pit deployed personnel. The primary outcome of interest in the systematic evidence review was self-reported provider-diagnosed new-onset asthma at follow-up.(28) The "Defense Health Board: Deployment Pulmonary Health" report (2015) cites a heterogeneous body of references, most of which did not meet criteria for the evidence review of this CPG.(29) The Work Group acknowledges that the Defense Health Board seeks to further develop recommendations for post-deployment screening and surveillance for pulmonary disease. Additional research is needed on the association between exposure to potential inhalational hazards during deployment (e.g., OIF/OEF burn pits exposure) and asthma or other adverse pulmonary health outcomes.

The Work Group systematically reviewed evidence related to this recommendation. The Work Group's confidence in the quality of the evidence was low, as the evidence relating to depression and current smoking was low, and clear evidence related to combat was described as lacking. (26,27) Therefore, this recommendation is categorized as *Reviewed, New-replaced*. The benefits of identifying known risk factors slightly outweigh the harm, as the patient must invest time into completing a survey, and there might be associated stigma with identifying risk factors. There is some variation in patient values and preferences, as some patients may not have time to answer questions. An additional implication is the associated provider time required to ask the questions. Thus, the Work Group decided on a *Weak for* recommendation.

Recommendation

2. In adults and children with asthma, we suggest identifying known risk factors of asthma-related outcomes including overweight/obesity, atopy, air quality, secondhand smoke exposure in children, and history of lower respiratory infection and screening for presence of anxiety or depression.
   (Weak for | Not Reviewed, Amended)

Discussion

As these are *Not Reviewed, Amended* 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.(30-42) The evidence for each identified risk factor is discussed as follows:

Obesity

The Work Group found evidence that overweight/obesity is a risk factor for asthma-related outcomes. Ahmadizar et al. (2016), from an SR of five studies, found that overweight/obesity was associated with an increased risk of asthma exacerbation in children.(31) 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).(32) 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.(33) 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.(34) 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).(43) 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 three retrospective cohort studies conducted in adults(35,36) (44), as well as two SRs of studies conducted in children.(37,38) 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.(37,39,40) 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.(41) 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).(35)

Depression

Zhang et al. (2016) found that adults with both depression and combined psychologic dysfunction (PD) had an increased risk of asthma exacerbation.(42) There was also an increased risk of unscheduled medical visits, ED visits, and hospitalizations for patients with depression and PD (SOE: low). Depression may lead to behaviors that cause poor asthma control including but not limited to poor adherence.(42)

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).(35) 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.(45) 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.

Two recent studies point to sex and sexual minorities as potential risk factors for asthma. However, the work group felt that further research is needed to clarify the role of sex and sexual minorities as risk factors for asthma and asthma related outcomes.(46,47)

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 2019 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 indoor and outdoor allergen risk factors, they have been identified by other expert review panels.(48) This information was not included in the systematic evidence review carried out for this CPG, so it 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 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

3. We suggest offering a written asthma action plan to improve asthma control and asthma-related quality of life.

(Weak for | Reviewed, Amended)

Discussion

This weak recommendation was based on low quality evidence by Dhippayom et al. (2022*).*(49) This SR and meta-analysis of 13 RCTs comparing the efficacy of different strategies to support the self-management of asthma in patients found that patients who received behavioral health care more than once per month via an electronic-Health method had greater improvement in their asthma control and that patient education with a combination of features was most likely to decrease asthma severity or exacerbations as measured by systemic corticosteroid use during hospitalizations. Additionally, Hodkinson et al. (2020)(50) found that regularly supported self-management was the approach most likely to decrease asthma related healthcare utilization. However, evidence review including Salim et al. (2020)(51), Jeminiwa (2024)(52), Kim et al. (2022)(53), Fedele et al. (2021)(54), Rhee et al. (2021)(55), Baptist (2020)(56), and Park et al. (2018)(57) which was conducted as part of this guideline update did not complete any comparative analysis of patient education components or asthma action plan (AAP) components, so we were unable to make any determinations of their effectiveness on the control of asthma or asthma-related quality of life. Of note, one SR, Kew et al. (2022)(58) did identify that stable and increased doses of inhaled corticosteroids (ICS) as part of an AAP were equivalent in reducing the need for systemic rescue corticosteroids as measured by the number and severity of asthma exacerbations, although this was not identified as a component of an AAP.

Patients are eager to know about and understand their medical conditions so that they can better manage their health. Educating patients with current, relevant, evidence-based information about their condition helps patients to be more involved in shared decision making with their healthcare team and successfully managing their health (59) and is generally considered the standard of care. Components of a patient-centered education plan should include: the goals of education, assessment of baseline asthma literacy, information about the disease and symptoms, identification of disease triggers and how to control them, skills training, identification of medications and their use, and when the patient should seek additional medical help to manage their asthma.(60)

Patient education should include a structured patient-centered conversation, evidence-based education documents, and a discussion about ongoing follow-up.(60) This education should be tailored to the patient's needs, values, and literacy. Educational programs for patients with asthma should include a written AAP as part of the education documents provided to the patient. Multiple different educational modalities are available and should be evaluated and utilized to ensure complete patient understanding. Formats for AAPs can vary significantly, but their main feature includes instructions to help patients maintain daily control of their asthma and to recognize and respond to loss of that control. The routine review and update of AAPs should be integrated into regular medical follow-up.

The patient focus group that was conducted for this CPG suggested that patients are receptive to the use of AAPs. These AAPs provide an organized approach for day-to-day management and a plan for what to do when loss of symptom control occurs. Education about the AAP can provide

an opportunity to ask questions, express concerns, learn valuable skills, and share values and preferences.

The patient focus group identified some variation regarding the use of AAPs, but overall AAPs were important to their care and the care of their child(ren) with asthma and provided them with multiple management options for their asthma care. Focus group attendees discussed how important it was to obtain the AAP and education on how to use it promptly after the diagnosis of asthma was made. Providers may see the AAP and education of patients as a burden. Healthcare staff knowledge and training on AAP completion and patient education varies widely within organizations. The time to complete and review the AAP and educate patients takes significant time especially if there are differences in language or health literacy.

Other considerations are the availability of printers in the office or electronic means for the patient to obtain the AAP. Integration of the AAP into the Electronic Health Record (EHR) can facilitate regular review and adjustment. Finally, patients have significant variation in their confidence of self-managing asthma; this can lead to patients overusing the healthcare system or delaying treatment. Healthcare providers should be aware of this. Example AAPs can be found in Appendix F.

The Work Group systematically reviewed evidence by Dhippoyon et al. (2022)(49), Kew et al. (2022)(58), Hodkinson et al. (2020)(50), Salim et al. (2020)(51), Jeminiwa (2024)(52), Kim et al. (2022)(53), Fedele et al. (2021)(54), Rhee et al. (2021)(55), Baptist (2020)(56), and Park et al. (2018)(57) related to this recommendation. Therefore, it is categorized as *Reviewed, Amended*. The Work Group's confidence in the quality of the evidence was very low. Our Work Group's *Weak for* recommendation reflects both the low quality of evidence and that the overall body of evidence has a major limitation in that components of an educational or AAP were not discussed or evaluated in the evidence review. The benefits of a written AAP to improve asthma control and asthma-related quality of life slightly outweighed the potential harm. Patient values and preferences varied somewhat due to different modalities used in the education process. Thus, the Work Group decided upon a *Weak For* recommendation.

Recommendation

4. There is insufficient evidence to recommend for or against offering any particular patient-oriented technology to augment usual care for asthma.
   (Neither for nor against | Reviewed, New-replaced)

Discussion

Medication adherence is a critical component of asthma management and can affect asthma control and risk of severe or life-threatening exacerbations. Use of patient-oriented digital technologies in addition to the usual care may increase medication adherence. The studies reviewed for the CPG did not have a standardized definition or classification of digital technologies for asthma intervention. In one SR of 17 RCTs, the digital technology interventions that provide feedback about medication-taking were classified as internet or mobile phone self-management

applications; adherence monitoring devices; games; and interactive voice recognition equipment. (61)

The Work Group reviewed the evidence to determine whether digital technologies can improve medication adherence to improve asthma control and other benefits versus usual care. There were three SRs, eight individual RCTs, and one informational study identified for review. In one SR (61) and three RCTs (62-64) mobile applications improved controller asthma medication adherence (in children and adults) based on validated questionnaires, which may have translated to the improved asthma control over usual care. The SR by Chan et al. (2022)(61), found that mobile text message intervention seemed to improve asthma control compared to usual care. While Coker et al. (2021)(65) found that mobile text message interventions showed no difference in healthcare utilization in the pediatric population. Another SR with 10 RCTs, found that adherence monitoring devices improved inhaler adherence in children but could not confirm actual inhalation of the medication.(66) Of the body of evidence reviewed, the overall quality was very low due to limitations including small number of studies for the various technologies, inconsistent methodologies, and some risk of bias between group compared to usual care. Also, the outcomes (e.g., FEV1, peak flow readings, inhalers skills, healthcare utilizations, and QOL) were not consistent across all studies. Most individual studies identified were relatively small, with short follow-up, and did not consider the effect of digital technologies on time off work or school.

As this is a *Reviewed, New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation. The overall quality of evidence is very low for technology as a means to reduce the number or severity of asthma-related exacerbations. However, there were some benefits seen and patients generally accepted the technological interventions. We recognize that there is large variation in patient values and preferences due to age, learning skills, physical abilities, and socioeconomic status. Patient-oriented technologies also require additional resources and have limitations (e.g., equipment, training, rurality, and internet connectivity) particularly for parents of the pediatric population. Finally, longitudinal research is needed to see if one digital technology is better than others; the cost-benefits; or long-term harms. Therefore, the Work Group offers a *Neither for nor against* recommendation.

b. Pharmacotherapy

The evidence review of the 2019 VA/DOD Asthma CPG included a systematic review and metanalysis (61) which compared a combination inhaled corticosteroid and a long-acting beta-agonist (ICS/LABA) as controller and quick relief therapy to maintenance ICS and to fixed dose maintenance ICS/LABA. There are currently several LABAs approved for patients with asthma. Some have a more rapid onset of action (e.g., formoterol) while others have a slower onset of action (e.g., salmeterol). The LABA which was used in the combined ICS/LABA controller/reliever was formoterol. Despite evidence showing reduced exacerbations using formoterol combined with ICS as both controller and reliever, this strategy was not recommended by the 2019 VA/DOD Asthma CPG. The Food and Drug Administration had approved ICS/LABAs as maintenance controller medications for asthma but not as fast acting relievers. This strategy was also considered novel and had not yet become a standard of care. Although ICS/formoterol combinations still do not have FDA approval as quick relief medications, later asthma guidelines have supported their use as controller/relievers (GINA) and this strategy has become adopted into

routine practice. This strategy is often referred to as maintenance and reliever therapy (MART) or single inhaler maintenance and reliever therapy (SMART). The 2025 VA/DOD Asthma CPG uses the terminology controller/reliever rather than maintenance and reliever as it is clearer with respect to mechanism of action and recognizes that particularly for mild asthma a symptom driven controller/reliever strategy does not require daily maintenance use.

The 2025 evidence review included additional evidence evaluating combination controller/reliever therapy. The majority of the studies evaluated a single inhaler combination of inhaled corticosteroid and formoterol. At the time of this guideline, formoterol is the only LABA that has been studied and demonstrated effectiveness in controller/reliever therapy, though due to concerns for use of LABA monotherapy in asthma, it is not FDA approved as a reliever medication. A small number of the studies in the evidence review evaluated a single inhaler combination of ICS/albuterol. Albuterol, like formoterol, is a fast-acting beta agonist but has a shorter duration of action so is considered a short acting beta agonist (SABA).

Access to combination inhalers may be limited for some patients due to cost or formulary considerations. With education it is likely that patients could duplicate the combined controller/reliever strategy by taking separate beta agonist and ICS inhalers at the same time. Close follow-up, however, would be necessary to ensure patients are taking both ICS and beta agonist inhalers together and not stopping their ICS. The patient focus group of this CPG identified the value of access to combination medication options to control their (or their child's) asthma. The Work Group also recognized the convenience of combination inhalers. Combination products simplify treatment plans and support improved adherence by avoiding the need for multiple devices or delivery systems. Whether as a combined inhaler, or in separate devices, patients will need to be educated regarding the purpose, frequency of use/overuse of medication as well as inhaler administration technique.

Recommendation

5. We recommend inhaled corticosteroids (ICS) for asthma control.
   (Strong for | Not reviewed, Amended

6. For patients (ages 12 and over) with asthma, we suggest inhaled corticosteroids combined with a rapid-onset long-acting beta agonist (e.g., formoterol), for control and relief of asthma.
   (Weak for | Reviewed, New-replaced)

Discussion

Inhaled corticosteroids (ICS) are an essential therapy for the control of asthma. This is a strong recommendation carried forward from the prior 2019 Clinical Practice Guideline (CPG). The evidence review from the prior 2019 CPG established that ICS as controller medication decreases asthma symptoms and exacerbations. The use of ICS for asthma control has become standard of care. The 2025 recommendation is modified from 2019. The 2019 CPG recommended ICS for persistent asthma. Prior distinctions between mild intermittent and mild persistent asthma were

based on frequency of symptoms, however, these distinctions were arbitrary and not evidence based. Labeling patients as intermittent asthma may lead to undertreatment with ICS and overuse of beta agonists. Additional evidence reviewed in the 2025 CPG continues to support the use of ICS as a controller medication in patients classified as mild. Based on the relevant studies from the 2019 and 2025 CPG evidence base, the 2025 CPG strongly recommends the use of ICS for the control of asthma, as it is a *Not Reviewed, Amended* recommendation. The confidence in the quality of the evidence is high. Benefits of therapy with ICS with respect to improved asthma symptoms and reduced exacerbations outweigh risks in patients of all ages and levels of severity. Thus, the Work Group decided on *Strong for* recommendation.

We suggest that ICS combined with a rapid-onset long-acting beta agonist (e.g., formoterol) as both controller and reliever be the preferred strategy for the treatment of asthma in patients 12 years and older. There was insufficient evidence to recommend this strategy in patients ages 4-11. The primary benefit of this strategy was a reduction in asthma exacerbations. This benefit was most clearly seen in studies which enrolled patients who were considered poorly controlled or classified as moderate to severe. These patients were instructed to use their ICS/rapid-onset long-acting beta agonist (e.g., formoterol) medications as everyday maintenance therapy and in addition as required for symptoms. In studies which enrolled patients classified as mild asthma, patients used combination ICS/rapid-onset long-acting beta agonist (e.g., formoterol) intermittently in response to symptoms. This combined controller/reliever strategy was superior to SABA alone and non-inferior to maintenance ICS plus SABA as needed for symptoms, with respect to asthma exacerbations. Although the inclusion of evidence for patients with mild asthma weakens the strength of this recommendation, it does importantly improve its clinical utility since asthma control and severity are dynamic.

The evidence review of the 2019 VA/ DOD Asthma CPG included a systematic review and metanalysis (67) which compared a combination inhaled corticosteroid and rapid-onset long-acting beta agonist (e.g., formoterol) as controller and for quick relief therapy to maintenance ICS plus SABA and to fixed dose maintenance ICS/LABA plus SABA. The LABA which was used in the combined ICS/LABA controller/reliever was formoterol which has a rapid onset of action. This review included 16 RCTs (N=22748 patients). The studies reviewed consistently showed ICS/LABA controller/reliever therapy reduced asthma exacerbations in patients 12 years and older compared to other strategies. Only one study in this systematic review classified patients as having mild to moderate asthma. Most studies either classified patients as moderate to severe or did not classify the patients but indicated that their asthma was not controlled, or they had had an exacerbation in the past year. The metanalysis of the included studies showed the following absolute percent reduction in asthma exacerbations, and strength of the evidence for the comparisons.

- ICS/rapid-onset LABA Controller/Reliever vs Same Dose ICS -8.1 Moderate
- ICS/rapid-onset LABA Controller/Reliever vs Higher Dose ICS -11 Low
- ICS/rapid-onset LABA Controller/Reliever vs ICS/ LABA Same dose ICS -6.6 High
- ICS/rapid-onset LABA Controller/Reliever vs ICS/LABA Higher dose ICS -2.8 High

Subgroup analysis of one study also showed a large reduction in asthma exacerbations for patients ages 4-11 (N 341) however, the strength of the evidence was low. This was considered insufficient evidence to recommend this strategy to patients 4-11.(68)

Despite consistent benefit in reducing asthma exacerbations, only one study comparing combination ICS/rapid-onset LABA as controller/reliever to a similar dose ICS/LABA maintenance showed a significant improvement in symptom control as measured by AQ-5 questionnaire. Other studies showed no difference in control of symptoms. The strength of evidence (SOE) for this finding was considered low.

A 2021 systematic review (69) compared combination inhaled steroid and rapid-onset long acting beta agonist (e.g., formoterol) (ICS/rapid-onset LABA) to other strategies in patients with asthma classified as mild. As in the prior metanalysis the rapid-onset LABA that was combined with ICS was formoterol. ICS/rapid-onset LABA as required for symptoms was shown to be superior to SABA alone as required for symptoms with respect to asthma exacerbations requiring systemic steroids. The SOE for this outcome was high. There was also a large reduction in exacerbations requiring hospitalization, ER or urgent care visits, however, events were less common so the SOE for this finding was low. Difference in asthma control questionnaire scores favored ICS/rapid-onset LABA over SABA alone, however, the difference was small and unlikely to be clinically important. The SOE for this finding was moderate. ICS/rapid-onset LABA used as required for symptom control was non-inferior to maintenance ICS and SABA as required for symptoms with respect to exacerbations requiring systemic steroids, (SOE: moderate) and superior with respect to exacerbations resulting in hospitalizations, ER or urgent care visits. (SOE: low). Patients on maintenance ICS + SABA for symptoms had improved AQ-5 symptom scores compared to ICS/rapid-onset LABA used only as required for symptoms. Although the SOE of this finding was high, the magnitude of this difference was not likely to be clinically significant.

There is considerably less evidence for the use of combined ICS/SABA. Combination budesonide/albuterol has been shown to be more effective in reducing exacerbations than albuterol alone in poorly controlled asthmatics already receiving maintenance ICS/LABA therapy (70) (SOE: Moderate). A FDA mandated study by Chips et al. 2023 (71) demonstrated in patients with mild asthma that combination budesonide/albuterol given on a scheduled basis functioned as both controller and reliever with respect to its effects on lung function. Although frequency of exacerbation was not a primary endpoint of the study, budesonide/ albuterol given four times a day on a scheduled basis had four times less exacerbations than the albuterol alone. One study (70), which was not reviewed in the 2019 or 2025 evidence reviews showed a combination beclomethasone and albuterol inhaler was superior to albuterol alone and was similar to patients receiving maintenance beclomethasone albuterol with respect to asthma exacerbations.

Based on the relevant studies from the 2019 and 2025 CPG evidence base, the 2025 CPG suggests a strategy of using ICS/rapid-onset LABA (e.g., formoterol) as both controller and reliever in patients 12 years and older with asthma, as it is a *Weak for, Reviewed, New-replaced* recommendation. This recommendation was based on clinical studies which included patients with moderate to severe or poorly controlled asthma who used an ICS/rapid-onset LABA) on a maintenance and symptom driven basis and in patients with mild asthma who used controller/reliever ICS/rapid-onset LABA only on a symptom driven basis. The former group

showed reduced exacerbations compared to ICS or ICS/LABA as maintenance only plus SABA for quick relief (SOE: Moderate) and the latter group showed non-inferiority to ICS maintenance plus SABA (SOE: Moderate) and marked superiority to SABA alone for symptoms (SOE: High). The effect of this strategy on asthma symptom control as measured by standardized asthma control questionnaires was mixed and showed unclear clinical significance. Combining data from these two separate groups of patients led to a weaker but simpler and more clinically useful recommendation. The benefits of this strategy for all patients with asthma 12 years and older outweigh the harms. Thus, the Work Group decided on *a Weak for* recommendation.

Recommendation

7. For patients with uncontrolled asthma on inhaled corticosteroids alone, we recommend the use of both inhaled corticosteroids and rapid-onset long-acting beta agonists (e.g., formoterol) as both controller and reliever.
   (Strong for | Reviewed, Amended)

Discussion

In patients who are uncontrolled on ICS alone, we recommend the addition of a LABA over other treatment options (e.g., increased dosing of ICS, addition of Leukotriene Receptor Antagonists (LTRA). The 2019 VA/DOD Asthma CPG also found the addition of a LABA to ICS therapy was more efficacious than increasing the intensity of ICS treatment alone. However, the 2019 Work Group noted that the overall confidence in the quality of the evidence was rated low because of issues concerning study designs and small sample sizes in a portion of the reviewed literature.

The 2025 Work Group reviewed three SRs, with a total evidence base of 100 RCTs, that met inclusion criteria for this specific recommendation. The safety and efficacy of the addition of LABA to ICS has been established in multiple research studies.

A SR by Oba et al. (2023) (72) of 35 RCTs comparing combination medium-dose ICS/LABA to monotherapy high-dose ICS showed a significant reduction in the number and severity of asthma exacerbations as well as improved asthma control, both of which were identified as critical outcomes. High-dose ICS/LABA combination therapy compared to monotherapy high-dose ICS documented similar results for these critical outcomes. The SOE supporting medium-dose ICS/LABA was moderate, while the SOE was high for the higher dose ICS/LABA combination therapy.

Oba, et al. (2022) (73), evaluated 17 RCTs involving over 17,000 adult patients. The RCTs compared the effectiveness and safety of dual and triple combination therapies, specifically the permutations included: high-dose ICS/LABA vs medium-dose ICS/LABA, high or medium-dose ICS/LABA/long-acting muscarinic antagonist (LAMA) vs medium or high-dose ICS/LABA and high-dose ICS/LABA/LAMA vs medium-dose ICS/LABA/LAMA. While medium-dose ICS/LABA/LAMA was preferred over medium-dose ICS/LABA and high-dose ICS/LABA/LAMA was favored over high-dose ICS/LABA for the critical outcome of number and severity of exacerbations, there was no clinically significant difference in asthma control/symptoms at 12 months.

Cividini et al. (2023)(74), a SR of 48 RCTs, evaluated the safety and effectiveness of LABA addition to patients currently on any dose of ICS (low-, medium-, and high-dose ICS) compared to LTRAs in patients less than 18 years of age. The combination of ICS and LABA produced results similar to Oba et al. (2023) (72) of decreased number and severity of exacerbations as well as improved asthma control compared to LTRA monotherapy. While the SOE for Cividini et al. (2023) (74) was moderate regarding the critical outcome of asthma severity and exacerbations, the studies involving the evaluation of over 8000 pediatric patients was worthy of inclusion in the recommendation.

