

Asthma Guidelines from the National Asthma Education and Prevention Program: Where Are We Now?

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The National Asthma Education and Prevention Program Guidelines for the Diagnosis and Management of Asthma were last published in 2007. New therapies and strategies for asthma management have been investigated in the last decade that merit evaluation and inclusion as revision to the guidelines. The National Heart, Lung, and Blood Institute initiated a process for an update on selected topics in 2014 with the final guideline update expected to be published by August 2019. Topics selected for update include the following: Systematic Review of Intermittent Inhaled Corticosteroids and of Long-acting Muscarinic Antagonists for Asthma; The Clinical Utility of Fractional Exhaled Nitric Oxide (FeNO) in Asthma Management; The Effectiveness of Indoor Allergen Reduction and the Role of Bronchial Thermoplasty in the Management of Asthma; and The Role of Immunotherapy in the Treatment of Asthma. The systematic reviews and meta-analyses of these topics will be published in peer-reviewed journals in 2018.

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A COMPLETE UPDATE of the National Asthma Education and Prevention Program Guidelines for the Diagnosis and Management of Asthma was last published in 2007 as the Expert Panel Report 3 (EPR-3).¹ Since that time, clinical practice strategies have changed, and new drugs have been approved for marketing by the Food and Drug Administration rendering the current guidelines as suboptimal. Over the next few issues in this column, Pharmacotherapy Update, the latest updates to the guidelines will be reviewed. This present publication will provide the background for the evolution of the guidelines and an introduction to the topics, which will be reported on in upcoming issues.

The National Asthma Education and Prevention Program (NAEPP) of the National Heart, Lung, and Blood Institute (NHLBI) comprises many national level organizations, professional societies, lay voluntary and patient groups, and federal agencies.¹ The NAEPP convenes the Expert Panel that prepares the guidelines and initially began developing science-based guidelines shortly after inception in 1989.² This initial panel was composed of asthma specialists from clinical care, research, academia, and representatives of other organizations and federal agencies that were invested in strategies for asthma management. These initial guidelines, developed through expert consensus, were published in 1991.³

The second review began in 1995, and a complete update to the guidelines was published in 1997 (EPR-2).^{4,5} To keep the guidelines dynamic, the NAEPP determined that review and publication of selected questions based upon published research activity or concerns and controversies of clinical practice would be an efficient process for guideline update.⁵ In 2002, the “Update on Selected Topics 2002” was published and centered on long-term asthma management that included medication use, monitoring, and prevention, with a focus on controller therapy in children.⁶ This update was the first to use the Agency for Healthcare Research and Quality (AHRQ) Evidence-Based Practice Center (EPC) (awarded to Blue Cross and Blue Shield Association Technology Evaluation Center) process to conduct a systematic review of the evidence and for the EPR to include the level of evidence (A, B, C, or D) to justify the recommendations in the EPR-2 guideline update.⁵

The process for another complete update to the guidelines was initiated in 2004, which used the EPR-2 and Update on Selected Topics 2002 as the framework to strategize the literature update. After an iterative process that included multiple EPR panel, consultant, and public