No Significant Adverse Events (SAE) were documented in either SR.

While solo LABA administration devices are available, the patient focus group of this CPG identified the value of access to combination medication options to control their (or their child's) asthma. The Work Group also recognized the convenience of combination ICS/LABA devices. 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. However, the Work Group did note some possible implications that should be addressed during the patient-provider encounter. Separate ICS and LABA administration devices may be preferred by the patient and/or provider due to cost, formulary or insurance considerations. In addition, separate administration devices allow individualized titration of ICS and LABA if indicated. Whether as a combined inhaler, or in separate devices, patients will need to be educated regarding the purpose, frequency of use/overuse of medication as well as inhaler administration technique.

The Work Group systematically reviewed evidence related to this recommendation.(72-74) Therefore, it is categorized as *Reviewed, Amended*. The Work Group's confidence in the quality of evidence was moderate. The benefits of addition of LABA to ICS as both controller and reliever therapy outweighed potential harms as there were no Serious Adverse Events noted with the addition of LABA in either the pediatric or adult populations studied. Patient values and preferences are similar, as the ICS/LABA combination does not add another inhaler and patients will likely be more compliant if asthma is well controlled. Other implications include acceptability and feasibility, as there are pharmacy formulary issues with multiple ICS/LABA brands and pharmacies may not provide spacers. Subgroup considerations also exist, as this is not FDA approved for children under the age of 6. Thus, the Work Group decided on a *Strong for* recommendation.

Recommendation

8. In patients with uncontrolled asthma on inhaled corticosteroids and long-acting beta agonists, who use short-acting beta agonists for relief, we suggest inhaled corticosteroids and rapid-onset long-acting beta agonists (e.g., formoterol) as both controller and reliever. **(Weak for | Reviewed, New-added)**

Discussion

The safety and efficacy of addition of LABA to ICS has been established in multiple research studies.(70,72,73) As noted in Recommendation 6 (above), evidence reviewed from the 2019 VA/DOD Asthma CPG consistently showed ICS/LABA controller/reliever therapy reduced asthma exacerbations in patients 12 years and older compared to other strategies.

These medications may be administered as two separate medications, however, are frequently administered together into one inhaler and are recommended for asthma control therapy. Currently, patients who experience asthma exacerbations may utilize a SABA for symptom relief as needed. We recommend patients currently on ICS and LABA for asthma control utilize a combined ICS and a LABA for symptom relief as needed. There are currently several LABAs approved for patients with asthma. Some have a more rapid onset of action (e.g., formoterol), while others have a slower onset of action (e.g., salmeterol). The LABA which was used in the combined ICS/LABA controller/reliever studies, and thus recommended by the Work Group, was formoterol which has a rapid onset of action as well as being a long-acting beta agonist.

Evidence from Beasley et al. (2022)(75) found that use of ICS/LABA as both controller and reliever therapy led to a significant reduction in severe exacerbation rate compared to remaining at the same dose of ICS/LABA maintenance plus SABA reliever, however, there was no statistically significant difference in ICS/LABA as control/reliever versus increased dose of ICS/LABA maintenance with addition of SABA as reliever. This SR (75) reported mixed evidence regarding the benefit of SMART over other ICS/LABA regimens. There was no difference in the SAEs or increased level of harm with a moderate quality of evidence. Study timeframe included up to 12 months in this literature review evidence.

The patient focus group of this CPG identified the value of access to combination medication for both control and reliever therapy for their (or their child's) asthma. The Work Group also recognized the convenience of combination ICS/LABA devices. Combination products simplify treatment plans and support improved adherence by avoiding the need for multiple devices or delivery systems. A plethora of LABA formulations are currently available. When prescribing ICS/LABA as reliever medication, care should be taken that patients are prescribed rapid-onset/long-acting beta agonists (e.g., formoterol) versus a LABA with longer onset of action (e.g., salmeterol). In addition, patients will need to be educated regarding the purpose, frequency of use/overuse of medication as well as inhaler administration technique.

The 2025 Work Group systematically reviewed the evidence related to this recommendation. (70,75) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of evidence was low. The body of evidence had some limitations, such as imprecision in measurement of outcomes.(69) The benefits of ICS/LABA use as both control and reliever medication outweighed potential harms as there were no SAEs noted. Patient values and preferences are similar, as patients will have one inhaler for both exacerbations and maintenance, and reduction in severe exacerbations is preferred by patients. Other implications include resource use and subgroup considerations, as inhaler shortages may occur if VA/DOD begins prescribing more ICS/LABA in lieu of SABA and is not FDA approved for children under 6 years old. Thus, the Work Group decided on a *Weak for* recommendation.

Recommendation

9. For patients with asthma (ages 12 and over) not controlled by medium or high dose inhaled corticosteroids and long-acting beta agonists, we suggest adding a long-acting muscarinic antagonist (LAMA).
   (Weak for | Reviewed, New-added)

Discussion

Evidence gathered from the Cochrane literature review (76) suggested the addition of a LAMA improved control in patients, ages 12 and over. The evidence base consisted of 5 SRs and 3 RCTs which included patients whose asthma was uncontrolled or only partly controlled despite treatment with ICS prior to study initiation. Studies from systematic evidence review included Oba et al. 2022 (73) and Oba et al. 2023 (72) with patients not well controlled on either medium or high dose inhaled corticosteroids/LABA alone. There were 17,000 patients in 17 RCTs, which included a network meta-analysis (NMA) and direct comparisons between interventions. Most of the studies showed statistical significance for triple therapy. Addition of a LAMA was associated with improvement and reduction in symptoms and decreased exacerbations. Beasley, et al. 2022 (75) supported this recommendation through reduction of severe exacerbations and Asthma Control Questionnaire (ACQ) (critical values), however there was no appreciable difference in the Asthma Quality of Life Quotient (AQLQ) score. Another SR (73) found that triple-therapy combinations (ICS medium or high-dose/LABA/LAMA) reduced moderate-to-severe asthma exacerbations compared to dual therapy (ICS medium or high-dose/LABA), although severe asthma exacerbations requiring hospitalization did not differ significantly between treatment regimens. Evidence in this same SR, Oba et.al. 2022, with 5 RCTs, found that the ICS-high dose/LABA/LAMA increased the number of ACQ responders at the 12 months follow-up significantly.

Another SR (73) found that triple-therapy combinations (ICS medium or high-dose/LABA/LAMA) reduced moderate-to-severe asthma exacerbations compared to dual therapy (ICS medium or high-dose/LABA), although severe asthma exacerbations requiring hospitalization did not differ significantly between treatment regimens.

The Work Group systematically reviewed evidence related to this recommendation.(72,73) It is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The evidence favored triple therapy but no clinically meaningful difference for AQLQ scores at 12 months. The body of evidence had some limitations including length of study, (less than 12 months,) and few pediatric patients. Oba et al. 2022 (73) favored triple therapy but again was not extended for long term review. Adding a long-acting muscarinic agonist agent led to benefits outweighing the harm of adverse events. Patient values and preferences varied somewhat because of preferences to add a medication versus trips to the ED for an exacerbation or another referral visit to a specialist. Other implications include feasibility and equity, as the triple therapy inhaler may not be available everywhere. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

10. In patients with exercise-induced bronchoconstriction, we suggest pre-exertional short-acting beta agonists.
    (Weak for | Reviewed, New-replaced)

Discussion

New evidence from LaForce (77) and Bar-Yoseph (78) did not result in significant updates to this recommendation. LaForce trial compared albuterol/budesonide (SABA/ICS) to placebo. SABA plus or minus ICS has been standard of care for exercise induced bronchospasm (EIB). We recommend future research comparing study agents against standard of care. Bar-Yoseph compared fluticasone/vilanterol to salbutamol (albuterol) with results showing no additional benefit in EIB with addition of ICS. The FDA boxed warning regarding Leukotriene Receptor Antagonists (LTRAs) resulted in the removal of the LTRAs as a recommendation in this update.

EIB, commonly referred to in the medical literature as exercise-induced asthma, 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.(79) 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 typically 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 short acting beta agonist medication 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 a SABA has been proven beneficial.(80,81)

The Work Group systematically reviewed evidence related to this recommendation.(77,78) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of evidence was low. Benefits slightly outweigh the harm. The Work Group carefully considered patient preferences, particularly in active populations, such as military personnel and athletes, where rapid and reliable symptom control during exercise is crucial. SABAs are preferred for their rapid onset and ease of use before physical activity in both groups of patients described above with EIB, those with Asthma diagnosis and those with no diagnosis of asthma, but symptomatic bronchospasm with exercise. Even in the case that an Asthma patient is on MART (ICS + rapid-onset LABA) therapy for asthma management, a SABA should be used with regards to EIB based on the available evidence. This mitigates any overuse of inhaled corticosteroid. While LTRAs offer convenience with daily dosing, the FDA boxed warning has prompted a shift toward using them only in specific circumstances. Resource use and adherence also favor SABAs as the primary recommendation, given their accessibility and fast-acting relief. Thus, the Work Group decide on a *Weak for* recommendation.

Recommendation

11. 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 | Not reviewed, Not changed)

Discussion

Standard practice for outpatient management of asthma involves a stepwise approach (see Module B of the 2025 Asthma CPG Algorithm and Sidebar F). 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 Asthma Control Questionnaire (ACQ) and the Asthma Control Test (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 B of the algorithm and Sidebar F). 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, recent acute illness, planned travel, peak allergen seasons, and/or for patients who cannot be closely monitored.

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 (76,82-84) and two RCTs (85,86). The strongest evidence was to avoid complete discontinuation of ICS in adults due to increased exacerbations and asthma symptoms. However, the SR showed asthma exacerbations were statistically no more likely among patients who reduced the ICS dose compared to those who maintained their ICS dose.(83) Another SR showed stepping down ICS therapy to a lower dose ICS versus continuing a stable dose ICS resulted in inconclusive evidence for the outcomes of exacerbations, asthma control, and quality of life.(84) However, the same SR demonstrated that stepping down the ICS component of a ICS/LABA 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. The impact on exacerbations was not statistically significant. Stepping down a patient on ICS/LABA to ICS alone versus continued stable dose ICS/LABA was studied in both the SR by Ahmad et al. (2015) (76) and the RCT by Rogers et al. (2018).(86) The SR found statistically significant differences favoring continued ICS/LABA therapy with respect to asthma control and asthma-related quality of life. However, the authors noted the evidence was insufficient to show whether this had an effect on important outcomes such as exacerbations requiring hospital admission and serious adverse events.(76) A more recent RCT examining the same LABA

step-off found no statistically significant difference in outcomes between groups.(86) Both studies were inconclusive with respect to exacerbations after LABA step-off. The safety for chronic ICS use was addressed and there were no recent studies found that addressed the long-term effects of cumulative exposure to corticosteroids in individuals who have asthma and a comorbid atopic disease for which corticosteroids are a standard for treatment.

As this is a *Not reviewed, Not changed* recommendation in 2025, the Work Group systematically reviewed evidence from 2019 and previous related to this recommendation.(76,82-86) The previous 2019 guideline update noted that "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

12. We suggest offering the treatment of gastroesophageal reflux disease in patients with gastroesophageal reflux disease and asthma for improving asthma control and lung function.
    (Weak for | Reviewed, New-added)

Discussion

Asthma and GERD are well-known to be commonly co-occurring conditions with various theories existing for the interactions of one disease on the other. A 2021 SR by Kopsaftis et al. (87) specifically explored the effect of treatment of GERD on asthma outcomes among patients with moderate-to-severe asthma and co-occurring GERD. This SR included 23 RCTs (n=2872), with most studies on adults and medical treatment of GERD compared to placebo. Fifteen studies included proton pump inhibitors as medical treatment of GERD and 8 studies included histamine 2 receptor antagonists. Only 2 trials included pediatric patients (n=274), 2 included surgical interventions for GERD (n=42), and 1 trial included lifestyle interventions (n=62). The strength of evidence for the outcomes varied from moderate to very low. Notably, there were no recent studies included in this SR, with publication dates of the 23 RCTs ranging from 1981 to 2010.

The SR by Kopsaftis et al.(87) demonstrated no significant difference in the rate of moderate-to-severe exacerbations or asthma-related quality of life with the medical treatment of GERD compared to placebo in this patient population. There were mixed results in the 20 RCTs that compared GERD to placebo on the effect on asthma symptoms scores, with 6/20 studies demonstrating a positive effect on asthma symptoms scores. No meta-analysis was performed. However, the SR by Kopsaftis et al. did favor medical treatment of GERD regarding several

important outcomes, including lung function and use of rescue inhalers (relievers), both of which had moderate certainty of evidence. GERD treatment compared to placebo was associated with a mean of 100 mL improvement in FEV1. Treatment of GERD was also associated with a mean of 0.71 less puffs per day of rescue inhalers, which the Work Group felt demonstrated a clinically meaningful improvement in asthma control.(87) There was insufficient evidence to recommend for any method of GERD treatment over another for improvement in asthma outcomes. This was largely due to the small number of comparative studies assessing surgical management of GERD or conservative management with lifestyle modifications compared to medical therapies of GERD and placebo.

It is worth noting that the studies within the SR that favored treatment of GERD for asthma outcomes were conducted on patients with self-reported symptomatic GERD. Additional studies have explored the question of whether asthma outcomes are improved in persons treated for asymptomatic GERD. One RCT (88) found no improvement in asthma outcomes in this subset of patients with co-occurring asymptomatic GERD. Based on such evidence, it may be reasonable to consider the symptomatic vs. asymptomatic nature of a patient's GERD when offering treatment of GERD for improved asthma outcomes, though this study was not included in the literature review for our recommendation in this clinical practice guideline. It is also worth mentioning that lifestyle modifications are routinely recommended as an important component of GERD management, despite the lack of studies in the reviewed SR specifically studying this treatment for asthma outcomes. These principles are considered established science in the management of GERD and there are minimal harms to recommending lifestyle modifications such as avoidance of known trigger foods and drinks, abstinence from eating within two hours of sleeping, elevation of the head of the bed, tobacco cessation, and weight loss in overweight persons.

Although the overall strength of evidence in the SR is low for the critical outcomes of acute exacerbations, outcomes with higher confidence of evidence did favor treatment of GERD for asthma outcomes while the others did not demonstrate any significant difference. Overall, the benefits of treating GERD as a co-occurring condition with asthma slightly outweigh the potential harms related to side effects from GERD therapy, such as polypharmacy, nutritional deficiencies, increased risk of pneumonia and clostridium difficile infections, and potential delay in escalation of asthma therapy. Work Group members felt it was important to explicitly emphasize that the treatment of GERD and other co-occurring conditions should not delay escalation of asthma therapy in uncontrolled patients.

There is some variation in patient preferences and values regarding the treatment of GERD for improvement in asthma outcomes. Patients may differ in perceptions of the role of GERD treatment in asthma management, individual preferences on additional testing and medications, and adherence. Considerations beyond acceptability among patients include resource allocation for testing and treatment, as well as distribution variables like financial and medical differences in the cost of copays and burden of polypharmacy. With this in mind, we suggest offering treatment of GERD in patients with GERD and asthma for improving asthma control and lung function, with consideration of patient preferences and characteristics.

The Work Group systematically reviewed evidence related to this recommendation. (87)

Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including small sample size and heterogeneity in treatments, duration and follow up (87) The benefits of treatment of GERD, including improvement in asthma control and lung function, slightly outweighed the potential harm of side effects of GERD therapy, increased infection risk, polypharmacy, and delay in escalation of asthma therapy. Patient values and preferences varied somewhat because patients vary in receptiveness to treatment of co-occurring conditions. Thus, the Work Group decided upon a *Weak for* recommendation.

c. Non-pharmacotherapy

Recommendation

13. We suggest weight loss in adults with asthma and obesity to improve asthma control. **(Weak for | Reviewed, New-added)**

Discussion

The evidence review for weight loss in patients with asthma and obesity included two RCTs. The available evidence suggests that weight loss in adults with asthma and obesity improves asthma control.(89,90)

The Ozbey et al. 2020 study evaluated asthma-related outcomes following a 10-week diet program with dietitian prepared meals and snacks, compared to no weight loss intervention. The study found that diet group had significant improvements in self-rated asthma control, Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), and pulmonary functions. These improvements were particularly noticed in individuals with a weight loss of more than 5%, compared to those who lost less than 5%. Conversely, the Sharma et al. (2023) study explored the effects of a diet program consisting of a 12-week liquid diet followed by food reintroduction over 4 weeks on asthma-related outcomes. The study demonstrated significant improvements in ACT and ACQ, but no changes in pulmonary functions. Both studies showed no difference in asthma-related healthcare utilization between the diet and control groups.

In the previous 2019 VA/DOD Asthma CPG, overweight/obesity was identified as a risk factor for asthma-related outcomes. The benefits of weight loss were found to slightly outweigh the burdens. Weight loss has an overall positive impact on health, including on asthma control and the benefits of weight loss were identified in the evidence reviewed for 2025 guidelines. However, the burden of being on a restricted diet program, suffering from not eating, and some side effects of malnutrition, including but not limited to hair loss and nutrient depletion cannot be ignored.

There are several limitations to this recommendation. Two studies were conducted over relatively short periods (12 weeks and 16 weeks), which may create uncertainty of long-term effects of weight loss on asthma control. Additionally, the dietary interventions in these studies were intensive, providing all meals to patients, which significantly limits both the real-world feasibility and the ability to generalize asthma-related outcomes to other weight loss methods. Depending on patient's preferences and values, some patients may be resistant to adhering to a restricted or specialized diet, which can affect weight loss and its maintenance. Implementing such interventions in family practice is not feasible due to limited resources and personnel.

Furthermore, resources are limited to patients due to extra cost of purchasing prepared or manufactured meals and snacks. Access to resources, quality of services, and opportunities may vary among different race groups, socioeconomic status, and ethnicity. This may pose additional challenges in program implementation.

The Work Group systematically reviewed evidence related to this recommendation.(89,90) As a result, this recommendation is categorized as *Reviewed, New added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had several limitations, including small sample size, short study duration, conflicted pulmonary function test results, and potential author bias. The benefits of weight loss and asthma outcome values slightly outweighed the potential harms or burdens. Patient values and preferences varied largely because of the uncertainty of long-term effects of weight loss, difficulties in achieving and maintaining weight loss in general, and challenges of adhering to a restricted diet. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

14. We suggest against the use of indoor air filtration devices such as high efficiency particulate air and nitric oxide filters, for asthma control.
    (Weak against | Reviewed, New-added)

Discussion

Six studies were included for review in the evidence base. They investigated the effects of nitric oxide (NO2) filters in the home, nocturnal temperature-controlled laminar airflow (TLA) devices in the home, high efficiency particulate air (HEPA) filters in the home and school, and integrated pest management (IPM) in the school. The studies investigated domains of asthma control and symptoms, number and severity of asthma exacerbations, asthma related healthcare utilization, pulmonary function, and quality of life. Two of these studies were industry sponsored by the device manufacturer (Airsonett TLA devices, Chauhan et al. 2021; Dyson HEPA filters, Fong et al. 2023).(91,92) The only study that demonstrated clinically and statistically significant differences between intervention and sham treatment groups involved severe persistent asthmatic patients and was industry sponsored.(91)

Regarding the critical outcome of asthma control and symptoms, Fong et al. 2023 (92) demonstrated no significant differences in asthma control between groups receiving HEPA and sham filters (p=0.08) and after multivariate analysis demonstrated no between-group differences in Asthma Control Questionnaire 6 (ACQ6) scores. Phipatanakul et al. 2021(93) demonstrated no statistically significant interaction between both classroom HEPA filters and IPM. Separately, IPM in the classroom produced no significant effect and classroom HEPA filters produced no significant effect. James et al. 2020 studied HEPA filters in bedrooms and found no clinically nor statistically significant changes in median ACQ scores and in subgroups found statistically but not clinically meaningful changes in ACQ scores. Under the same critical outcome but studying NO_2 filters, Gent et al. 2023 described a positive association of increase of 0.7 symptom days in 14 days for every 10 parts per billion (ppb) increase in household NO_2 but found no significant reduction in symptom days between NO_2 reduction and control treatments.

The only study that evaluated the critical outcome of number and severity of asthma exacerbations was Chauhan et al. 2021.(91) The study was limited to severe persistent asthmatic patients, and populations from two separate prior studies for analysis, “Neither Study A nor Study B2 separately showed a statistically significant difference between TLA and placebo for severe asthma exacerbations,” but after analyzing the data described significant reduction in asthma exacerbation risk ratio in patients with ACQ7 > 3 and ACT < 18 (RR: 0.59 [0.38-0.90]; p=0.015) and for greater ACQ7 scores but not at lower scores ACQ7 > 2.5 (p=0.096).

Phipatanakul et al. 2021 (93) investigated IPM and HEPA filters in the classroom environment and was the only study that included the important outcome of asthma-related healthcare utilization. Defined as the sum of unscheduled clinic visits, emergency department visits, and overnight hospitalizations, measures of asthma-related healthcare utilization comparing school IPM (IRR: 0.94 [0.38 to 2.31]) and classroom HEPA filters were not statistically significant.

Three studies investigated the important outcome of pulmonary function. The industry study of living room and bedroom HEPA filters (Fong et al. 2023) (92) showed no significant differences in objective spirometric measures between intervention and sham filter groups compared with baseline evaluation in FEV_1, FVC, and FEV_1:FVC ratio. In an evaluation of mold burden with indoor and outdoor exposures, indoor dust burden, and classroom HEPA filter intervention, Vesper et al. 2023 (94) described no significant differences in the average FEV_1 percentile before and after intervention. In an investigation of IPM and HEPA filters in the classroom environment, Phipatanakul et al. 2021 (93) found no significant mean differences (MD) in spirometric measures in IPM intervention classrooms of FEV_1 mean percent predicted or in HEPA intervention classrooms of FEV_1 or FEV_1:FVC mean ratio.

Three studies investigated the important outcome of quality of life. The industry study of living room and bedroom HEPA filters (Fong et al. 2023)(92) showed no between-group differences in quality of life (AQLQ) scores and, after multivariate analysis, there were no differences in AQLQ between groups. In a study of bedroom HEPA filters, James et al. 2020 found AQLQ scores were not significantly different between HEPA and “dummy” treatments and AQLQ scores in subjects with ‘impaired’ quality of life scores were not significantly different between seasons. In the industry sponsored study of TLA devices in severe asthmatic patients, Chauhan et al. 2021 showed a reduction in severe asthma exacerbations in patients with total AQLQ scores ≤ 3 and with AQLQ symptom domains of ≤ 3.

The interpretation of the above suggests that HEPA filters and NO_2 filters have no significant improvements in asthma control, exacerbations, health-care utilization, objective measures of lung function, or in quality of life, and can only be obtained at personal cost. These costs may be pernicious to families with limited resources, i.e., a demand on limited funds that could be spent on other healthcare needs and could thus be a harm to certain populations. While the use of devices to improve one’s home environment seems an obvious benefit subject to marketing, the data do not convincingly show a healthful benefit and consistently so across multiple studies in this analysis and describing these competing merits may be complicated and subject to the health literacy of individual patients. No conclusions should be drawn from a single study sponsored by the manufacturer of a particular TLA device in a narrow patient population. While no improvement

in measures of asthma were found in studies of IPM, it would not be prudent to discourage the removal of rodents from a home or school for other concerns of health and hygiene.

The results from this limited pool of evidence are largely consistent with previous trials and reviews of larger bodies of evidence. A review and report on the effectiveness of indoor allergen control in asthma management (Leas et al. 2018) (95) found no significant effects from single interventions with low to moderate strength of evidence. These included use of acaricides for dust mites, air purification devices, impermeable mattress covers, carpet removal, HEPA vacuums, mold removal, pest control, and pet removal. Studies of multicomponent interventions had variable study design preventing meta-analysis and with low to high strength of evidence found certain improvements in such measures as school absenteeism but not consistently asthma control, rates of asthma exacerbations, quality of life, or hospitalizations.

A more recent review (Kalayci et al. 2022) (96) echoes these findings. While house dust mite (HDM) interventions have been described and proven beneficial for allergic rhinitis, they have not consistently been described as beneficial for asthma, describing effects of HDM interventions on asthma outcomes as controversial. Molds can be ubiquitous in outdoor air and generally mold abatement would be recommended in any home environment, yet the molds associated with indoor environments (*Aspergillus* spp., *Penicillium* spp.) are different than outdoor molds associated with adverse outcomes on asthmatics (*Alternaria* spp., *Cladosporium* spp.). While rodent exposure and allergen sensitization is associated with symptoms, removal of rodents through IPM is not consistently associated with symptom improvement. Similarly, while cockroach exposure and allergen sensitization are associated with symptoms, no clear benefits have been demonstrated with abatement. Not a subject included with our data review, cat and dog dander are shown to result in adverse asthma symptoms in those sensitized and may persist in a home for up to six months after animal removal. The most common recommendation is to rehome an animal for sensitized patients. Yet while animal dander is carried into school and workplace environments where they do not reside, studies of HEPA filters have not shown consistent clinical benefit for asthma.

The Work Group systemically reviewed evidence related to this recommendation.(91-94,96-98) As a result, this recommendation is categorized as *Reviewed, New-added*. The literature review conducted for this clinical practice guideline has been consistent with literature across a two-decade period prior to literature review period that has not shown any consistent clinically meaningful or statistically significant benefits for HEPA or NO_2 filters across large populations or consistently in asthmatic patients. These specific devices come at a cost to patients and may compete for an individual patient's healthcare budget with interventions that may have greater demonstrated benefit. While clinical benefit has been inconsistently shown for pest management such as for rodents and cockroaches, removal of these pests from the environment may be beneficial for reasons other than asthma. Thus, the Work Group decided upon a *Weak against* recommendation.

Recommendation

15. We suggest a multidisciplinary treatment approach to improve asthma-related quality of life, asthma control, and treatment adherence.

(Weak for | Not reviewed, Not changed)

Discussion

The evidence base for this recommendation consisted of three SRs (58,99,100) and nine RCTs (101-109). 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(99), culturally specific education(101), holistic self-management education(102), community pharmacist education,(103,104) asthma management program education (105), and behavioral modification education.(58,106-108) 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.."(58) 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 (99), holistic self-management education (102), community pharmacist education (103),and behavioral modification education.(58) "A significant positive correlation was demonstrated between asthma control and asthma-related quality of life scores."(103) Improved asthma control from behavioral modification may be a secondary outcome as identified through patient self-reported increases in quality of life.(58)

Asthma treatment adherence, per patient self-reported satisfaction, increased with community pharmacist education.(100,109) 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).(100) A patient diary-keeping method showed improvement in medication adherence only after "the 3rd follow up to 4th follow-up".(109)

The Work Group systematically reviewed the unaligned 2019 recommendation and did not review the evidence or change the recommendation. Therefore, it remains categorized as *Not reviewed, Not changed*. The body of evidence had some limitations including overall confidence in the quality of evidence continued to be low in the support of the 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). Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

16. We suggest patients with asthma participate in regular exercise to improve quality of life and asthma control.
    (Weak for | Not reviewed, Not changed)

Discussion

Patients with asthma should participate in regular exercise to improve quality of life and asthma control. As noted in the 2013 Cochrane SR (110) (which updated the 2005 review 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." The 2013 Cochrane SR (110) compared several studies, showing that the benefits of exercise outweigh the risks for patients with asthma. 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 several mechanisms including strengthening respiratory muscles. The SR (110) 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 (110) 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)(79), 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. In the research conducted by Flapper et al. (2008)(111), 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. Thus, physical activity should be recommended as a supplementary therapy to medication.

In 2019, the Work Group's confidence in the quality of the evidence was low, specifically regarding outcomes including asthma control/symptoms, exacerbations, and quality of life. In 2025, the Work Group reviewed the recommendation and determined it should be carried forward. It was discussed that some patients may have an aversion to exercise due to exercise-induced asthma, but the quality of life studies showed the need to maintain a physical exercise program. Practitioners may need to address patient concerns for pediatric safety when playing outside in some areas and air quality issues (dependent on location and/or some modifications as needed) when air quality is borderline. Patients with individual co-occurring conditions may need to have some modifications to exercise program.

As this is a *Not-Reviewed, Not-Changed* recommendation, the Work Group did not review any new evidence for this CPG update and considered the assessment of the evidence put forth in the

2019 CPG. There was some evidence of benefit, however 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. Eichenberger et al. (2013)(79) states about 90% of patients with asthma suffer from exercise-induced bronchoconstriction (i.e., airway narrowing and increased airway resistance, during and after exercise), which might prevent patients with asthma from performing regular physical exercise. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

17. 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 asthma.
    (Weak for | Not reviewed, Not changed)

Discussion

In a 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.(112) 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.(112) 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. 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.(112) 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.(113)

The Work Group systematically reviewed the unaligned 2019 recommendation and did not review the evidence or change the recommendation. Therefore, it remains categorized as a *Not reviewed, Not changed*. The Work Group determined the confidence in the evidence remains 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 benefits of this recommendation slightly outweigh the associated harms and burdens. Patient values and preferences may vary somewhat, as patients may not prefer to engage due to stigma of mental health treatment, the number of sessions involved competing with other scheduling needs, and assigned homework required. Costs relating to treatment, including copays, required childcare, transportation and time spent away from other tasks may also be a deterrent. While most mental health providers are trained in CBT, availability may be affected due to other competing referrals received. Behavioral health clinicians already embedded within primary care clinics may be able

to mitigate concerns related to resources and stigma. Thus, the Work Group decided upon a *Weak for* recommendation.

d. Monitoring and Follow-up

Recommendation

18. We suggest against utilizing spirometry for routine monitoring of patients with stable asthma.
    (Weak against | Not reviewed, Not changed)

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.(114) 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.(115) 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 and 2019 VA/DOD Asthma CPGs, these recommendations were 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 at advanced age) 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.(114) 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.(114,115) 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

19. 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 | Not Reviewed, Not changed)

Discussion

Fractional exhaled nitric oxide (FeNO) is a biomarker that reflects eosinophilic airway inflammation, and its use has been explored in various studies to manage asthma in primary care. However, there is conflicting evidence regarding its clinical utility. Wang et al. (2015)(40) and Petsky et al. (2018)(116) provided moderate-quality evidence from systematic reviews that demonstrated a reduction in asthma exacerbations in the FeNO-monitored group, compared to controls.(40) Although these findings suggest that FeNO could play a role in managing asthma, several other clinically important outcomes, such as exacerbations requiring systemic corticosteroids and healthcare utilization, did not differ significantly between FeNO monitoring and usual care.

Moreover, Szefler et al. (2008)(117) conducted a RCT comparing FeNO-guided asthma management to standard care, but this trial also failed to show significant improvements in healthcare utilization or treatment adherence. While some improvement in milder forms of asthma exacerbations was observed, the overall benefit remains unclear, particularly in the primary care setting, where resource use, availability and implementation of FeNO monitoring might pose challenges. Given the lack of consistent clinical benefit, the evidence does not support a strong recommendation for implementation of routine FeNO monitoring in primary care for asthma management.

The Work Group considered patient preferences and values, noting that patients are generally accepting of FeNO testing due to its ease and non-invasive nature, especially in those patients who cannot easily undergo spirometry, with almost immediate results allowing for clinician decision making. However, the cost and resource burden associated with introducing this test into routine primary care settings might outweigh the modest clinical benefits observed. The ease of use of FeNO, combined with the availability of other tools like spirometry, led the Work Group to conclude that FeNO should not be routinely recommended for asthma management in primary care. Additionally, the availability of FeNO equipment varies across different healthcare systems, further complicating its routine implementation.

The Work Group determined there is insufficient evidence to recommend for or against the routine use of FeNO in monitoring patients in primary care settings to improve asthma-related clinical outcomes. This recommendation remains categorized as a *Not reviewed, Not changed*. The

quality of evidence was rated at low. The prior Work Group for the VA DOD 2019 Asthma guidelines systematically reviewed evidence on the use of FeNO for managing asthma in primary care settings. Based on the studies by Wang et al. (2015)(40), Petsky et al. (2018)(116), and Szefler et al. (2008)(117), the confidence in the quality of evidence was deemed to be low, (and is being carried forward) as the available studies provided inconsistent results regarding key clinical outcomes and no new studies were reviewed by this Work Group. While some reduction in mild exacerbations was observed in prior studies, other important measures, such as healthcare utilization and treatment adherence, did not show significant improvements. The benefits of FeNO were determined as slightly outweighing the harms/burdens. The general availability in primary care of FeNO monitoring appear to be limited and must be weighed against the resource use and potential implementation challenges. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

20. For patients with asthma, there is insufficient evidence to recommend for or against offering telemedicine as an alternative to in-person treatment.
    (Neither for nor against | Reviewed, New-added)

Discussion

Low quality of evidence from a single study was found to show telemedicine, as an alternative option to in-person treatment, lowers the likelihood of emergency room visits, shows improvement from baseline FeNO levels, and more symptom-free days. Halterman et al. 2018(118) identified one RCT identifying school-based children between ages 3-10 that noted no serious or adverse reactions, telemedicine showed more symptom free days, lower likelihood of emergency room visits, and improvement from baseline FeNO levels. Study of statistical or clinical significance related to exacerbations and Quality of Life (QOL). Evidence found was very low for both critical and important outcomes, with wide confidence intervals and no intention to treat analysis.

The Work Group systematically reviewed evidence related to this recommendation from Halterman et al. 2018.(118) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low for both critical and important outcomes. The body of evidence had some limitations including evaluating only 400 children ages 3-10. Overall, the quality of the included study was poor, confidence intervals were wide, and the study did not include an intention to treat analysis. Telemedicine usage showed beneficial outcomes, with significantly more symptom-free days in the telemedicine group, a significantly lower likelihood of emergency room visits, and improved baseline FeNO levels. The benefits slightly outweighed the harms and burdens for the patients using telemedicine visits [e.g., resulted in more symptom-free days in the telemedicine group, lowered the likelihood of having emergency room visits and improved baseline FeNO levels] outweighed any harms - no serious or adverse reactions were noted in these studies. Patient values and preferences were similar because some patients prefer the convenience and intimacy of virtual visits. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

21. We suggest leveraging electronic health record capabilities, such as trackers and reminders, in the care of patients with asthma.
    (Weak for | Not reviewed, Not changed)

Discussion

Fiks et al. (2015)(119) showed that families with asthmatic children using an EHR-linked patient portal engaged both parents and the clinical team, and had better outcomes with fewer missed school days by the children and fewer missed parent workdays. The portal was used more frequently in those patients with moderate to severe asthma. The proprietary system used in this study showed some improvement in symptom-free days. Reminders to improve inhaler adherence were mostly ineffective; however, the confidence in the quality of the evidence was very low. Smith et al. (2012)(120) was able to demonstrate the use of asthma risk registers in primary care practices reduced asthma related hospitalizations but did not reduce the number of treated exacerbations. This study showed an increase in prescriptions for recommended preventive therapies in primary care practices using electronic alerts compared to practices using routine care alone. Another cluster-randomized trial showed a reduced rate of uncontrolled asthma episodes in patients using an asthma management system.

As this is a *Not reviewed, Not changed* recommendation, the Work Group based this recommendation on the evidence cited in the previous guideline.(119-123) 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 some 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.

X. Research Priorities

During the development of the 2025 VA/DOD asthma CPG, the Work Group identified topics needing additional research, including areas requiring stronger evidence to support current recommendations and research exploring new areas to guide future CPGs.

A. Pharmacotherapy

Many research priorities regarding pharmacotherapy were identified during the creation of this CPG. Future research should focus on comparative efficacy trials of head-to-head active medications versus placebo, as placebo is not the standard of care. Also, the efficacy and safety of long-term ICS/LABA therapy should be studied in both the adult and pediatric populations.

More research is also needed to determine when and how to progress from a low dose ICS/LABA through high dose ICS/LABA regimen in patients with uncontrolled asthma and then to progress to the addition of a LAMA. Additional research is also needed regarding ICS/LABA as control/reliever therapy in the pediatric population, and to suggest for or against addition of vitamin D3 to reduce exacerbations when added to an ICS regimen compared to ICS alone in patients with uncontrolled asthma. Studies which satisfy FDA regulatory requirements to allow for formal approval of combination ICS and formoterol as a combined controller and reliever therapy should be conducted, as well as further studies to investigate the effectiveness of ICS/rapid-onset LABA combinations which contain rapid-onset LABAs other than formoterol.

Future studies should also be focused on the most optimal treatment of co-occurring conditions, including GERD and obesity, as well as the safety of de-escalating GERD therapy in patients with asthma.

B. Asthma Education

Further research with more focus on AAPs to include how different components and practice settings effect patient outcomes, how tailoring of the education and AAP content to the patient's severity of disease and health literacy effects the outcomes, an analysis of specific patient education and AAPs compared against each other, and higher quality of studies about differing modalities of education is required to improve the confidence in the effect of these interventions on asthma outcomes. Longitudinal research is also needed to explore if one patient-oriented digital technology is better than others, the cost-benefit tradeoff, and potential long-term harms.

C. Non-pharmacotherapy

While asthma remains a prevalent condition, healthcare economics do not favor rigorous study of indoor environments that vary across the panoply of home and school environments. Multicomponent interventions can be summarized as changing one's living environment, and that can be logistically difficult and monetarily expensive even when one is reimbursed for the exercise such as for permanent change of station moves. A small signal was seen in TLA devices in an industry sponsored paper of combined study populations, these should be independently investigated in rigorously designed studies. Rather than continue to address these considerations through individual interventions, large multicomponent multicenter trials with uniform design might be the only conclusive means to address the questions of clinically meaningful interventions.

Future research may be needed to evaluate potential new exercise programs, AI and technology benefits for new physical exercise programs and compare these to control groups.

Additional research is needed to determine the optimal delivery method, format, and target population for CBT when treating patients with asthma in primary care

Further research with sufficiently powered studies on the efficacy of AAPs is required to improve confidence on asthma outcomes.

D. Monitoring and Follow-Up

Since many of the studies were predominately adults, further research is warranted to include younger ages, adolescents and pediatric populations.

Future research should determine the impact on patient management in primary care and in augmenting available spirometric results instead of availability.

Further research may evaluate whether telemedicine is effective for follow-up of adult and pediatric patients with asthma, as well as if telemedicine decreases ER visits and hospital admissions, and if there is a difference in medication adherence between face-to-face and telehealth visits. Research can also look at the cost-effectiveness of implementing at home spirometers for telehealth visits, as well as longer term research projects and follow-up.

Appendix A: Guideline Development Methodology

A. Developing Key Questions to Guide the Systematic Evidence Review

To guide this CPG's systematic evidence review, the Work Group drafted 12 KQs on clinical topics of the highest priority for the VA and DOD populations. The KQs followed the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework, as established by the Agency for Healthcare Research and Quality (AHRQ) (see **Table A-1**).

Table A-1. PICOTS (124)

P	Patients, Population, or Problem	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.
I	Intervention or Exposure	Treatment (e.g., drug, surgery, lifestyle changes), approach (e.g., doses, frequency, methods of administering treatments), or diagnostic/screening test used with the patient or population.
C	Comparison	Treatment(s) (e.g., placebo, different drugs) or approach(es) (e.g., different dose, different frequency, standard of care) that are being compared with the intervention or exposure of interest described above.
O	Outcome	Results of interest (e.g., mortality, morbidity, quality of life, complications). Outcomes can include short, intermediate, and long-term outcomes.
(T)	Timing, if applicable	Duration or follow-up of interest for the particular patient intervention and outcome to occur (or not occur).
(S)	Setting, if applicable	Setting or context of interest. Setting can be a location (e.g., primary, specialty, inpatient care) or type of practice.

Abbreviation: PICOTS: population, intervention, comparison, outcome, timing, and setting

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-4** contains the final set of KQs used to guide the systematic evidence review for this CPG.

Using the GRADE approach, 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 critical outcomes were used to determine the overall quality of evidence (see Determining Recommendation Strength and Direction).

a. Population(s)

The patient population of interest for this CPG is children and adults (aged 5 years or older) with asthma treated in a VA/DOD primary or ambulatory care setting.

b. Interventions and Comparators

KQ	Intervention(s)	Comparator(s)
1	Exposure • Aviation fuel • Burn pits • Nitric oxide • Other chemicals and air pollutants encountered during military service	• Differing levels of exposure • No exposure • Use of personal protective equipment
2	AIR (anti-inflammatory budesonide albuterol) • MART Therapy: ICS + formoterol (LABA) in combination therapy • ICS • Beclomethasone (QVAR) • Budesonide (Pulmicort) • Ciclesonide (Alvesco) • Flunisolide (Aerospan) • Fluticasone (Flovent, Armonair, Arnuity) • Mometasone (Asmanex) • Triamcinolone acetonide (Azmacort) Inhaled steroids/long-acting beta agonists (ICS/LABA) • Budesonide/Formoterol (Symbicort) • Fluticasone/Salmeterol (Advair, AirDuo) • Fluticasone/vilanterol (Breo Ellipta) • Mometasone/formoterol (Dulera) Leukotriene receptor antagonist • Montelukast (Singulair) • Zafirlukast (Accolate) • Zileuton (Zyflo) Long-acting anticholinergic/muscarinic receptor antagonists • Tiotropium (Spiriva) • Short-acting beta agonists • Albuterol (Ventolin, Pro-Air, Proventil) • Levalbuterol (Xopenex)	• Listed interventions compared to each other (head-to-head)

KQ	Intervention(s)	Comparator(s)
	Systemic corticosteroids • Dexamethasone (Decadron) • Methylprednisolone (Medrol) • Prednisolone (Prelone) • Prednisone (Deltasone) Other medications • Cromolyn sodium • Theophylline • Vitamin D (prescribed)	
3	**ICS** • Beclomethasone (QVAR) • Budesonide (Pulmicort) • Ciclesonide (Alvesco) • Flunisolide (Aerospan) • Fluticasone (Flovent, Armonair, Arnuity) • Mometasone (Asmanex) • Triamcinolone acetonide (Azmacort) **ICS/LABA** • Budesonide/Formoterol (Symbicort) • Fluticasone/Salmeterol (Advair, AirDuo) • Fluticasone/vilanterol (Breo Ellipta) • Mometasone/formoterol (Dulera)	• Daily vs intermittent ICS or ICS/LABA • Head-to-head comparison of ICS types • Higher vs lower ICS doses • ICS/LABA vs ICS alone
4	Pharmacotherapy, addition/modification of treatment: (e.g., adding medication, increasing dose) **ICS** • Beclomethasone (QVAR) • Budesonide (Pulmicort) • Ciclesonide (Alvesco) • Flunisolide (Aerospan) • Fluticasone (Flovent, Armonair, Arnuity) • Mometasone (Asmanex) • Triamcinolone acetonide (Azmacort) **Inhaled steroids/long-acting beta agonists (ICS/LABA)**	• Other addition/ modification in treatment (e.g., maintaining dose of ICS and adding another agent [e.g., leukotrienes, tiotropium, LABA, LAMA])

KQ	Intervention(s)	Comparator(s)
	• Budesonide/Formoterol (Symbicort) • Fluticasone/Salmeterol (Advair, AirDuo) • Fluticasone/vilanterol (Breo Ellipta) • Mometasone/formoterol (Dulera) **Leukotriene receptor antagonist** • Montelukast (Singulair) • Zafirlukast (Accolate) • Zileuton (Zyflo) **Long-acting anticholinergic/muscarinic receptor antagonists** • Tiotropium (Spiriva) **Short-acting beta agonists** • Albuterol (Ventolin, Pro-Air, Proventil) • Levalbuterol (Xopenex) **Systemic corticosteroids** • Dexamethasone (Decadron) • Methylprednisolone (Medrol) • Prednisolone (Prelone) • Prednisone (Deltasone) **Other medications** • Cromolyn sodium • Theophylline • Vitamin D (prescribed)	
5	• Content/ components of asthma action plan including non-urgent, management of acute exacerbation • Patient education (including on inhaler use) • Patient self-management approaches/ strategies	• Different self-management approach • One AAP vs. another AAP • One education strategy vs. another
6	• Mobile apps/technology focused on self-management • Other wearable devices • Oxygen monitoring • Propeller sensor	• Attention control • Sham intervention • Usual care

KQ	Intervention(s)	Comparator(s)
	• Text messages • Web/internet-based management approaches	
7	• Budesonide/Albuterol (Airsupra) • ICS with or without LABA • Leukotriene Receptor Antagonists (LTRA) • Mast Cell Stabilizing Agents (MCSA) pre-exercise • Short-acting beta agonists (SABA) pre-exercise	For patients with only exercise-induced bronchospasm: • Placebo vs. rescue med For patients with asthma and exercise-induced bronchospasm: • Maintenance treatment vs. same treatment used as rescue • Maintenance vs. same maintenance treatment plus add-on rescue for exercise
8	• Air filters/purifiers • Mattress covers/pillow covers • Mold removal • Pest control methods (cockroach, rodent, bird droppings etc.) • Reduced exposure to household fragrance products and cleaning products with strong scents, chemicals, or volatile organic compounds	• Sham intervention
9	• Any lifetime use of inhaled or oral corticosteroid prescribed for asthma, together with any lifetime use of intranasal, oral, or injectable corticosteroids prescribed for another condition	• Daily vs intermittent corticosteroid use • Higher vs lower doses • Type of ICS used
10	• Interactive telemedicine conducted via telephone or video conferencing using technologies (e.g., telephone, tablet, laptop, and/or desktop computer) for routine management and follow-up of patients with asthma	• Usual care (face-to-face)
11	• Any asthma medication plus prescription or nonprescription treatment for GERD (e.g., famotidine, antacids, omeprazole)	• Asthma medication plus placebo treatment for GERD
12	• Treatments for obesity, including: ▪ bariatric surgery ▪ combined programs ▪ diet ▪ exercise	• No treatment for obesity

KQ	Intervention(s)	Comparator(s)
	▪ pharma therapies (GLP-1, SGLT-2)	

c. Outcomes

KQ	Critical Outcome(s)	Important Outcome(s)
1	• Asthma Control/Symptoms • New (Incident) Diagnosis of Asthma • Number/Severity of Exacerbations	• Asthma Related Healthcare Utilization • Pulmonary Function • Quality of Life • Treatment Adherence
2	• Asthma Control/Symptoms • Number/Severity of Exacerbations • Treatment Adherence	• Asthma Related Healthcare Utilization • Pulmonary Function • Quality of Life • Serious Adverse Events
3	• Asthma Control/Symptoms • Number/Severity of Exacerbations • Reduced Need for Other Systemic Steroids • Serious Adverse Events	• Asthma Related Healthcare Utilization • Quality of Life • Treatment Adherence
4	• Asthma Control/Symptoms • Number/Severity of Exacerbations • Treatment Adherence •	• Asthma Related Healthcare Utilization • Pulmonary Function • Quality of Life • Serious Adverse Events
5	• Asthma Control/Symptoms • Number/Severity of Exacerbations	• Asthma Related Healthcare Utilization • Pulmonary Function • Quality of Life • Serious Adverse Events • Treatment Adherence
6	• Asthma Control/Symptoms • Patient Satisfaction/Experience	• Adherence to other asthma interventions • Cost of Care/Resource Use • Ease of Use • Feasibility • Quality of Life
7	• Ability to Exercise/Maintain Fitness	• Asthma Related Healthcare Utilization

KQ	Critical Outcome(s)	Important Outcome(s)
	• Asthma Control/Symptoms • Treatment Adherence	• Number/Severity of Exacerbations • Quality of Life • Serious Adverse Events
8	• Asthma Control/Symptoms • Number/Severity of Exacerbations	• Asthma Related Healthcare Utilization • Pulmonary Function • Quality of Life • Treatment Adherence
9	• Adverse Events Associated with Cumulative Corticosteroid Exposure (i.e., adrenal insufficiency, atrial fibrillation, cataract, diabetes, fractures, hypertension, myocardial infarction, osteonecrosis, osteoporosis)	• Quality of Life
10	• Asthma Control/Symptoms • Asthma-Related Healthcare Utilization • Number/Severity of Exacerbations	• Pulmonary Function • Quality of Life • Serious Adverse Events • Treatment Adherence
11	• Asthma Control/Symptoms • Number/Severity of Exacerbations	• Asthma Related Healthcare Utilization • Pulmonary Function • Quality of Life • Serious Adverse Events • Treatment Adherence
12	• Asthma Control/Symptoms • Number/Severity of Exacerbations	• Asthma Related Healthcare Utilization • Pulmonary Function • Quality of Life • Serious Adverse Events • Treatment Adherence

d. Timing

KQ	Timing
KQ1, KQ4-8	No minimum follow-up
KQ2	3-6 months of treatment; no minimum follow-up
KQ3	Minimum 6 months of treatment; no minimum follow-up
KQ9	≥1 year of corticosteroid use for any diagnosis
KQ10	Minimum 3 months follow-up
KQ11	Minimum treatment time for GERD of 3 months
KQ12	>3 months follow-up

e. Setting(s)

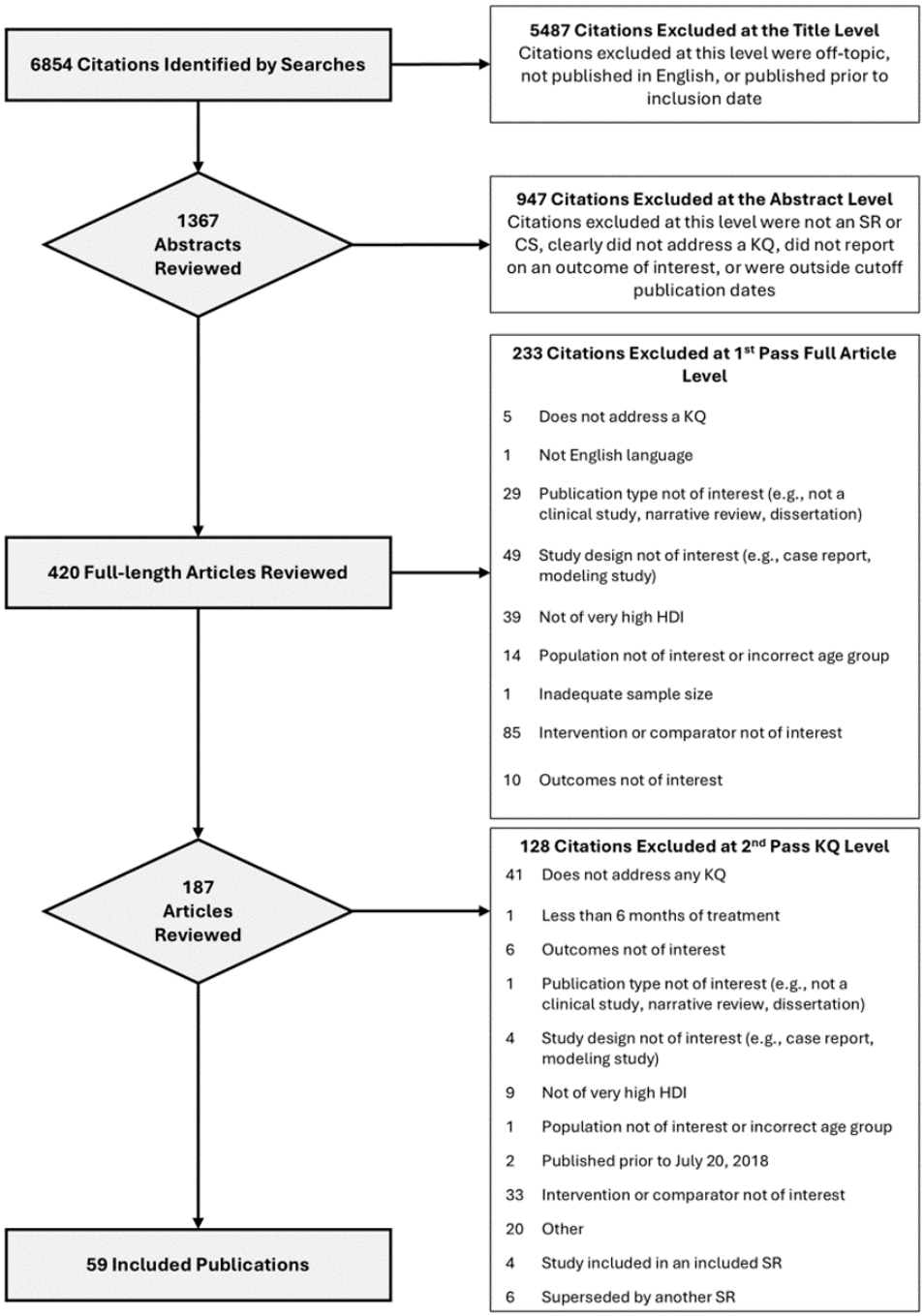
KQ	Setting(s)
KQs 1-7, 9-11	Primary care
KQ8	Patient home
KQ12	Primary care and/or weight management program

C. Conducting the Systematic Review

Extensive literature searches identified 6,854 citations potentially addressing the key questions of interest to this evidence review. Of those, 5,487 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, 1,367 abstracts were reviewed with 947 of those being excluded for the following reasons: not a systematic review or clinical study, did not address a key question of interest to this review, did not enroll a population of interest, or published prior to July 20, 2018. A total of 420 full-length articles were reviewed. Of those, 233 were excluded at a first pass review for the following: not addressing a key question of interest, not in in English, publication type not of interest, study design not of interest, not of very high HDI, population not of interest or incorrect age group, inadequate sample size, intervention or comparator not of interest, or outcomes not of interest. A total of 187 full-length articles were thought to address one or more key questions and were further reviewed. Of these, 128 were ultimately excluded. Reasons for their exclusion are presented in Figure A-1 below.

Overall, 59 publications addressed one or more of the Key Questions and were considered as evidence in this review. Table 5 indicates the number of studies that addressed each of the questions, and some papers were used for more than one Key Question. Table A-2 indicates the number of studies that addressed each of the KQs.

Figure A-1. Study Flow Diagram



Abbreviations: CS: clinical study; HDI: human developmental index; 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: 6,854 citations identified by searches.
    a. Right to Box 2: 5,487 excluded at the title level. Excluded citations were off topic, not published in English, or published prior to inclusion date.
    b. Down to box 3.
2. Box 3: 1,367 abstracts reviewed.
    a. Right to Box 4: 947 citations excluded at the abstract level. Citations excluded were not an SR or CS, clearly did not address a KQ, did not report an outcome of interest, or were outside cutoff publication dates.
    b. Down to Box 5.
3. Box 5: 420 full-length articles reviewed.
    a. Right to Box 6: 233 citations excluded at 1st pass full-article level.
        i. 5 or doesn't address KQ.
        ii. 1 not English language.
        iii. 29 publication type not of interest.
        iv. 49 study design not of interest.
        v. 39 not of very high HDI.
        vi. 14 population not of interest or incorrect age group.
        vii. 1 inadequate sample size.
        viii. 85 intervention or comparator not of interest.
        ix. 10 outcomes not of interest.
    b. Down to Box 7.
4. Box 7: 187 articles reviewed.
    a. Right to Box 8: 128 citations excluded at 2nd pass full-article level.
        i. 41 doesn't address a KQ.
        ii. 1 less than 6 months of treatment.
        iii. 6 outcomes not of interest.
        iv. 1 publication type not of interest.
        v. 4 study design not of interest.
        vi. 9 not of very high HDI.

vii. 1 population not of interest or incorrect age group.
viii. 2 published prior to July 20, 2018.
ix. 33 intervention or comparator not of interest.
x. 20 other.
xi. 4 study included in an included SR.
xii. 6 superseded by another SR.

b. Down to Box 9.

5. Box 9: 59 included studies.

Table A-2. Evidence Base for KQs

KQ Number	KQ	Number and Study Type
1	How do environmental exposures during the course of military service predict: • Onset of asthma • Exacerbations of asthma?	2 SRs
2	What is the comparative effectiveness of various initial treatments for asthma? How does this vary for mild vs. severe asthma?	2 RCTs
3	What are the long-term comparative benefits and harms of chronic inhaled corticosteroids?	3 SRs, 8 RCTs (in 11 publications) (14 publications total)
4	For patients with treated but uncontrolled asthma, what strategies or additions/modifications in pharmacologic intervention are effective at controlling asthma?	5 SRs, 3 RCTs
5	For patients with asthma, what is the comparative effectiveness of self-management approaches, asthma action plan (AAP) components, or patient education components on asthma-related outcomes?	4 SRs (2 with NMA), 6 RCTs
6	For patients with asthma, what is the effectiveness of patient-oriented technologies?	4 SRs, 8 RCTs
7	For patients with or without asthma who also experience exercise-induced bronchospasm, what pharmacotherapies are effective in the prevention of exercise-induced bronchospasm?	2 RCTs
8	Among individuals with asthma, what is the effectiveness of interventions to reduce or remove indoor inhalant allergens on asthma control and other outcomes?	4 RCTS, 2 Post-Hoc Analyses
9	What are the long-term effects of cumulative exposure to corticosteroids in individuals who have asthma and a comorbid atopic disease for which corticosteroids are a standard treatment?	No studies identified
10	Are telemedicine checkups a safe and effective alternative to being seen in person for routine asthma management?	1 RCT
11	In patients with asthma and gastroesophageal reflux disease (GERD), does treating GERD improve asthma outcomes?	1 SR
12	In patients with asthma and obesity, does treating obesity improve asthma outcomes?	2 RCTs
Total Evidence Base		**57 studies (in 60 publications)**

Abbreviations: AAP: asthma action plan; GERD: gastro esophageal reflux disease; KQ: key question; NMA: network meta-analysis RCT: randomized controlled trial; SR: systematic review

a. General Criteria for Inclusion in Systematic Evidence Review

- Randomized control trials (RCTs) or systematic reviews of RCTs published on or after July 20, 2018, to May 15, 2024. If multiple systematic reviews addressed a key question, we selected the most recent and/or comprehensive review.
- Studies had to be published in English.
- Publication had to be a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, research protocols, and other publications that were not full-length clinical studies were not accepted as evidence.
- Systematic reviews 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 Evidence-based Practice Centers of the Agency for Healthcare Research and Quality). If an existing review did not assess the overall quality of the evidence, evidence from the review was 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.
- RCTs had to have an independent control group. Randomized crossover trials were only included if data from the first period (prior to treatment crossover) was reported separately and an adequate washout period was used.
- If no RCTs were available to address KQs 1 (environmental exposure), 3 (chronic inhaled corticosteroids), 8 (indoor allergens), or 9 (cumulative exposure to corticosteroids), prospective, non-randomized comparative studies were included. In the event there was no data identified for these KQs, we then looked at longitudinal cohort studies. Similarly, if no systematic reviews of RCTs were available for KQs 1, 3, 8, or 9, SRs of eligible non-RCT designs were used.
- Study had to have enrolled at least 20 patients (10 per study group for RCTs and 20 for prospective non-randomized studies) unless otherwise noted.
- Study had to have enrolled at least 85% of patients who meet the study population criteria: children and adults aged 5 years or older with asthma, or the population appropriate to the KQ. If the patient population fell below this threshold but the relevant population of patients with asthma was reported separately, then that study was included.
- To ensure applicability to the VA/DOD healthcare systems, and ensure consistency across the CPG program, inclusion of individual studies was limited to very high Human Development Index (HDI), countries with an index ≥0.8 where standards of healthcare are comparable (e.g., United States, Canada, United Kingdom, Western Europe, Israel, Japan, Hong Kong, Australia, and New Zealand). Inclusion of systematic reviews was limited to those including more than half of the studies from eligible regions.
- These regions of interest are listed in Table 1 of the Statistical Annex of the 2023/24 Human Development Report produced by the United Nations Development Programme.
- Study must have reported on at least one outcome of interest.

b. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in Table A-5, below. Additional information on the search strategies, including topic-specific search terms and search strategies can be found in Appendix L.

Table A-3. Bibliographic Database Information

Name		Date Limits	Platform/ Provider
Bibliographic Databases	The Cochrane Database of Systematic Reviews (Cochrane Reviews)	July 20, 2018, through May 15, 2024	Wiley
	CINAHL	July 20, 2018, through May 15, 2024	Wiley
	EMBASE (Excerpta Medica)	July 20, 2018, through May 15, 2024	Elsevier
	MEDLINE/PreMEDLINE	July 20, 2018, through May 15, 2024	Elsevier
	PsycINFO	July 20, 2018, through May 15, 2024	OVIDSP
Gray Literature Resources	PubMed (In-process and Publisher records)	July 20, 2018, through May 15, 2024	NLM
	AHRQ	July 20, 2018, through May 15, 2024	AHRQ

c. Rating the Quality of Individual Studies and the Body of Evidence

The Sigma Team assessed the methodological risk of bias of individual diagnostic, observational, and interventional studies using the USPSTF method. Each study is assigned a rating of *Good*, *Fair*, or *Poor* based on a set of criteria that vary depending on study design. Detailed lists of criteria and definitions appear in Appendix VI of the USPSTF procedure manual.(16)

Next, the Sigma team assessed the overall quality of the body of evidence for each critical and important outcome using the GRADE approach. This approach considers the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence. The overall quality of the body of evidence is rated as *High*, *Moderate*, *Low*, and *Very Low.*

D. Developing Evidence-Based Recommendations

In consultation with the VA Office of Quality and Patient Safety and the Clinical Quality Improvement Program, Defense Health Agency, and the Sigma Team convened a 3.5 day in-person recommendation development meeting from September 17-20, 2024, to develop this CPG's evidence-based recommendations. Two weeks before the meeting, the Sigma Team finalized the systematic evidence review and distributed the report to the Work Group; findings were also presented during the recommendation development meeting.

Led by the Champions, the Work Group interpreted the systematic evidence review's findings and developed this CPG's recommendations. The strength and direction of each recommendation were determined by assessing the quality of the overall evidence base, the associated benefits and harms, patient values and preferences, and other implications (see Determining Recommendation Strength and Direction).

Determining Recommendation Strength and Direction

Per GRADE methodology, each recommendation's strength and direction is determined by the following four domains.(13) Information on each domain, questions to consider, and the resulting judgement can be found in Table A-4.

1. Confidence in the Quality of the Evidence

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 their strength. The evidence review used for the development of recommendations for asthma, conducted by the Sigma Team, assessed the confidence in the quality of the evidence base and assigned a rate of "High," "Moderate," "Low," or "Very Low."

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?

2. Balance of Desirable and Undesirable Outcomes

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 most clinicians will offer patients therapeutic or preventive measures if 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?

3. Patient Values and Preferences

Patient 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?

4. Other Implications

Other implications consider the practicality of the recommendation, including resources 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 patients 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 practicality of the recommendation.

Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgement
Balance of desirable and undesirable outcomes	▪ What is the magnitude of the anticipated desirable outcomes? ▪ What is the magnitude of the anticipated undesirable outcomes? ▪ Given the best estimate of typical values and preferences, are you confident that benefits outweigh harms/burdens or vice versa?	▪ Benefits outweigh harms/burdens ▪ Benefits slightly outweigh harms/burdens ▪ Benefits and harms/burden are balanced ▪ Harms/burden slightly outweigh benefits ▪ Harms/burden outweigh benefits
Confidence in the quality of the evidence	▪ Among the designated critical outcomes, what is the lowest quality of relevant evidence? ▪ How unlikely is further research to change the confidence in the estimate of effect?	▪ High ▪ Moderate ▪ Low ▪ Very low
Patient 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

E. Recommendation Categorization

1. Recommendation Categories and Definitions

For use in the 2025 Asthma CPG, a set of recommendation categories was adapted from those used by the United Kingdom National Institute for Health and Clinical Excellence (NICE).(17,18) These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2019 Asthma CPG.

2. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether 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 2019 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.

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.

3. 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 SR of the evidence. Due to time and budget constraints, the update of the Asthma CPG could not review all available evidence on the 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.

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, 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. Recommendations 2, 3, 5, 7, 11, 15-19, and 21 were carried forward from the 2019 Asthma CPG using this method. The categories for the recommendations from the 2019 Asthma CPG are noted in Appendix A.

F. Drafting and Finalizing the 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 2019 Asthma CPG to support the amended "carried forward"

recommendations. The Work Group also considered tables, appendices, and other sections from the 2019 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 revise the CPG. Once they were developed, the first two drafts of the CPG were posted on the Asthma Wiki Website for a period of 10-20 business days for internal review and comment by the Work Group. Draft 3 was made available for a 14-day peer review and comment period (see External Peer Review). All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG. Following the Draft 3 review and comment period, the Work Group reviewed external feedback and created a final draft of the CPG. The Champions then presented the CPG to the VA/DOD EBPWG for approval, and the final CPG was approved in March 2025. To accompany the CPG, the Work Group produced toolkit products, including a provider summary, quick reference guide, and patient summary.

Appendix B: Patient Focus Group Methods and Findings

A. Methods

VA and DOD Leadership recruited seven participants for the focus group, with support from the Champions and other Work Group members as needed. A convenience sample was utilized in selection of participants, and therefore the sample of patients used is not generalizable for the entirety of VA and DOD patients with asthma. The goal of recruitment for this Patient Focus Group was to have engaging, diverse patients, who would be able to cogently explain their experience with Asthma receiving VA or DOD healthcare services.

The Work Group, with support from the Sigma Team, identified topics on which patient input was important to consider in developing the CPG. The Sigma Team developed, and the Work Group approved and patient focus group guide covering these topics. The focus group facilitator led the discussion used the guide to elicit the patients' perspectives about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all questions were addressed.

B. Patient Focus Group Findings

a. Participants would benefit from accessible and customized asthma education and information resources.

- Participants emphasized the need for trusted educational resources.
- Patients noted that further education and training from providers would be beneficial.

b. Participants discussed the value of clear and concise communication about available asthma treatment options, as well as having shared decision making between asthma patients and their providers about treatment goals.

- Patients stated that they viewed their providers as the most trustworthy source of asthma information and the patient-provider relationship is highly regarded.
- The participants noted that they valued access to a combination of care/medications.

c. Participants voiced the importance of receiving coordinated care that uses a 'whole person' approach and comprehensive Asthma Treatment Plans from their providers.

- Participants found collaborative and holistic care models valuable in asthma treatment.
- Participants liked receiving thorough Asthma Treatment Plans from their providers that included multiple management options.

d. Participants emphasized the need for peer connection and support between individuals with asthma to better address asthma-associated stigmas.

- Participants expressed the need for opportunities to connect with others who have asthma.

- Participants discussed the importance of de-stigmatizing asthma in patient populations of all ages.

Appendix C: Assessments of Asthma Severity and Control

A. Assessment of Asthma Severity

Table C-1. Assessment of Asthma Severity[a, b, c, d]

Asthma Severity (assess after trial of 2-3 months of treatment)	Description of Asthma Control
Mild	Controlled on low-intensity treatment (ex: prn low dose ICS-formoterol or low dose ICS + prn rapid-onset LABA/SABA)
Moderate	Controlled with low or medium-dose ICS-LABA
Severe	Controlled with high-dose ICS-LABA (with or without add-on therapies such as LAMA, biologic therapies, or chronic oral corticosteroids) OR Uncontrolled despite high-dose ICS-LABA (with or without add-on therapies)

[a] Severity classification does not apply to the active duty population due to different occupational requirements.
[b] Asthma severity is determined by retrospective assessment of the minimum the level of treatment required to obtain control of asthma symptoms and exacerbations after a trial of at least 2-3 months of therapy.
[c] Severe asthma should be distinguished from asthma that is difficult to treat due to modifiable factors such as inappropriate therapy, poor adherence, poor inhaler technique, uncontrolled co-morbidities and persistent exposures to sensitizing agents [GINA and ATS].] (3,125)
[d] This table has been modified with guidance from the Global Initiative for Asthma [2024] (3) and ATS/ERS Task Force (125).

B. Assessment of Asthma Control

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

Assessing Asthma Control (All Ages)		
Components of Control (over 4 weeks)	**Controlled**	**Not Controlled**
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 relief (not for prevention of EIB)	≤2 treatments/week	>2 treatments/week
ACT score ages ≥4 years	≥ 20	≤19

* This table has been carried forward from the 2009 and 2019 VA/DOD Asthma CPG. It has been modified from guidance from other organizations (ATS/ERS [2021] (125) and the Global Initiative for Asthma [2024] (3)).

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

Table C-3. Risk Factors for Poor Asthma Outcomes[*, a]

Risk Factors for Poor Asthma Outcomes		
Risk Factors for Exacerbations	**Risk Factors for Developing Persistent Airflow Limitation**	**Risk Factors for Medication Side Effects**
■ Uncontrolled asthma symptoms ■ History of 1 or more exacerbations in the previous year requiring oral corticosteroids ■ History of ever requiring intensive care admission or intubation for an asthma exacerbation ■ Therapy without ICS (i.e., using SABA as both controller and reliever) ■ Overuse of SABA ■ Socioeconomic factors ■ Poor treatment adherence ■ Poor inhaler technique ■ Low FEV1, especially <60% predicted and/or with high bronchodilator responsiveness ■ High subjective response OR spirometry with significant reversibility post-BD (i.e., more than 2 times per week) ■ Elevated FeNO ■ Exposure to smoking (including e-cigarettes), allergens, and air pollution ■ Blood eosinophilia	■ History of preterm birth or low birth weight and greater infant weight gain ■ Chronic mucus hypersecretion ■ Therapy without ICS ■ Exposure to tobacco smoke, noxious chemicals, occupational or domestic exposures ■ Low initial FEV1 ■ Sputum or blood eosinophilia	■ Frequent corticosteroids for asthma and/or other conditions ■ Long-term or high-dose ICS ■ Poor inhaler technique

Risk Factors for Poor Asthma Outcomes		
Risk Factors for Exacerbations	**Risk Factors for Developing Persistent Airflow Limitation**	**Risk Factors for Medication Side Effects**
■ Other medical conditions including pregnancy, obesity, chronic rhinosinusitis, GERD, and confirmed food allergies		

[a] Although poor control of asthma symptoms is a strong risk factor for exacerbations, it is important to recognize that even patients with well-controlled asthma symptoms may remain at risk for exacerbations (GINA 2024) (3).

* This table has been created and modified with guidance from other organizations (ATS/ERS [2021] (125) and the Global Initiative for Asthma [2024] (3)).

C. Indications for Specialist Referral

Patients may benefit from specialist referral to pulmonology, allergy/immunology, ENT and others, for assistance in asthma management in the following circumstances:

- Patient has ever had a life-threatening asthma exacerbation
- Patients needing advanced therapies, such as biologics, roflumilast, or a chronic macrolide antibiotic. Also, any patients requiring more than two courses 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], aspirin exacerbated respiratory disease [AERD], severe rhinitis, vocal cord dysfunction, GERD, COPD) that do not respond to appropriate management
- Additional diagnostic testing is indicated (e.g., allergy testing, rhinoscopy, complete pulmonary function studies, bronchoscopy)
- If persistent airflow limitation is present on pulmonary function testing
- Patient is being considered for specialized treatments including immunotherapy, biological agents or bronchial thermoplasty
- 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 C-4. 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 C-5. Identifying Alternative Diagnosis Based on Symptoms and Tests: Adult and Pediatric Causes (in Addition to Table C-4)

Diagnosis	Presentation	Test: Results	Radiographic Findings (CT, chest X-ray)	Pulmonary Function Tests
Allergic bronchopulmonary aspergillosis	▪ Brownish sputum ▪ Wheezing ▪ Shortness of breath ▪ Fever ▪ Malaise	▪ Blood: eosinophilia ▪ Serum precipitins to aspergillus ▪ Very elevated IgE	▪ Recurrent fleeting infiltrates ▪ Bronchiectasis ▪ Mucoid impaction ▪ Centrilobular nodules	▪ Airflow obstruction (variable response to bronchodilator)
Allergic rhinitis	▪ Seasonal or chronic rhinorrhea/nasal obstruction ▪ Daytime and/or morning cough	▪ Trial of antihistamines	▪ N/A	▪ Normal spirometry with allergies alone ▪ However, allergic rhinitis is a common co-occurring condition with asthma
Bronchiectasis - Airway enlargement	▪ Chronic productive cough ▪ Wheezing ▪ Shortness of breath	▪ Variable depending on cause	▪ High resolution CT: localized infiltrates, airway enlargement	▪ Normal or mild airflow obstruction
Bronchiolitis - Asthma exacerbation caused by viruses	▪ Diffused wheeze and/or bronchi	▪ No response to beta-2 agonist ▪ Respiratory syncytial virus testing	▪ N/A	▪ N/A
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	▪ N/A

Diagnosis	Presentation	Test: Results	Radiographic Findings (CT, chest X-ray)	Pulmonary Function Tests
Congestive heart failure/ coronary artery disease	▪ Fatigue ▪ Orthopnea ▪ Paroxysmal nocturnal dyspnea ▪ Dyspnea on exertion ▪ Edema ▪ Weight gain	▪ Echocardiogram: Low left ventricular ejection fraction and/or diastolic dysfunction ▪ B-type natriuretic peptide: elevated	▪ Cardiomegaly ▪ Pulmonary congestion ▪ Pleural effusions	▪ Variable, though reversible obstruction is uncommon
COPD	▪ See Table C-4, See VA/DOD COPD CPG[3]	▪ Arterial blood gas: hypercapnia	▪ Bullous disease ▪ Hyperinflation	▪ Airflow obstruction (variable response to bronchodilator) ▪ FEV1/FEC ratio less <0.7
Cystic fibrosis	▪ Recurrent productive cough ▪ Recurrent pneumonia ▪ Malabsorption ▪ Sinusitis ▪ Pancreatic insufficiency	▪ Sweat chloride test abnormal	▪ Hyperinflation ▪ Cystic changes ▪ Bronchiectasis	▪ Airflow obstruction, often without response to bronchodilators
Foreign body (Age: 6 months to 6 years)	▪ Unilateral wheeze ▪ Sudden onset ▪ Choking history	▪ Bronchoscopy	▪ Chest X-ray – Unilateral hyperinflation or atelectasis ▪ Failure to deflate on expiratory or decubitus chest X-ray	▪ N/A

[3] See the 2021 VA/DOD Clinical Practice Guideline for the Management of Chronic Obstructive Pulmonary Disease. Available at: https://www.healthquality.va.gov/

Diagnosis	Presentation	Test: Results	Radiographic Findings (CT, chest X-ray)	Pulmonary Function Tests
GERD	▪ Heartburn ▪ Irritable after feeding (children) ▪ Hoarseness ▪ Dry cough ▪ Commonly asymptomatic	▪ Trial of H2-blocker or proton pump inhibitors ▪ Consider gastrointestinal referral for pH probe: reflux	▪ N/A	▪ N/A
Laryngomalacia (Onset prior to 6 weeks of age)	▪ Inspiratory wheeze ▪ Improves when prone ▪ No bronchodilator response	▪ Laryngoscopy	▪ N/A	▪ N/A
Trachea/bronchomalacia	▪ Inspiratory or expiratory monophonic wheeze ▪ No bronchodilator response	▪ Bronchoscopy	▪ N/A	▪ N/A
Pulmonary embolus	▪ Unresponsive to bronchodilator ▪ Hemodynamic compromise ▪ Sudden chest pain ▪ Presence of risk factors ▪ Tachycardia ▪ Hypoxemia	▪ D-dimer: elevated ▪ Arterial blood gas: hypoxemia	▪ CT: Chest pulmonary embolus protocol ▪ Ventilation/ perfusion mismatch ▪ Chest X-ray normal	▪ N/A
Recurrent upper respiratory infection	▪ Common cold symptoms	▪ Reduction of respiratory symptoms after bulb suction or decongestion	▪ N/A	▪ N/A

Diagnosis	Presentation	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	▪ Normal imaging ▪ Hilar adenopathy ▪ Pulmonary infiltrates ▪ Nodules ▪ Fibrosis	▪ Normal, restriction, 20% show obstruction
Subglottic stenosis	▪ History of intubation ▪ Biphasic wheeze, loudest in neck ▪ No bronchodilator response	▪ Bronchoscopy	▪ N/A	▪ N/A
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

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 Veterans Affairs

Appendix D: 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, note that patients usually, but not always, present with two or more symptoms:
  - 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 and/or pollutants: pollens, molds
  - Primary or Secondary tobacco or vape 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 and/or burning stoves, chemicals
  - Co-occurring 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, for example: frequency and/or response of SABA, inhaled and/or oral steroid bursts
- Family history:
  - Asthma
  - Allergic Rhinitis
  - Sinusitis
  - Nasal Polyps
  - Eczema
- Social history:
  - Daycare, workplace, school characteristics
  - Social factors interfering with adherence such as substance abuse, tobacco and/or e-cigarette exposure
  - Social support networks
  - Level of education/Healthcare literacy
  - 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, to include compliance and adherence with current treatment plan
- Level of support
- Economic resources
- Sociocultural beliefs
- Environmental factors from travel
- Deployment

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.

- Observation: cough, audible wheeze or stridor, hypernasal speech
- 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 D-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, unilateral wheeze, productive cough
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 E: DOD Service-Specific Regulation Concerning Asthma

A. General

Uniformed service members will be evaluated for fitness according to the DOD Instruction for Medical Standards and Service-Specific 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:

- DOD: DODI 6130.03 v1: Medical Standards for Military Service: Appointment, Enlistment, or Induction
- Air Force: AFI 48-123, Medical Examinations and Standards
- Army: AR 40-501, Standards of Medical Fitness
- Coast Guard:
- Navy and Marine Corps: NAVMED P-117, The Manual of the Medical Department
- Space Force: N/A

B. Deployment Issues

Uniformed service members deploying or stationed Outside of the Continental United States (OCONUS) 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 OCONUS.

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 F: Example Asthma Action Plan Templates

Providers should choose the Asthma Action Plan (AAP) appropriate for patient's age and primary language to increase understanding of instructions and adherence. Below are example AAP templates for adults from the National Heart, Lung, and Blood Institute and the DOD. For an example of an AAP template that can be used for children or in different languages, see links below or check with your local and state health and education departments.

- Create an Asthma Action Plan | American Lung Association
- My Asthma Action Plan (lung.org)
- My Asthma Action Plan for Home and School (lung.org)
- School or Child Care Asthma/Allergy Action Plan March 2024 (aafa.org)
- Asthma Action Plan April 2018 (aafa.org)
- CDC Asthma Action Plan
- Asthma Action Plan (nih.gov)
- SMART Asthma Action Plan (allergyasthmanetwork.org)

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

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: _____

Daily Medicines

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)

1st **Add: quick-relief medicine—and keep taking your GREEN ZONE medicine.**

_____ (quick-relief medicine) _____ Number of puffs **or** ☐ Nebulizer, once — Can repeat every _____ minutes up to maximum of _____ doses

2nd **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: _____ (quick-relief medicine) _____ Number of 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,
- 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:

☐ _____ (quick-relief medicine) _____ Number of 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 _____ puffs of _____ (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. Keep in mind that controlling any allergen usually requires a combination of approaches, and reducing allergens is just one part of a comprehensive asthma management plan. Here are some tips to get started. These tips tend to work better when you use several of them together. Your health care provider can help you decide which ones may be right for you.

ALLERGENS

❒ Dust Mites

These tiny bugs, too small to see, can be found in every home—in dust, mattresses, pillows, carpets, cloth furniture, sheets and blankets, clothes, stuffed toys, and other cloth-covered items. If you are sensitive:

- Mattress and pillow covers that prevent dust mites from going through them should not be used alone; consider using them along with air filtration or carpet removal.
- Consider reducing indoor humidity to below 60 percent. Dehumidifiers or central air conditioning systems can do this.

❒ Cockroaches and Rodents

Pests like these leave droppings that may trigger your asthma. If you are sensitive:

- Consider an integrated pest management plan.
- Keep food and garbage in closed containers to decrease the chances for attracting roaches and rodents.
- Use poison baits, powders, gels, or paste (for example, boric acid) or traps to catch and kill the pests.
- If you use a spray to kill roaches, stay out of the room until the odor goes away.

❒ Animal Dander

Some people are allergic to the flakes of skin or dried saliva from animals with fur or hair. If you are sensitive and have a pet:

- Consider keeping the pet outdoors.
- Try limiting to your pet to commonly used areas indoors.

❒ Indoor Mold

If mold is a trigger for you, you may want to:

- Explore professional mold removal or cleaning to support complete removal.
- Wear gloves to avoid touching mold with your bare hands if you must remove it yourself.
- Always ventilate the area if you use a cleaner with bleach or a strong smell.

❒ Pollen and Outdoor Mold

When pollen or mold spore counts are high you should try to:

- Keep your windows closed.
- If you can, stay indoors with windows closed from late morning to afternoon, when pollen and some mold spore counts are at their highest.
- If you do go outside, change your clothes as soon as you get inside, and put dirty clothes in a covered hamper or container to avoid spreading allergens inside your home.
- Ask your health care provider if you need to take or increase your anti-inflammatory medicine before the allergy season starts.

IRRITANTS

❒ Tobacco Smoke

- If you smoke, visit smokefree.gov or ask your health care provider for ways to help you quit.
- Ask family members to quit smoking.
- Do not allow smoking in your home or car.

❒ Smoke, Strong Odors, and Sprays

- If possible, avoid using a wood-burning stove, kerosene heater, or fireplace. Vent gas stoves to outside the house.
- Try to stay away from strong odors and sprays, such as perfume, talcum powder, hair spray, and paints.

❒ 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 must vacuum yourself, using high efficiency participate air-filtration (HEPA) filter vacuum cleaners may be helpful.

❒ 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

NIH National Heart, Lung, and Blood Institute

NIH Publication No. 20-HL-5251
December 2020

For more information and resources on asthma, visit *nhlbi.nih.gov/BreatheBetter*.

LEARN MORE BREATHE BETTER™

B. Department of Defense Asthma Action Plan Template

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

DA FORM **4700** FEB 2003

C. CDC Asthma Action Plan Templates

Asthma Action Plan

Name: _____ Date: ____ / ____ / _____

Doctor's Name: _____ Main Emergency Contact: _____

Doctor's Phone Number: _____ Backup Emergency Contact: _____

Green Zone: No coughing, wheezing, chest tightness, or shortness of breath. Can do usual activities.

Doing Well

Every day: Take these medicines, even if you're not having any symptoms. Avoid triggers that you know make your asthma worse.

Medicine	How much to take	When to take

Before you exercise: Take [ ]2 or [ ]4 Puffs of _____ 5 minutes before you start, as needed.

Yellow Zone: One or more of these symptoms: coughing, wheezing, chest tighness, breathing trouble, waking up at night due to asthma. Or, if you can only do some, but not all, usual activities.

Some Symptoms

Keep taking your Green Zone medicine and avoiding triggers as usual **AND** take this medicine:

Medicine	How much to take and how often		
(Quick-relief)	_____ Puffs Can repeat every ___ minutes, Up to ___ times	**OR**	[ ] Nebulizer: Use it once

If you return to the Green Zone after 1 hour, keep monitoring to be sure you stay in the Green Zone.

If you do **not** return to the Green Zone after 1 hour take this medicine:

Medicine	How much to take and how often		
(Quick-relief)	_____ Puffs	**OR**	[ ] Nebulizer: Use it once
AND: (Oral Steroid)	Take _____ mg each day for ____ (3 to 10) days		

Call your doctor (or have someone call) just before you take the oral steroid OR _____ minutes/hours after taking the oral steroid, based on the instructions your doctor gave when the medicine was prescribed.

Asthma Action Plan

Name: _____ Date: ____ / ____ / _____

Doctor's Name: _____ Main Emergency Contact: _____

Doctor's Phone Number: _____ Backup Emergency Contact: _____

Red Zone: EMERGENCY! Very short of breath, or quick-relief medicines have not helped, or symptoms are the same or worse after 24 hours in the Yellow Zone. Or, if you cannot do any of your usual activities.

Severe Symptoms Emergency

Take this medicine	How much to take		
(Quick-relief)	_____ Puffs Can repeat every ___ minutes, up to ___ times	**OR**	[ ] Nebulizer: Can repeat every ___ minutes, up to ___ times
(Oral steroid)	Take _____ mg.		

After you take your medicine, call your doctor right away!
If you're still in the Red Zone after 15 minutes and have not reached your doctor, go to the hospital or call 911!

If you have these DANGER SIGNS: trouble walking or talking due to shortness of breath or your lips or fingernails are blue, pale, or gray, take ____ puffs of your quick-relief medicine and GO to the hospital or call 911 NOW!

These DANGER SIGNS mean you need help right away. Don't wait to hear back from your doctor.
GO to the hospital or call 911 NOW!

If you use a peak flow meter you can use these scores to determine your current zone:

Your best score	Your green zone	Your yellow zone	Your red zone
_____	_____ or higher (80% of best score)	_____ to _____ (50 to 80% of best score)	_____ or lower (50% of best score)

Know Your Asthma Triggers.

Learn how to avoid triggers to control your asthma.

Triggers are things that make your asthma symptoms worse. People with asthma do not all have the same triggers. Avoiding your triggers is one step you can take to help keep your asthma under control. Work with your healthcare provider to check whether any of these things make your asthma worse, then take the related steps below. Check CDC's webpage for other steps you can take: www.cdc.gov/asthma

Outdoor Triggers

Weather
Air Quality
Pollen

- Pay attention to radio, television, the internet, or newspaper reports about things that might trigger your asthma. These might include reports about weather, air quality, pollen count, or wildfire conditions.
- Plan outdoor activities for when the air quality is best.
- If pollen triggers your asthma, close windows and turn on air conditioning (if possible) when pollen levels are high.
- When there are wildfires, stay away from areas where there is smoke or vapors. Stay indoors, if possible, to avoid smoke or vapors.
- When it is cold, wear a scarf or face mask that covers your nose and mouth to keep airflow as warm as possible.

Indoor Triggers

If you are allergic to dust mites, cockroaches, rodents, indoor mold, or pets, use an air purifier with a high-energy particulate air (HEPA) filter, and use HEPA filters for vacuum cleaners. Keep your home as clean as possible. If you can, ask someone else to clean your home regularly, or wear a dust mask while you clean.

Pets

If you are allergic to your pet, the best way to avoid exposure is to remove the pet from your home and have the house cleaned. If you can't remove the pet:

- Keep the pet out of your bedroom.
- Ask a family member to wash your pet regularly.
- Use allergen-proof pillow and mattress covers.
- Use an air cleaner with HEPA filter.

Note: Pet fur, skin, and saliva trigger some people's asthma.

Dust mites

(tiny bugs that live in dust and fabric)

- Keep relative humidity levels in your home low, around 30%–50%.
- Wash your bedding every week and dry completely.
- Use allergen-proof pillow and mattress covers.

Know Your Asthma Triggers.

Indoor Triggers

Cockroaches **Mice** **Rats** 	• Keep your kitchen clean and store food and garbage in closed containers. • Don't leave out any standing water or other liquids. • Seal cracks or openings in cabinets, walls, floorboards, and around plumbing. • Use traps or poison bait to get rid of roaches, mice, or rats. Keep bait away and out of reach of children and pets. Avoid sprays and foggers.
Mold **Humidity** 	• Fix water leaks as soon as possible and dry damp or wet items within 48 hours. • Remove all moldy items from your home. • Use an air conditioner or dehumidifier to keep the air dry in your home. Keep relative humidity levels in your home low, around 30%–50%. • Empty and clean refrigerator and air conditioner drip pans regularly. • Use bathroom exhaust fans or open windows when you shower.
Smoke **Sprays** **Scents** **Disinfectants** 	• Avoid places where people smoke. If you smoke, ask your healthcare provider how to quit. • Don't use a wood-burning stove, kerosene heater, or fireplace. • Avoid perfume, paint, hairspray, and talcum powder. • Try to stay away when cleaners or disinfectants are being used and right after their use. • Increase air flow by opening doors and windows and turning on exhaust fans.

Other Common Triggers

Illness 	• Contact your healthcare provider if you think you have another health problem that is making it harder for you to breathe. Such problems might include the flu, a cold, acid reflux (heartburn), a sinus infection, severe allergies, or another health concern.
Emotions 	• Talk to your healthcare provider if anxiety, stress, or other emotions make your asthma worse.

Notes:

Appendix G: 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, tezepelumab) approved for treatment of asthma.

Of note, though currently limited in availability in the clinical setting, FeNO testing can be a valuable tool for identifying airway inflammation in asthma patients, helping to determine eligibility for biologic medications targeting eosinophilic inflammation. By providing a non-invasive and objective measure of airway eosinophilia, FeNO testing can aid clinicians in selecting appropriate biologic therapies and optimizing asthma management.

Biologic agents targeting immunoglobulin E (IgE) (omalizumab), interleukin-5 (mepolizumab, reslizumab)interleukin-5α benralizumab, interleukin-4α (dupilumab), and thymic stromal lymphopoietin blockingTSLP (tezepelumab) are used as add-on maintenance therapy for moderate-to-severe asthma that is inadequately controlled (e.g., asthma exacerbations, poor symptom control) with optimized treatment with ICS and other controller medications (LABA, LAMA) including assessment of proper inhaler technique and adherence to therapy. Compared to placebo, these agents have reduced the rate of exacerbations and have shown modest improvement in patient symptoms and quality of life.

An oral steroid-sparing effect with benralizumab, mepolizumab, dupilumab, and reslizumab has been demonstrated in randomized controlled trials in patients who were oral steroid dependent. Tezepelumab was not shown to reduce ICS dose, while maintaining asthma control, compared to placebo. Data from real world studies with omalizumab have shown reduction in oral steroid maintenance doses.

Omalizumab is indicated for moderate-to-severe persistent asthma in patients six years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen ~~serum IgE~~. Mepolizumab, benralizumab, and reslizumab are indicated for patients with severe asthma who have an eosinophilic phenotype. Mepolizumab and benralizumab are approved for those who are six years of age and older and reslizumab is approved for those who are 18 years of age and older. Dupilumab is indicated for moderate-to-severe asthma in those who are six years of age and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma. Tezepelumab is indicated for severe asthma in those who are 12 years of age or older without regards to phenotype or biomarkers. Higher blood eosinophils at baseline is a predictor of a good asthma outcome to biologic therapy.

When biologics are started, other controller treatments are continued. Do not discontinue ICS. A trial of at least 4 months is needed to assess initial response. Assessments include asthma symptom control, exacerbations, lung function, side effects to therapy, and patient satisfaction. Where applicable, the effect of the biologics on other type 2 co-morbidities such as nasal polyps and atopic dermatitis should be assessed. Primary care and specialist should work in

collaboration to monitor and manage treatment. This would include de-escalation of other asthma treatments in those with a good response, extending the trial of the biologic where response is unclear, or discontinuing the biologic or switching to another biologic if there is no response.

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. Ongoing and continued cigarette smoking also poses increased clearance of theophylline. Patients on theophylline should be maintained at a serum level of 5-15 mcg/ml with routine trough level monitoring appropriate for the formulation of theophylline being prescribed. Theophylline might be considered as a non-preferred alternative when other options cannot be used or have been unsuccessful.

C. Additional Information on Drugs Used in Treatment of Asthma

Table G-1. Drugs Used in Treatment of Asthma[a, b, c]

Drug Class[a]	Place in Therapy	Clinical Considerations[b]
Rapid-onset LABA ▪ Albuterol (HFA MDI/Neb SOLN) ▪ Levalbuterol (HFA MDI/Neb SOLN) ▪ Albuterol DPI	▪ 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 (HFA MDI) ▪ Budesonide (DPI/Neb SOLN) ▪ Ciclesonide (HFA MDI) ▪ Fluticasone (HFA MDI/DPI) ▪ Mometasone (HFA 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

Drug Class[a]	Place in Therapy	Clinical Considerations[b]
		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
SAMA ▪ Ipratropium (HFA MDI) and Neb SOLN	▪ Add-on agent to inhaled corticosteroids beta agonists (SABA or formoterol) cannot be used as rescue. ▪ Note: SMI only approved for COPD.	▪ May cause bitter taste in mouth, dry mouth, dry nasal mucosa, sinusitis
Combination Inhalers ▪ Budesonide/albuterol (HFA MDI) ▪ Budesonide/formoterol (HFA MDI) ▪ Fluticasone/salmeterol (HFA MDI/DPI) ▪ Mometasone/formoterol (MDI) ▪ Fluticasone/vilanterol (DPI) ▪ Mometasone/formoterol (MDI) ▪ Ipratropium/albuterol (MDI) or Neb SOLN Triple Agent Inhalers ▪ Fluticasone/umeclidium/vilanterol (DPI) ▪ Budesonide/glycopyrrolate/formoterol (MDI)[C]	▪ Fixed-dose combination ICS/LABA is preferred over using both drugs as separate inhalers to encourage adherence to therapy. Separate ICS + LABA is alternative and effective with optimal adherence. ▪ SAMA/SABA not	▪ See comments for SAMA, ICS and beta agonists ▪ LAMA may cause headache, dry mouth, constipation, ▪ Albuterol and Formoterol onset for both 5 min. Albuterol lasts 6 hours, Formoterol lasts 12 hours. No evidence for budesonide/albuterol as more effective than Budesonide/formoterol ▪ ICS plus rapid-onset

Drug Class[a]	Place in Therapy	Clinical Considerations[b]
	preferred in Asthma as recommended MART therapy should include ICS ■ Triple agents appropriate when LABA/ICS adherent with continued symptoms. These can be triple agent inhaler or separate ingredient inhalers with appropriate adherence	LABA preferred for MART therapy ■ See comments for SAMA, ICS, Beta Agonists and LAMA above
Leukotriene Modifiers ■ Montelukast (tablets, chewable tablets, oral grandules) ■ 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

Drug Class[a]	Place in Therapy	Clinical Considerations[b]
		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 Soft Mist Inhaler 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; HFA: Hydrofluoroalkane; ICS: inhaled corticosteroid; LABA: long-acting beta agonist; LAMA: long-acting muscarinic antagonist; MDI: metered dose inhaler; mL: milliliter; SABA: short-acting beta agonist; SAMA: selective beta-2 adrenergic agonists; SMI: soft mist inhaler; Neb SOLN: nebulizer solution

Table G-2. Inhaled Steroids[a, b, c, d, e]

Inhaled Steroid Strengths	Usual dosing interval	FDA-approved ages	Ages	Comparative Dose (mcg/day)			Highest recommended dose per product labeling (mcg/day)
				Low Dose	Medium Dose	High Dose	
Beclomethasone HFA 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 *Also available in Neb SOLN	Twice daily	≥6 years	≥18 years 6-17 years	180-540 180-360	>540-1170 >360-720	>1200 >800	1440 720
Ciclesonide HFA MDI (*ALVESCO*) 80, 160 mcg	Twice daily	≥12 years[c]	≥12 years	80-160	>160-320	>320	640
Fluticasone propionate HFA 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)

				Comparative Dose (mcg/day)			
Inhaled Steroid Strengths	**Usual dosing interval**	**FDA-approved ages**	**Ages**	**Low Dose**	**Medium Dose**	**High Dose**	**Highest recommended dose per product labeling (mcg/day)**
Mometasone HFA MDI (*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 and Global Initiative for Asthma

[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 H: Evidence Table

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

#	Recommendation	2019 Strength of Recommendation[a]	Evidence[b]	2025 Strength of Recommendation[c]	2025 Recommendation Category[d]
1.	We suggest identifying known risk factors (e.g., deployment, smoking) for developing asthma and asthma-associated conditions (e.g., depression, anxiety disorders).	Weak for	(26,27) **Additional Reference** (28,29)	Weak for	Reviewed, New-replaced
2.	In adults and children with asthma, we suggest identifying known risk factors of asthma-related outcomes including overweight/obesity, atopy, air quality, secondhand smoke exposure in children, and history of lower respiratory infection and screening for presence of anxiety or depression.	Weak for	(30-42) **Additional Reference** (43,45,48)	Weak for	Not reviewed, Amended
3.	We suggest offering a written asthma action plan to improve asthma control and asthma-related quality of life.	Weak for	(49-58) **Additional Reference** (59,60)	Weak for	Reviewed, Amended

[a] 2019 Strength of Recommendation column: "Not applicable" indicates that the 2025 VA/DOD Asthma CPG recommendation was a new recommendation and therefore does not have an associated 2017 strength of recommendation.
[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 a systematic evidence review carried out as part of the initial development or update of this 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 identified through a systematic evidence review. These references were, therefore, not included in the evidence base for the recommendation and did not influence the strength and direction of the recommendation.
[c] 2025 Strength of Recommendation column: The 2025 VA/DOD Asthma CPG was developed using the GRADE approach to determine the strength of each recommendation. Refer to the Grading Recommendations section for more information.
[d] Recommendation Category column: Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category

#	Recommendation	2019 Strength of Recommendation [a]	Evidence [b]	2025 Strength of Recommendation [c]	2025 Recommendation Category [d]
4.	There is insufficient evidence to recommend for or against offering any particular patient-oriented technology to augment usual care for asthma.	Neither for nor against	(61-66)	Neither for nor against	Reviewed, New-replaced
5.	We recommend inhaled corticosteroids (ICS) for asthma control.	Strong for	(67-71)	Strong for	Not reviewed, Amended
6.	For patients (ages 12 and over) with asthma, we suggest inhaled corticosteroids combined with a rapid-onset long-acting beta agonist (e.g., formoterol), for control and relief of asthma.	Weak for	(67-71)	Weak for	Reviewed, New-replaced
7.	For patients with uncontrolled asthma on inhaled corticosteroids alone, we recommend the use of both inhaled corticosteroids and rapid-onset long-acting beta agonists (e.g., formoterol) as both controller and reliever.	Weak for	(72-74)	Strong for	Reviewed, Amended
8.	In patients with uncontrolled asthma on inhaled corticosteroids and long-acting beta agonists, who use short-acting beta agonists for relief, we suggest inhaled corticosteroids and rapid-onset long-acting beta agonists (e.g., formoterol) as both controller and reliever.	Not applicable	(75),69) **Additional Reference** (72),(73)	Weak for	Reviewed, New-added
9.	For patients with asthma (ages 12 and over) not controlled by medium or high dose inhaled corticosteroids and long-acting beta agonists, we suggest adding a long-acting muscarinic antagonist (LAMA).	Not applicable	(72,73,75) **Additional Reference** (74)	Weak for	Reviewed, New-added

#	Recommendation	2019 Strength of Recommendation [a]	Evidence [b]	2025 Strength of Recommendation [c]	2025 Recommendation Category [d]
10.	In patients with exercise-induced bronchoconstriction, we suggest pre-exertional short-acting beta agonists.	Weak for	(77,78) **Additional Reference** (79-81)	Weak for	Reviewed, New-replaced
11.	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	(76,82-86)	Weak for	Not reviewed, Not changed
12.	We suggest offering the treatment of gastroesophageal reflux disease in patients with gastroesophageal reflux disease and asthma for improving asthma control and lung function.	Not applicable	(87) **Additional Reference** (88)	Weak for	Reviewed, New-added
13.	We suggest weight loss in adults with asthma and obesity to improve asthma control.	Not applicable	(89,90)	Weak for	Reviewed, New-added
14.	We suggest against the use of indoor air filtration devices such as high efficiency particulate air and nitric oxide filters, for asthma control.	Not applicable	(91-94,96-98) **Additional Reference** (95,96)	Weak against	Reviewed, New-added
15.	We suggest a multidisciplinary treatment approach to improve asthma-related quality of life, asthma control, and treatment adherence.	Weak for	(58,99-109,112)	Weak for	Not reviewed, Not changed
16.	We suggest patients with asthma participate in regular exercise to improve quality of life and asthma control.	Weak for	(79,110,111,126)	Weak for	Not reviewed, Not changed

#	Recommendation	2019 Strength of Recommendation[a]	Evidence[b]	2025 Strength of Recommendation[c]	2025 Recommendation Category[d]
17.	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 asthma.	Weak for	(112) **Additional Reference** (113)	Weak for	Not reviewed, Not changed
18.	We suggest against utilizing spirometry for routine monitoring of patients with stable asthma.	Weak against	(114,115)	Weak against	Not reviewed, Not changed
19.	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	(40,116,117)	Neither for nor against	Not reviewed, Not changed
20.	For patients with asthma, there is insufficient evidence to recommend for or against offering telemedicine as an alternative to in-person treatment.	Weak for	(118)	Neither for nor against	Reviewed, New-added
21.	We suggest leveraging electronic health record capabilities, such as trackers and reminders, in the care of patients with asthma.	Weak for	(119-123)	Weak for	Not reviewed, Not changed

Appendix I: 2019 Recommendation Categorization

Table I-1. 2019 Asthma CPG Recommendation Categorization Table[a, b, c, d, e, f]

2019 CPG Recommendation #[a]	2019 Recommendation Text[b]	2019 CPG Strength of Recommendation[c]	2019 CPG Recommendation Category[d]	2025 CPG Recommendation Category[e]	2025 CPG Recommendation #[f]
1	We suggest spirometry if there is a need to confirm a clinical diagnosis of asthma.	Weak for	Reviewed, New-replaced	Not reviewed, Deleted	NA
2	In primary care, we suggest against whole-body plethysmography as part of the diagnostic evaluation of asthma.	Weak against	Reviewed, New-replaced	Not reviewed, Deleted	NA
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	Not reviewed, Deleted	NA
4	If bronchoprovocation testing is considered, we suggest methacholine challenge testing.	Weak for	Reviewed, New-replaced	Not reviewed, Deleted	NA
5	We recommend against offering computed tomography scan to diagnose asthma in patients with persistent airflow obstruction post- bronchodilator.	Strong against	Reviewed, New-added	Not reviewed, Deleted	NA

[a] The 2019 Recommendation # column indicates the recommendation number of the recommendation in the 2019 VA/DOD Asthma CPG.
[b] The 2019 CPG Recommendation text column contains the wording of each recommendation from the 2019 VA/DOD Asthma CPG.
[c] The 2019 CPG Strength of Recommendation column contains the strength determined in the 2019 VA/DOD Asthma CPG.
[d] The 2019 CPG Recommendation Category column contains the recommendation category assigned during the development of the 2019 VA/DOD Asthma CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and definitions for each category.
[e] The 2025 CPG Recommendation Category column contains the recommendation category assignevd during the development of the 2025 VA/DOD Asthma CPG.
[f] The 2025 CPG Recommendation # column contains the new recommendations to which recommendations carried forward from the 2019 VA/DOD Asthma CPG correspond.

2019 CPG Recommendation #[a]	2019 Recommendation Text[b]	2019 CPG Strength of Recommendation[c]	2019 CPG Recommendation Category[d]	2025 CPG Recommendation Category[e]	2025 CPG Recommendation #[f]
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	Reviewed, New-replaced	1
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	TBD	2
8	We suggest offering a written asthma action plan to improve asthma-related quality of life.	Weak for	Reviewed, New-replaced	Reviewed, Amended	3
9	We suggest offering asthma education.	Weak for	Reviewed, New-replaced	Not reviewed, Deleted	NA
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	Not reviewed, Deleted	NA
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	Not reviewed, Deleted	NA
12	For patients with persistent asthma, we recommend inhaled corticosteroids as initial controller medication.	Strong for	Reviewed, Amended	Not reviewed, Deleted	NA
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	Not reviewed, Deleted	NA

2019 CPG Recommendation #[a]	2019 Recommendation Text[b]	2019 CPG Strength of Recommendation[c]	2019 CPG Recommendation Category[d]	2025 CPG Recommendation Category[e]	2025 CPG Recommendation #[f]
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	Reviewed, Amended	7
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	Not Reviewed, Not changed	11
16	We suggest short-acting beta agonists or leukotriene receptor antagonists for prevention of exercise-induced bronchospasm.	Weak for	Not reviewed, Amended	Reviewed, New-replaced	10
17	We suggest a multidisciplinary treatment approach to improve asthma-related quality of life, asthma control, and treatment adherence.	Weak for	Reviewed, New-replaced	Not reviewed, Not changed	15
18	We suggest patients with asthma participate in regular exercise to improve quality of life and asthma control.	Weak for	Reviewed, Amended	Not reviewed, Not changed	16
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	Not reviewed, Not changed	17
20	We suggest against utilizing spirometry for routine monitoring of patients with stable asthma.	Weak against	Reviewed, New-replaced	Not reviewed, Not changed	18
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	Not reviewed, Not changed	19
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	Not reviewed, Not changed	21

Appendix J: Participant List

Elizabeth Rees Atayde, RN, MSN, FMP, CCM-R
CPHM Quality Management Coordinator
Southern Arizona VA Healthcare System
Tucson, AZ

Donald Curran, MD
Primary Care Community Based Outpatient Clinical Firm Chief
Veterans Administration Connecticut Health Care System
West Haven, CT

Kimberly Fabyan, MD
Pulmonary and Critical Care Physician
Walter Reed National Military Medical Center
Bethesda, MD

LaToya Huff, RT
Acting National RRT Program Manager
Atlanta VA Healthcare System
Atlanta, GA

Brian Nibbelink, PharmD
Element Chief
United States Air Force Joint Refill Processing Center
San Antonio, TX

Christina Nguyen, RT
Respiratory Therapist
Michael E. Debakey VA Medical Center
Houston, TX

Kimberly Schnacky, PharmD, BCPS, BCACP, DPLA
VISN 8 PBM Clinical Pharmacy Program Manager
Orlando VA Medical Center
Orlando, FL

MAJ Juhyun Cho, FNP-BC
Battalion Surgeon
1-78 Fired Artillery Battalion, 428 Field Artillery Brigade, Fires Center of Excellence
Fort Still, OK

Deona Eickhoff, MBA, BSN, RN, CCM
Clinical Disease Case Management Consultant
Government Civilian Defense Health Agency (DHA), Medical Affairs Division
Aurora, CO

Mary Gollings, LCSW
Social Work Supervisor, Health Care Programming
Jesse Brown VA Medical Center
Chicago, IL

Jane Jacknewitz-Woolard, DNP, CRNP-BC, AE-C
Nurse Practitioner, Pediatric Pulmonology Service
Walter Reed National Military Medical Center
Bethesda, MD

Lan-Anh Ngo, MD
Primary Care Physician
Taylor Burk Clinic, Brooke Army Medical Center
San Antonio, TX

Katherine Richards, MD
Staff Pulmonologist, Medical Care
Michael E. Debakey VA Medical Center
Houston, TX

Jonathan Schroeder, MD
Pediatric Pulmonologist
Brooke Army Medical Center
San Antonio, TX

Amir Sharafkhaneh, MD, PhD
Staff Pulmonologist, Medical Care
Michael E. Debakey VA Medical Center
Houston, TX

Daniel Steigelman, MD
Allergy/Immunology Department Chair
Wilford Hall Ambulatory Surgical Center,
Joint Base San Antonio
San Antonio, TX

William Wilson, RRT
NICU/PICU Respiratory Educator
Brooke Army Medical Center
San Antonio, TX

William C. "Claibe" Yarbrough, MD
National Program Executive Director,
Pulmonary and Critical Care
Office of Specialty Care, VA Central Office
North Texas Healthcare System
Dallas, TX

Appendix K: Alternative Text Descriptions of Algorithms

The following outlines narratively describe Module A and Module B, 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 symptoms and signs compatible with asthma (see Sidebar A)”
2. Box 1 connects to Box 2, in the shape of a hexagon: “Is the patient acutely ill?”
    a. If the answer is “Yes” to Box 2, then Box 3 in the shape of a rectangle: “Treat exacerbation”, and Box 4 in the shape of a circle: “Follow-up as appropriate”
    b. If the answer is “No” to Box 2, then Box 5 in the shape of a hexagon: “Is there a confidence clinical diagnosis of asthma? (Sidebar B and Appendix C)
        i. If the answer is “Yes” to Box 5, then Box 12 in the shape of a circle: “Continue to Module B: Initiation of Therapy for Initial Treatment or Continuation of therapy”
        ii. If the answer is “No” to Box 5, then Box 6 in the shape of a hexagon: “Is there an alternative diagnosis?”
            1. If the answer is “Yes” to Box 6, then Box 7 in the shape of a rectangle: “Treat alternative diagnosis”
            2. If the answer is “No” to Box 6, then Box 8 in the shape of a hexagon: “Is the patient capable of spirometry and is it readily available?”
                a. If the answer is “Yes” to Box 8, then Box 9 in the shape of a rectangle “Obtain spirometry”
                b. If the answer is “No” to Box 8, then Box 12 in the shape of a circle: “Continue to Module B: Initiation of Therapy for Initial Treatment or Continuation of therapy”
3. 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 then Box 12 in the shape of an oval: “Continue to Module B: Initiation of Therapy for Initial Treatment or Continuation of therapy”
4. If the answer is “No” to Box 10, then Box 11, in the shape of a rectangle: “Consider other options according to site availability and patient/provider preferences and characteristics (Refer to Sidebar C, Sidebar D, and Appendix C)”

5. Box 11 connects to Box 13, in the shape of a hexagon, asks the question: "Was asthma diagnosis or decision to treat confirmed?"
    a. If the answer is "Yes" to Box 13, then Box 12, in the shape of an oval: "Continue to Module B: Initiation of Therapy for Initial Treatment or Continuation of therapy"
    b. If the answer is "No" to Box 13, then Box 14 in the shape of an oval: "Refer to specialist (e.g., pulmonary, immunology, allergy) (see Sidebar J)"

B. Module B: Initiation of Therapy

6. Module B begins with Box 15, in the shape of a rounded rectangle: "Patient with confirmed or suspected diagnosis of asthma (see Sidebar A and Sidebar B)"
7. Box 15 connects to Box 16, in the shape of a rectangle: "Start or continue therapy with an ICS and rapid-onset LABA as a reliever and initiate asthma education and care management (see Sidebars E, F, and G and Recommendation 6)"
8. Box 16 connects to Box 17, in the shape of a hexagon, asks "Does the patient have more than mild symptoms?"
    a. If the answer is "Yes" to Box 17, then Box 23, in the shape of a rectangle: "Initiate ICS and rapid-onset LABA as controller and reliever (see Sidebar G)"
    b. If the answer is "No" to Box 17, then Box 18, in the shape of a hexagon: "Are the patient's symptoms controlled?"
        i. If the answer is "Yes" to Box 18, then Box 20, in the shape of a rectangle: "Reassess in 3 months or at next visit: Symptom Control, Adherence, and Inhaler Technique. Revise Asthma Action Plan and coordinate with case manager, as needed. (see Appendix F and Sidebar I)"
        ii. If the answer is "No" to Box 18, then Box 19 in the shape of a rectangle: "Address adherence and proper inhaler technique and/or dose escalation as appropriate (see Sidebar G and Box 25)", then Box 20, in the shape of a rectangle: "Reassess in 3 months or at next visit: Symptom Control, Adherence, and Inhaler Technique. Revise Asthma Action Plan and coordinate with case manager, as needed. (see Appendix F and Sidebar I)"
9. Box 23 connects to Box 24, in the shape of a hexagon, asks the question: "Are the patient's symptoms controlled?"
    a. If the answer is "Yes" to Box 24, then Box 20, in the shape of a rectangle: "Reassess in 3 months or at next visit: Symptom Control, Adherence, and Inhaler Technique. Revise Asthma Action Plan and coordinate with case manager, as needed. (see Appendix F and Sidebar I)"

   b. If the answer is “No“ to Box 24, then Box 25 in the shape of a rectangle: “Increase to moderate dose ICS and rapid-onset LABA as controller and reliever (see Sidebar G)”

10. Box 25 connects to Box 26, in the shape of a hexagon: “Are the patient’s symptoms controlled?”
    a. If the answer is “Yes” to Box 26, then Box 20, in the shape of a rectangle: “Reassess in 3 months or at next visit: Symptom Control, Adherence, and Inhaler Technique. Revise Asthma Action Plan and coordinate with case manager, as needed. (see Appendix F and Sidebar I)”
    b. If the answer is “No” to Box 26, then Box 27 in the shape of a rectangle: “Continue moderate dose ICS and rapid-onset LABA as controller and reliever, and add LAMA (Consider specialist referral, see Sidebar G and Sidebar J)”
11. Box 27 connects to Box 20, in the shape of a rectangle: Reassess in 3 months or at next visit: Symptom Control, Adherence, and Inhaler Technique. Revise Asthma Action Plan and coordinate with case manager, as needed. (see Appendix F and Sidebar I)”
12. Box 20 connects to Box 21, in the shape of a hexagon: “Are symptoms stable for >90 days?”
    a. If the answer is “Yes” to Box 21, then Box 22, in the shape of a rectangle: “Consider initiating step-down therapy (see Sidebar H)”, then Box 21, in the shape of a rectangle: “Reassess in 3 months or at next visit: Symptom Control, Adherence, and Inhaler Technique. Revise Asthma Action Plan and coordinate with case manager, as needed. (see Appendix F and Sidebar I)”
    b. If the answer is “No” to Box 21, then Box 19, in the shape of a rectangle: “Address adherence and proper inhaler technique and/or dose escalation as appropriate (see Sidebar G and Box 25)”

Appendix L: Literature Review Search Terms and Strategy

A. Topic-specific Search Terms

Table L-1. Key Question Specific Concept Tables for Populations: PubMed, and EMBASE

Concept	Subject Headings	Key Words
Asthma	**EMBASE (EMTREE)** allergic asthma asthma bronchospasm bronchus hyperreactivity exercise induced asthma respiratory function respiratory tract allergy sinonasal polyp **PubMed/Medline (MeSH)** asthma asthma and nasal polyps asthma, aspirin-induced asthma, exercise-induced bronchial hyperreactivity bronchial spasm respiratory physiological phenomena respiratory sounds	acute* asthma* asthmatic bronchial* bronchus hyperreactivity chronic* chronic* exacerbation* fixed airflow obstruction fixed obstruction lung function* patient* progress* severe* wheeze* *word variations have been searched

Table L-2. Key Question Specific Concept Tables for Interventions: PubMed and EMBASE

Concept	Subject Headings	Key Words
KQ1 Environmental Exposures	**EMBASE (EMTREE)** air pollution allergen disease exacerbation environmental exposure fungus gastroesophageal reflux indoor air pollution military personnel nitric acid nitric oxide occupational exposure occupational health open burning respiratory tract infection risk assessment sleep apnea syndromes veteran **PubMed/Medline (MeSH**) air pollution air pollution, indoor allergens disease progression environmental exposure fungi gastroesophageal reflux inhalation exposure military health military personnel nitric acid nitric oxide occupational exposure occupational health open waste burning respiratory tract infections risk assessment	active duty aspergillus aviation fuel burn pits chemical exposure exposure response

	sleep apnea syndromes veterans	
KQ2 Initial Treatment	**EMBASE (EMTREE)** anti-asthmatic agent beclomethasone budesonide budesonide plus formoterol ciclesonide cromoglycate disodium dexamethasone disease exacerbation flunisolide fluticasone fluticasone furoate plus vilanterol fluticasone propionate plus salmeterol formoterol fumarate plus mometasone furoate leukotriene receptor blocking agent levalbuterol methylprednisolone mometasone furoate montelukast prednisolone prednisone salbutamol tiotropium bromide triamcinolone acetonide vitamin D zafirlukast zileuton **PubMed/Medline (MeSH)** albuterol anti-asthmatic agents beclomethasone budesonide budesonide, formoterol fumarate drug combination	anti-inflammatory budesonide albuterol beclometasone inhaled corticosteroids long-acting beta agonists short-acting beta agonists SMART Therapy inhaled steroids systemic corticosteroids

	ciclesonide cromolyn sodium dexamethasone disease progression flunisolide fluticasone fluticasone furoate-vilanterol trifenatate fluticasone-salmeterol drug combination leukotriene receptor antagonist levalbuterol methylprednisolone mometasone mometasone furoate, formoterol fumarate drug combination montelukast prednisolone prednisone theophylline tiotropium triamcinolone acetonide vitamin d zafirlukast zileuton	
KQ3 Long-Term Effects of Chronic Inhaled Corticosteroids	**EMBASE (EMTREE)** beclomethasone budesonide budesonide plus formoterol ciclesonide corticosteroid flunisolide fluticasone fluticasone furoate plus vilanterol fluticasone propionate plus salmeterol formoterol fumarate plus mometasone furoate mometasone furoate triamcinolone acetonide	beclometasone

	PubMed/Medline (MeSH) adrenal cortex hormones beclomethasone budesonide budesonide, formoterol fumarate drug combination ciclesonide flunisolide fluticasone fluticasone furoate-vilanterol trifenatate fluticasone-salmeterol drug combination mometasone furoate mometasone furoate, formoterol fumarate drug combination triamcinolone acetonide	
KQ4 Treated but Uncontrolled	**EMBASE (EMTREE)** beclomethasone budesonide budesonide plus formoterol ciclesonide corticosteroid cromoglycate disodium dexamethasone flunisolide fluticasone fluticasone furoate plus vilanterol fluticasone propionate plus salmeterol formoterol fumarate plus mometasone furoate leukotriene receptor blocking agent levalbuterol methylprednisolone mometasone furoate montelukast prednisolone prednisone	beclometasone inhaled corticosteroids inhaled steroids long-acting beta agonists short-acting beta agonists SMART Therapy systemic corticosteroids

	salbutamol theophylline tiotropium bromide triamcinolone acetonide vitamin D zafirlukast zileuton **PubMed/Medline (MeSH)** adrenal cortex hormones albuterol beclomethasone budesonide budesonide, formoterol fumarate drug combination ciclesonide cromolyn sodium dexamethasone flunisolide fluticasone fluticasone furoate-vilanterol trifenatate fluticasone-salmeterol drug combination leukotriene antagonists levalbuterol methylprednisolone mometasone furoate mometasone furoate, formoterol fumarate drug combination montelukast prednisolone prednisone theophylline tiotropium bromide triamcinolone acetonide vitamin d zafirlukast zileuton	
KQ5 Self-Management	**EMBASE (EMTREE)**	asthma action plan

	behavioral medicine educational model health literacy inhalational exposure patient care planning patient care team patient education patient-reported outcome program evaluation psychotherapy questionnaire self care self concept self evaluation self report social adaptation social participation **PubMed/Medline (MeSH)** behavioral medicine diagnostic self evaluation health literacy models, education patient care planning patient care team patient education as topic patient reported outcome measures program evaluation psychotherapy self care self management self report self-concept social adjustment social participation surveys and questionnaires	lifestyle modifications
KQ6 Patient-Oriented Technology	**EMBASE (EMTREE)** medical record	

	mobile application oximetry text messaging transcutaneous oxygen monitoring wearable computer web browser web-based intervention **PubMed/Medline (MeSH)** blood gas monitoring, transcutaneous internet-based intervention mobile applications oximetry patient portals text messaging wearable electronic devices web browser	
KQ7 Exercise-Induced Bronchospasm	**EMBASE (EMTREE)** beclomethasone budesonide budesonide plus formoterol ciclesonide cromoglycate disodium dexamethasone flunisolide fluticasone fluticasone furoate plus vilanterol fluticasone propionate plus salmeterol formoterol fumarate plus mometasone furoate leukotriene receptor blocking agent levalbuterol methylprednisolone mometasone furoate montelukast prednisolone	airsupra anti-inflammatory reliever beclometasone mast cell stabilizing agents short-acting beta agonists systemic corticosteroids exercise bronchospasm

	prednisone salbutamol theophylline tiotropium bromide triamcinolone acetonide vitamin D zafirlukast zileuton **PubMed/Medline (MeSH)** albuterol beclomethasone budesonide budesonide, formoterol fumarate drug combination ciclesonide cromolyn sodium dexamethasone flunisolide fluticasone fluticasone furoate-vilanterol trifenatate fluticasone-salmeterol drug combination leukotriene antagonists levalbuterol methylprednisolone mometasone mometasone furoate, formoterol fumarate drug combination montelukast prednisolone prednisone theophylline tiotropium triamcinolone acetonide vitamin d zafirlukast zileuton	
KQ8 Indoor Inhalant Allergens	**EMBASE (EMTREE)**	household cleaners

	air filter allergen biological pest control pest control safety **PubMed/Medline (MeSH)** air filters allergens pest control pest control, biological rodent control safety management	indoor inhalant allergens pest control methods pesticides rodents
KQ9 Comorbid Atopic Disease	**EMBASE (EMTREE)** allergic rhinitis asthma-chronic obstructive pulmonary disease overlap syndrome beclomethasone budesonide chronic obstructive lung disease ciclesonide corticosteroid flunisolide fluticasone mometasone sinonasal polyp sinusitis triamcinolone acetonide **PubMed/Medline (MeSH)** adrenal cortex hormones asthma-chronic obstructive pulmonary disease overlap syndrome beclomethasone budesonide ciclesonide flunisolide fluticasone	beclometasone chronic rhinosinusitis

	mometasone nasal polyps pulmonary disease, chronic obstructive rhinitis, allergic sinusitis triamcinolone acetonide	
K10 Telemedicine	**EMBASE (EMTREE)** artificial intelligence medical record mobile application teleconsultation telemedicine videoconferencing web browser web-based intervention **PubMed/Medline (MeSH)** artificial intelligence internet-based intervention mobile applications patient portals remote consultation telemedicine videoconferencing web browser	
KQ11 GERD	**EMBASE (EMTREE)** antacid agent antihistaminic agent cisapride famotidine gastroesophageal reflux omeprazole proton pump inhibitor **PubMed/Medline (MeSH)** antacids cisapride famotidine	GERD GORD potassium-competitive acid blocker

	gastroesophageal reflux histamine antagonists omeprazole proton pump inhibitor	
KQ12 Obesity	**EMBASE (EMTREE)** antiobesity agent bariatric surgery body weight loss diet exercise exercise induced asthma glucagon like peptide 1 low calorie diet obesity sodium glucose cotransporter 2 inhibitor weight loss program weight trajectory (body weight) **PubMed/Medline (MeSH)** anti-obesity agents asthma, exercise-induced bariatric surgery body-weight trajectory diet diet, reducing exercise glucagon-like peptide 1 obesity physical exertion sodium-glucose transporter 2 inhibitors weight loss weight reduction programs	

B. Search Strategies

Table L-3. Search Limits, EMBASE

Concept	Thesaurus Term	Key Word

INCLUDE Study Design	meta-analyses systematic review	'systematic review'/exp OR 'systematic review' OR 'meta analysis'/exp OR 'meta analysis'
	randomized controlled trials	'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)
	NO retrospective trials	'latin square design'/de OR 'controlled study'/exp OR 'clinical trial'/exp OR 'comparative study'/exp OR 'cohort analysis'/de OR 'follow up'/de OR 'intermethod comparison'/de OR 'parallel design'/de OR 'control group'/de OR 'prospective study'/de OR 'case control study'/exp OR 'major clinical study'/de OR 'evaluation study'/exp OR 'validation study'/exp OR 'longitudinal study'/exp
EXCLUDE Publication Types		NOT (abstract:nc OR annual:nc OR 'book'/exp OR 'case study'/exp OR conference:nc OR 'conference abstract':it OR 'conference paper'/exp OR 'conference paper':it OR 'conference proceeding':pt OR 'conference review':it OR congress:nc OR 'editorial'/exp OR editorial:it OR 'erratum'/exp OR letter:it OR 'note'/exp OR note:it OR meeting:nc OR sessions:nc OR 'shortsurvey'/exp OR symposium:nc OR [conferenceabstract]/lim OR [conference paper]/lim OR conference review]/lim OR [editorial]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR comment:ti OR book:pt OR 'case report'/de OR 'case report':ti OR 'a case':ti)
Humans		
Date		2018-2024

Table L-4. Search Limits, PubMed

Concept	Thesaurus Term	Key Word
INCLUDE Study Design	meta-analysis systematic review	meta-analysis/exp OR systematic review/exp OR "research synthesis" OR "systematic review*" OR "meta analysis" OR "meta analyses"
	randomized controlled trials	(random allocation[mh] OR "randomized controlled trials"[pt] OR "phase 3"[tiab] OR "phase iii"[tiab] OR random*[tiab] OR RCT[tiab])
	NO retrospective trials	"latin square design"[tiab] OR "controlled study"[tiab] OR "clinical trial"[tiab] OR "comparative study"[tiab] OR "cohort analysis"[tiab] OR "follow up"[tiab] OR "intermethod comparison"[tiab] OR "parallel design"[tiab] OR "control group"[tiab] OR "prospective study"[tiab] OR "case control study"[tiab] OR "major clinical study"[tiab] OR "evaluation study"[tiab] OR "validation study"[tiab] OR "longitudinal study"[tiab]
EXCLUDE Publication Types		NOT (booksdocs[Filter] OR "case reports"[pt] OR comment[pt] OR congress[pt] OR editorial[pt] OR letter[pt] OR "case report"[ti] OR comment*[ti] OR editorial[ti] OR letter[ti] OR news[ti])
Humans		
Date		July 20, 2018, to May 15, 2024

Appendix M: Abbreviation List

Abbreviation	Definition
AAP	asthma action plan
ACQ	Asthma Control Questionnaire
ACT	Asthma Control Test
ATS	American Thoracic Society
AQLQ	Asthma Quality of Life Questionnaire
BMI	body mass index
CBT	cognitive behavioral therapy
COI	conflict of interest
COPD	chronic obstructive pulmonary disease
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
FCC	family-centered care
FeNO	functional exhaled nitric oxide
FEV1	forced expiratory volume
FVC	forced vital capacity
GERD	gastroesophageal reflux disease
GINA	Global Initiative for Asthma
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HEPA	high efficiency particulate air
ICS	inhaled corticosteroids
IgE	Immunoglobulin E
IOM	Institute of Medicine
IPM	integrated pest management
KQs	key questions
LABA	long-acting beta agonist
LAMA	long-acting muscarinic antagonists
LTRA	leukotriene receptor antagonists
MART	maintenance and reliever therapy
mL	milliliter
NAM	National Academy of Medicine
Neb SOLN	nebulizer solution

NICE	National Institute for Health and Care Excellence
NO	nitric oxide
OIF/OEF	Operation Iraqi Freedom/Operation Enduring Freedom
OR	odds ratio
PCC	patient-centered care
PD	psychologic dysfunction
QOL	quality of life
RCT	randomized controlled trial
RR	relative risk
SABA	short-acting beta agonist
SAE	serious adverse event
SDM	shared decision making
SMART	single maintenance and reliever therapy
SOE	strength of evidence
SR	systematic review
TLA	temperature-controlled laminar airflow

References

1. Evidence Based Practice Work Group Charter (2017).
2. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol*. Apr 2011;64(4):395-400. doi:10.1016/j.jclinepi.2010.09.012
3. GINA. 2023 GINA Main Report 2023;
4. Prevention CfDCa. Most Recent Asthma Data.
5. Prevention USCfDCa. 2021 NHAMCS Questionnaires, Datasets, and Documentation. 2021.
6. Prevention CfDCa. 2020 NAMCS Questionnaires, Datasets, and Documentation. 2020;
7. Asthma (2017).
8. Song HJ, Blake KV, Wilson DL, Winterstein AG, Park H. Medical Costs and Productivity Loss Due to Mild, Moderate, and Severe Asthma in the United States. *J Asthma Allergy*. 2020;13:545-555. doi:10.2147/jaa.S272681
9. DoD instruction 6130.03. Medical Standards for Appointment, Enlistment, or Induction into the Military Services (2018).
10. Morris MJ, Walter RJ, McCann ET, et al. Clinical Evaluation of Deployed Military Personnel With Chronic Respiratory Symptoms: Study of Active Duty Military for Pulmonary Disease Related to Environmental Deployment Exposures (STAMPEDE) III. *Chest*. Jun 2020;157(6):1559-1567. doi:10.1016/j.chest.2020.01.024
11. Guideline for guidelines. Veterans Health Administration, Office of Quality & Performance, Evidence Review Subgroup (2019).
12. Ransohoff DF, Pignone M, Sox HC. How to decide whether a clinical practice guideline is trustworthy. *Jama*. Jan 9 2013;309(2):139-40. doi:10.1001/jama.2012.156703
13. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol*. Jul 2013;66(7):719-25. doi:10.1016/j.jclinepi.2012.03.013
14. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health Res Policy Syst*. Dec 5 2006;4:22. doi:10.1186/1478-4505-4-22
15. Newberry SJ, Ahmadzai N, Motala A, et al. AHRQ Methods for Effective Health Care. *Surveillance and identification of signals for updating systematic reviews: Implementation and early experience*. Agency for Healthcare Research and Quality (US); 2013.
16. Standards for Guideline Development (2018).
17. National Institute for Health and Care Excellence. *The Guidelines Manual*. 2012. https://www.nice.org.uk/process/pmg6/chapter/introduction
18. Martínez García L, McFarlane E, Barnes S, Sanabria AJ, Alonso-Coello P, Alderson P. Updated recommendations: an assessment of NICE clinical guidelines. *Implementation Science*. 12/2014 2014;9(1):72. doi:10.1186/1748-5908-9-72
19. Financial Relationships Between VHA Health Care Professionals and Industry (2014).
20. Robinson JH, Callister LC, Berry JA, Dearing KA. Patient-centered care and adherence: Definitions and applications to improve outcomes. *Journal of the American Academy of Nurse Practitioners*. 12/2008 2008;20(12):600-607. doi:10.1111/j.1745-7599.2008.00360.x
21. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. *J Fam Pract*. Sep 2000;49(9):796-804.
22. Fiscella K, Meldrum S, Franks P, et al. Patient Trust: Is It Related to Patient-Centered Behavior of Primary Care Physicians? *Medical Care*. 11/2004 2004;42(11):1049-1055. doi:10.1097/00005650-200411000-00003
23. Veterans Health Library. https://www.veteranshealthlibrary.va.gov/

24. Institute of Medicine Committee on Quality of Health Care in A. *Crossing the Quality Chasm: A New Health System for the 21st Century*. National Academies Press (US)

Copyright 2001 by the National Academy of Sciences. All rights reserved.; 2001.
25. Society for Medical Decision Making Committee on Standardization of Clinical Algorithms. Proposal for Clinical Algorithm Standards: Society for Medical Decision Making Committee on Standardization of Clinical Algorithms*. *Medical Decision Making*. 06/1992 1992;12(2):149-154. doi:10.1177/0272989X9201200208
26. McLean J, Anderson D, Capra G, Riley CA. The Potential Effects of Burn Pit Exposure on the Respiratory Tract: A Systematic Review. *Military Medicine*. 2021;186(7/8):672-681. doi:10.1093/milmed/usab070
27. Williams LG, Ross D. Impact of poor air quality while deployed on respiratory health: a systematic review. Article in Press. *BMJ Military Health*. 2023;doi:10.1136/military-2023-002381
28. Rivera AC, Powell TM, Boyko EJ, et al. New-Onset Asthma and Combat Deployment: Findings From the Millennium Cohort Study. *American Journal of Epidemiology*. 2018-10-01 2018;187(10):2136-2144. doi:10.1093/aje/kwy112
29. Deployment pulmonary health (2015).
30. Rivera AC, Powell TM, Boyko EJ, et al. New-Onset Asthma and Combat Deployment: Findings From the Millennium Cohort Study. *Am J Epidemiol*. Oct 1 2018;187(10):2136-2144. doi:10.1093/aje/kwy112
31. Ahmadizar F, Vijverberg SJH, Arets HGM, et al. Childhood obesity in relation to poor asthma control and exacerbation: a meta-analysis. *European Respiratory Journal*. 10/2016 2016;48(4):1063-1073. doi:10.1183/13993003.00766-2016
32. Egan KB, Ettinger AS, Bracken MB. Childhood body mass index and subsequent physician-diagnosed asthma: a systematic review and meta-analysis of prospective cohort studies. *BMC Pediatrics*. 12/2013 2013;13(1):121. doi:10.1186/1471-2431-13-121
33. Koebnick C, Fischer H, Daley MF, et al. Interacting effects of obesity, race, ethnicity and sex on the incidence and control of adult-onset asthma. *Allergy, Asthma & Clinical Immunology*. 12/2016 2016;12(1):50. doi:10.1186/s13223-016-0155-8
34. Schatz M, Zeiger RS, Yang S-J, et al. Prospective Study on the Relationship of Obesity to Asthma Impairment and Risk. *The Journal of Allergy and Clinical Immunology: In Practice*. 07/2015 2015;3(4):560-565.e1. doi:10.1016/j.jaip.2015.03.017
35. Jamrozik E, Knuiman MW, James A, Divitini M, Musk AB. Risk factors for adult-onset asthma: A 14-year longitudinal study. *Respirology*. 08/2009 2009;14(6):814-821. doi:10.1111/j.1440-1843.2009.01562.x
36. Moshe S, Slodownik D, Yagev Y, et al. Atopy as a risk factor for the development of asthma in young recruits. *Journal of Asthma*. 2015-05-28 2015;52(5):453-457. doi:10.3109/02770903.2014.982287
37. Ardura-Garcia C, Stolbrink M, Zaidi S, Cooper PJ, Blakey JD. Predictors of repeated acute hospital attendance for asthma in children: A systematic review and meta-analysis. *Pediatric Pulmonology*. 09/2018 2018;53(9):1179-1192. doi:10.1002/ppul.24068
38. Buelo A, McLean S, Julious S, et al. At-risk children with asthma (ARC): a systematic review. *Thorax*. 09/2018 2018;73(9):813-824. doi:10.1136/thoraxjnl-2017-210939
39. Tinuoye O, Pell JP, Mackay DF. Meta-Analysis of the Association Between Secondhand Smoke Exposure and Physician-Diagnosed Childhood Asthma. *Nicotine & Tobacco Research*. 2013-09-01 2013;15(9):1475-1483. doi:10.1093/ntr/ntt033
40. Wang Z, May SM, Charoenlap S, et al. Effects of secondhand smoke exposure on asthma morbidity and health care utilization in children: a systematic review and meta-analysis. *Ann Allergy Asthma Immunol*. Nov 2015;115(5):396-401.e2. doi:10.1016/j.anai.2015.08.005

41. Van Meel ER, Den Dekker HT, Elbert NJ, et al. A population-based prospective cohort study examining the influence of early-life respiratory tract infections on school-age lung function and asthma. *Thorax*. 02/2018 2018;73(2):167-173. doi:10.1136/thoraxjnl-2017-210149
42. Zhang L, Zhang X, Zheng J, et al. Co-morbid psychological dysfunction is associated with a higher risk of asthma exacerbations: a systematic review and meta-analysis. *Journal of Thoracic Disease*. 06/2016 2016;8(6):1257-1268. doi:10.21037/jtd.2016.04.68
43. Luthe SK, Hirayama A, Goto T, Faridi MK, Camargo CA, Hasegawa K. Association Between Obesity and Acute Severity Among Patients Hospitalized for Asthma Exacerbation. *The Journal of Allergy and Clinical Immunology: In Practice*. 11/2018 2018;6(6):1936-1941.e4. doi:10.1016/j.jaip.2018.02.001
44. Tohidinik HR, Mallah N, Takkouche B. History of allergic rhinitis and risk of asthma; a systematic review and meta-analysis. *World Allergy Organ J*. Oct 2019;12(10):100069. doi:10.1016/j.waojou.2019.100069
45. Global strategy for asthma management and prevention (2007).
46. Tran NK, Lunn MR, Schulkey CE, et al. Prevalence of 12 Common Health Conditions in Sexual and Gender Minority Participants in the All of Us Research Program. *JAMA Netw Open*. Jul 3 2023;6(7):e2324969. doi:10.1001/jamanetworkopen.2023.24969
47. Veldhuis CB, George M, Everett BG, Liu J, Hughes TL, Bruzzese JM. The Association of Asthma, Sexual Identity, and Inhaled Substance Use among U.S. Adolescents. *Ann Am Thorac Soc*. Feb 2021;18(2):273-280. doi:10.1513/AnnalsATS.202001-062OC
48. National Heart L, and Blood Institute, U.S. Department of Health and Human Services,,. Expert Panel Report-4 (EPR-4) Working Group.
49. Dhippayom T, Wateemongkollert A, Mueangfa K, Im H, Dilokthornsakul P, Devine B. Comparative Efficacy of Strategies to Support Self-Management in Patients with Asthma: A Systematic Review and Network Meta-Analysis. Article. *Journal of Allergy and Clinical Immunology: In Practice*. 2022;10(3):803-814. doi:10.1016/j.jaip.2021.09.049
50. Hodkinson A, Bower P, Grigoroglou C, et al. Self-management interventions to reduce healthcare use and improve quality of life among patients with asthma: systematic review and network meta-analysis. Article. *BMJ (Clinical research ed)*. 2020;370:m2521. doi:10.1136/bmj.m2521
51. Salim H, Ramdzan SN, Ghazali SS, et al. A systematic review of interventions addressing limited health literacy to improve asthma self-management. Article. *Journal of global health*. 2020;10(1):010427. doi:10.7189/jogh.10.010428
52. Jeminiwa R, Garza KB, Chou C, Franco-Watkins A, Fox BI. Effects of Framed Mobile Messages on Beliefs, Intentions, Adherence, and Asthma Control: A Randomized Trial. Article. *Pharmacy*. 2024;12(1)doi:10.3390/pharmacy12010010
53. Kim SH, Park SH, Kang I, et al. Environmental management education using immersive virtual reality in asthmatic children in Korea: a randomized controlled study (secondary publication). *J Educ Eval Health Prof*. 2022;19:15. doi:10.3352/jeehp.2022.19.15
54. Fedele DA, Thomas JG, McConville A, et al. Using Mobile Health to Improve Asthma Self-Management in Early Adolescence: A Pilot Randomized Controlled Trial. *J Adolesc Health*. Dec 2021;69(6):1032-1040. doi:10.1016/j.jadohealth.2021.06.011
55. Rhee H, Love T, Wicks MN, et al. Long-term Effectiveness of a Peer-Led Asthma Self-management Program on Asthma Outcomes in Adolescents Living in Urban Areas: A Randomized Clinical Trial. *JAMA Network Open*. 2021;4(12):e2137492-e2137492. doi:10.1001/jamanetworkopen.2021.37492
56. Baptist AP, Hao W, Song PX, Carpenter L, Steinberg J, Cardozo LJ. A behavioral intervention can decrease asthma exacerbations in older adults. *Annals of Allergy, Asthma & Immunology*. 2020;124(3):248-248. doi:10.1016/j.anai.2019.12.015

57. Park HJ, Byun MK, Kwon JW, et al. Video education versus face-to-face education on inhaler technique for patients with well-controlled or partly-controlled asthma: A phase IV, open-label, non-inferiority, multicenter, randomized, controlled trial. *PLoS One*. 2018;13(8):e0197358. doi:10.1371/journal.pone.0197358
58. Kew KM, Flemyng E, Quon BS, Leung C. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev*. Sep 26 2022;9(9):Cd007524. doi:10.1002/14651858.CD007524.pub5
59. Bhattad PB, Pacifico L. Empowering Patients: Promoting Patient Education and Health Literacy. *Cureus*. Jul 2022;14(7):e27336. doi:10.7759/cureus.27336
60. Dineen-Griffin S, Garcia-Cardenas V, Williams K, Benrimoj SI. Helping patients help themselves: A systematic review of self-management support strategies in primary health care practice. *PLoS One*. 2019;14(8):e0220116. doi:10.1371/journal.pone.0220116
61. Chan A, De Simoni A, Wileman V, et al. Digital interventions to improve adherence to maintenance medication in asthma. *Cochrane Database Syst Rev*. Jun 13 2022;6(6):Cd013030. doi:10.1002/14651858.CD013030.pub2
62. Kandola A, Edwards K, Straatman J, Dührkoop B, Hein B, Hayes J. Digital Self-Management Platform for Adult Asthma: Randomized Attention-Placebo Controlled Trial. *J Med Internet Res*. Apr 29 2024;26:e50855. doi:10.2196/50855
63. Karakul A, Düzkaya DS, Bozkul G, Çapanoğlu M. The effect of mobile game training designed for asthmatic children on asthma management and quality of life. *J Pediatr Nurs*. May-Jun 2024;76:e149-e158. doi:10.1016/j.pedn.2024.02.025
64. Al Raimi AM, Chong MC, Tang LY, Chua YP, Al Ajeel LY. Effect of Health Education via Mobile Application in Promoting Quality of Life Among Asthmatic Schoolchildren in Urban Malaysia During the COVID-19 Era: A Quasi-experimental Study. *Comput Inform Nurs*. Sep 1 2022;40(9):648-657. doi:10.1097/cin.0000000000000927
65. Mitchell SJ, Rangel A, Klein EJ, et al. Sociodemographic Differences in Asthma Self-Management Knowledge of Parents Seeking Asthma Care for their Children in Pediatric Emergency Departments. *J Health Care Poor Underserved*. 2021;32(4):2191-2201. doi:10.1353/hpu.2021.0191
66. Lee JR, Leo S, Liao S, et al. Electronic adherence monitoring devices for children with asthma: A systematic review and meta-analysis of randomised controlled trials. *International Journal of Nursing Studies*. 2021;122:N.PAG-N.PAG. doi:10.1016/j.ijnurstu.2021.104037
67. Sobieraj DM, Weeda ER, Nguyen E, et al. Association of Inhaled Corticosteroids and Long-Acting β-Agonists as Controller and Quick Relief Therapy With Exacerbations and Symptom Control in Persistent Asthma: A Systematic Review and Meta-analysis. *Jama*. Apr 10 2018;319(14):1485-1496. doi:10.1001/jama.2018.2769
68. Bisgaard H, Le Roux P, Bjåmer D, Dymek A, Vermeulen JH, Hultquist C. Budesonide/formoterol maintenance plus reliever therapy: a new strategy in pediatric asthma. *Chest*. Dec 2006;130(6):1733-43. doi:10.1378/chest.130.6.1733
69. Crossingham I, Turner S, Ramakrishnan S, et al. Combination fixed-dose beta agonist and steroid inhaler as required for adults or children with mild asthma. *Cochrane Database Syst Rev*. May 4 2021;5(5):Cd013518. doi:10.1002/14651858.CD013518.pub2
70. Papi A, Chipps BE, Beasley R, et al. Albuterol-Budesonide Fixed-Dose Combination Rescue Inhaler for Asthma. *N Engl J Med*. Jun 2 2022;386(22):2071-2083. doi:10.1056/NEJMoa2203163
71. Chipps BE, Israel E, Beasley R, et al. Albuterol-Budesonide Pressurized Metered Dose Inhaler in Patients With Mild-to-Moderate Asthma: Results of the DENALI Double-Blind Randomized Controlled Trial. *Chest*. Sep 2023;164(3):585-595. doi:10.1016/j.chest.2023.03.035

72. Oba Y, Anwer S, Patel T, Maduke T, Dias S. Addition of long-acting beta2 agonists or long-acting muscarinic antagonists versus doubling the dose of inhaled corticosteroids (ICS) in adolescents and adults with uncontrolled asthma with medium dose ICS: a systematic review and network meta-analysis. Article. *Cochrane Database of Systematic Reviews*. 2023;2023(8)doi:10.1002/14651858.CD013797.pub2
73. Oba Y, Anwer S, Maduke T, Patel T, Dias S. Effectiveness and tolerability of dual and triple combination inhaler therapies compared with each other and varying doses of inhaled corticosteroids in adolescents and adults with asthma: a systematic review and network meta-analysis. *Cochrane Database Syst Rev*. Dec 6 2022;12(12):Cd013799. doi:10.1002/14651858.CD013799.pub2
74. Cividini S, Sinha I, Donegan S, et al. Best step-up treatments for children with uncontrolled asthma: a systematic review and network meta-analysis of individual participant data. Article. *European Respiratory Journal*. 2023;62(2)doi:10.1183/13993003.01011-2023
75. Beasley R, Harrison T, Peterson S, et al. Evaluation of Budesonide-Formoterol for Maintenance and Reliever Therapy among Patients with Poorly Controlled Asthma: A Systematic Review and Meta-analysis. Article in Press. *JAMA Network Open*. 2022;doi:10.1001/jamanetworkopen.2022.0615
76. Ahmad S, Kew KM, Normansell R. Stopping long-acting beta2-agonists (LABA) for adults with asthma well controlled by LABA and inhaled corticosteroids. *Cochrane Database Syst Rev*. Jun 19 2015;2015(6):Cd011306. doi:10.1002/14651858.CD011306.pub2
77. LaForce C, Chipps BE, Albers FC, et al. Albuterol/budesonide for the treatment of exercise-induced bronchoconstriction in patients with asthma: The TYREE study. *Ann Allergy Asthma Immunol*. Feb 2022;128(2):169-177. doi:10.1016/j.anai.2021.10.020
78. Bar-Yoseph R, Gur M, Zuckerman S, et al. Short- and long-term effects of fluticasone furoate/vilanterol in exercising asthmatic adolescents: A randomized and open label trial. *Basic Clin Pharmacol Toxicol*. Nov 2021;129(5):369-375. doi:10.1111/bcpt.13640
79. Eichenberger PA, Diener SN, Kofmehl R, Spengler CM. Effects of exercise training on airway hyperreactivity in asthma: a systematic review and meta-analysis. *Sports Med*. Nov 2013;43(11):1157-70. doi:10.1007/s40279-013-0077-2
80. Pearlman DS, Rees W, Schaefer K, Huang H, Andrews WT. An evaluation of levalbuterol HFA in the prevention of exercise-induced bronchospasm. *J Asthma*. Nov 2007;44(9):729-33. doi:10.1080/02770900701595667
81. Pearlman DS, van Adelsberg J, Philip G, et al. Onset and duration of protection against exercise-induced bronchoconstriction by a single oral dose of montelukast. *Ann Allergy Asthma Immunol*. Jul 2006;97(1):98-104. doi:10.1016/s1081-1206(10)61377-4
82. Hagan JB, Samant SA, Volcheck GW, et al. The risk of asthma exacerbation after reducing inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials. *Allergy*. Apr 2014;69(4):510-6. doi:10.1111/all.12368
83. Rank MA, Hagan JB, Park MA, et al. The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials. *J Allergy Clin Immunol*. Mar 2013;131(3):724-9. doi:10.1016/j.jaci.2012.11.038
84. Crossingham I, Evans DJ, Halcovitch NR, Marsden PA. Stepping down the dose of inhaled corticosteroids for adults with asthma. *Cochrane Database Syst Rev*. Feb 1 2017;2(2):Cd011802. doi:10.1002/14651858.CD011802.pub2
85. Obase Y, Ikeda M, Kurose K, et al. Step-down of budesonide/formoterol in early stages of asthma treatment leads to insufficient anti-inflammatory effect. *J Asthma*. Sep 2013;50(7):718-21. doi:10.3109/02770903.2013.795588

86. Rogers L, Sugar EA, Blake K, et al. Step-Down Therapy for Asthma Well Controlled on Inhaled Corticosteroid and Long-Acting Beta-Agonist: A Randomized Clinical Trial. *J Allergy Clin Immunol Pract*. Mar-Apr 2018;6(2):633-643.e1. doi:10.1016/j.jaip.2017.07.030
87. Kopsaftis Z, Yap HS, Tin KS, Hnin K, Carson-Chahhoud KV. Pharmacological and surgical interventions for the treatment of gastro-oesophageal reflux in adults and children with asthma. *Cochrane Database Syst Rev*. May 17 2021;5(5):Cd001496. doi:10.1002/14651858.CD001496.pub2
88. Mastronarde JG, Anthonisen NR, Castro M, et al. Efficacy of esomeprazole for treatment of poorly controlled asthma. *N Engl J Med*. Apr 9 2009;360(15):1487-99. doi:10.1056/NEJMoa0806290
89. Özbey Ü, Balaban S, Sözener Z, Uçar A, Mungan D, Mısırlıgil Z. The effects of diet-induced weight loss on asthma control and quality of life in obese adults with asthma: a randomized controlled trial. *J Asthma*. Jun 2020;57(6):618-626. doi:10.1080/02770903.2019.1590594
90. Sharma V, Ricketts HC, McCombie L, et al. A Total Diet Replacement Weight Management Program for Difficult-to-Treat Asthma Associated With Obesity: A Randomized Controlled Feasibility Trial. *Chest*. May 2023;163(5):1026-1037. doi:10.1016/j.chest.2023.01.015
91. Chauhan AJ, Brown TP, Storrar W, et al. Effect of nocturnal Temperature-controlled Laminar Airflow on the reduction of severe exacerbations in patients with severe allergic asthma: a meta-analysis. Article. *European Clinical Respiratory Journal*. 2021;8(1)doi:10.1080/20018525.2021.1894658
92. Fong WCG, Kadalayil L, Lowther S, et al. The efficacy of the Dyson air purifier on asthma control: A single-center, investigator-led, randomized, double-blind, placebo-controlled trial. *Ann Allergy Asthma Immunol*. Feb 2023;130(2):199-205.e2. doi:10.1016/j.anai.2022.10.010
93. Phipatanakul W, Koutrakis P, Coull BA, et al. Effect of School Integrated Pest Management or Classroom Air Filter Purifiers on Asthma Symptoms in Students with Active Asthma: A Randomized Clinical Trial. Article. *JAMA - Journal of the American Medical Association*. 2021;326(9):839-850. doi:10.1001/jama.2021.11559
94. Vesper SJ, Wymer L, Coull BA, et al. HEPA filtration intervention in classrooms may improve some students' asthma. Article. *Journal of Asthma*. 2023;60(3):479-486. doi:10.1080/02770903.2022.2059672
95. Leas BF, D'Anci KE, Apter AJ, et al. Effectiveness of indoor allergen reduction in asthma management: A systematic review. Article. *Journal of Allergy and Clinical Immunology*. 2018;141(5):1854-1869. doi:10.1016/j.jaci.2018.02.001
96. Kalayci O, Miligkos M, Pozo Beltrán CF, et al. The role of environmental allergen control in the management of asthma. *World Allergy Organ J*. Mar 2022;15(3):100634. doi:10.1016/j.waojou.2022.100634
97. Gent JF, Holford TR, Bracken MB, et al. Childhood asthma and household exposures to nitrogen dioxide and fine particles: a triple-crossover randomized intervention trial. Article. *Journal of Asthma*. 2023;60(4):744-753. doi:10.1080/02770903.2022.2093219
98. James C, Bernstein DI, Cox J, et al. HEPA filtration improves asthma control in children exposed to traffic-related airborne particles. *Indoor Air*. Mar 2020;30(2):235-243. doi:10.1111/ina.12625
99. Peytremann-Bridevaux I, Arditi C, Gex G, Bridevaux PO, Burnand B. Chronic disease management programmes for adults with asthma. *Cochrane Database Syst Rev*. May 27 2015;2015(5):Cd007988. doi:10.1002/14651858.CD007988.pub2

100. Mes MA, Katzer CB, Chan AHY, Wileman V, Taylor SJC, Horne R. Pharmacists and medication adherence in asthma: a systematic review and meta-analysis. *Eur Respir J*. Aug 2018;52(2)doi:10.1183/13993003.00485-2018
101. Griffiths C, Bremner S, Islam K, et al. Effect of an Education Programme for South Asians with Asthma and Their Clinicians: A Cluster Randomised Controlled Trial (OEDIPUS). *PLoS One*. 2016;11(12):e0158783. doi:10.1371/journal.pone.0158783
102. Grammatopoulou EPP, Skordilis EKP, Haniotou AMF, John ZM, Athanasopoulos SPP. The effect of a holistic self-management plan on asthma control. *Physiother Theory Pract*. Aug 2017;33(8):622-633. doi:10.1080/09593985.2017.1331479
103. Bereznicki BJ, Peterson GM, Jackson SL, Walters H, Fitzmaurice K, Gee P. Pharmacist-initiated general practitioner referral of patients with suboptimal asthma management. *Pharm World Sci*. Dec 2008;30(6):869-75. doi:10.1007/s11096-008-9242-3
104. Petkova VB. Pharmaceutical care for asthma patients: a community pharmacy-based pilot project. *Allergy Asthma Proc*. Jan-Feb 2008;29(1):55-61. doi:10.2500/aap2008.29.3083
105. Shelledy DC, Legrand TS, Gardner DD, Peters JI. A randomized, controlled study to evaluate the role of an in-home asthma disease management program provided by respiratory therapists in improving outcomes and reducing the cost of care. *J Asthma*. Mar 2009;46(2):194-201. doi:10.1080/02770900802610068
106. Szczepanski R, Jaeschke R, Spindler T, Ihorst G, Forster J. Preschoolers' and parents' asthma education trial (P2AET)--a randomized controlled study. *Eur J Pediatr*. Sep 2010;169(9):1051-60. doi:10.1007/s00431-010-1173-z
107. Tousman SA, Zeitz H, Bond D, et al. A Randomized Controlled Behavioral Trial of a New Adult Asthma Self-management Program. *Journal of Asthma & Allergy Educators*. 2011;2(2):91-96. doi:10.1177/2150129710395752
108. Sun HW, Wang JP, Wang SZ, et al. Effect of educational and psychological intervention on the quality of life of asthmatic patients. *Respir Care*. Jun 2010;55(6):725-8.
109. D.S A, Adepu R, Parthasarathi G, P A M. Impact of Community Pharmacist Provided Patient Education in Asthma Patients on Treatment Outcomes-A Study. *Indian Journal of Pharmaceutical Education and Research*. 04/01 2009;43:125-133.
110. Carson KV, Chandratilleke MG, Picot J, Brinn MP, Esterman AJ, Smith BJ. Physical training for asthma. *Cochrane Database Syst Rev*. Sep 30 2013;(9):Cd001116. doi:10.1002/14651858.CD001116.pub4
111. Flapper BC, Duiverman EJ, Gerritsen J, Postema K, van der Schans CP. Happiness to be gained in paediatric asthma care. *Eur Respir J*. Dec 2008;32(6):1555-62. doi:10.1183/09031936.00140407
112. Kew KM, Nashed M, Dulay V, Yorke J. Cognitive behavioural therapy (CBT) for adults and adolescents with asthma. *Cochrane Database Syst Rev*. Sep 21 2016;9(9):Cd011818. doi:10.1002/14651858.CD011818.pub2
113. Robinson PJ RJ. *Behavioral consultation in primary care: A guide to integrating service*. Springer; 2016. https://link.springer.com/book/10.1007/978-3-319-13954-8
114. Oei SM, Thien FC, Schattner RL, et al. Effect of spirometry and medical review on asthma control in patients in general practice: a randomized controlled trial. *Respirology*. Jul 2011;16(5):803-10. doi:10.1111/j.1440-1843.2011.01969.x
115. Murray C, Foden P, Lowe L, Durrington H, Custovic A, Simpson A. Diagnosis of asthma in symptomatic children based on measures of lung function: an analysis of data from a population-based birth cohort study. *The Lancet Child & Adolescent Health*. 10/2017 2017;1(2):114-123. doi:10.1016/S2352-4642(17)30008-1
116. Petsky HL, Cates CJ, Kew KM, Chang AB. Tailoring asthma treatment on eosinophilic markers (exhaled nitric oxide or sputum eosinophils): a systematic review and meta-analysis. *Thorax*. Dec 2018;73(12):1110-1119. doi:10.1136/thoraxjnl-2018-211540

117. Szefler SJ, Mitchell H, Sorkness CA, et al. Management of asthma based on exhaled nitric oxide in addition to guideline-based treatment for inner-city adolescents and young adults: a randomised controlled trial. *Lancet*. Sep 20 2008;372(9643):1065-72. doi:10.1016/s0140-6736(08)61448-8
118. Halterman JS, Fagnano M, Tajon RS, et al. Effect of the school-based telemedicine enhanced asthma management (SB-TEAM) program on asthma morbidity: A randomized clinical trial. Article. *JAMA Pediatrics*. 2018;172(3)doi:10.1001/jamapediatrics.2017.4938
119. Fiks AG, Mayne SL, Karavite DJ, et al. Parent-reported outcomes of a shared decision-making portal in asthma: a practice-based RCT. *Pediatrics*. Apr 2015;135(4):e965-73. doi:10.1542/peds.2014-3167
120. Smith JR, Noble MJ, Musgrave S, et al. The at-risk registers in severe asthma (ARRISA) study: a cluster-randomised controlled trial examining effectiveness and costs in primary care. *Thorax*. Dec 2012;67(12):1052-60. doi:10.1136/thoraxjnl-2012-202093
121. Halterman JS, Szilagyi PG, Fisher SG, et al. Randomized Controlled Trial to Improve Care for Urban Children With Asthma: Results of the School-Based Asthma Therapy Trial. *Archives of Pediatrics & Adolescent Medicine*. 2011-03-01 2011;165(3)doi:10.1001/archpediatrics.2011.1
122. Normansell R, Kew KM, Stovold E. Interventions to improve adherence to inhaled steroids for asthma. *Cochrane Database Syst Rev*. Apr 18 2017;4(4):Cd012226. doi:10.1002/14651858.CD012226.pub2
123. Tamblyn R, Ernst P, Winslade N, et al. Evaluating the impact of an integrated computer-based decision support with person-centered analytics for the management of asthma in primary care: a randomized controlled trial. *J Am Med Inform Assoc*. Jul 2015;22(4):773-83. doi:10.1093/jamia/ocu009
124. Agency for Health Research and Quality. The Effective Health Care Program stakeholder guide Appendix D: Research questions & PICO(TS) 2011. http://www.ahrq.gov/clinic/epcpartner/stakeholderguide/
125. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. *European Respiratory Journal*. 2020;55(1):1900588. doi:10.1183/13993003.00588-2019
126. Ram FS, Robinson SM, Black PN, Picot J. Physical training for asthma. *Cochrane Database Syst Rev*. Oct 19 2005;(4):Cd001116. doi:10.1002/14651858.CD001116.pub2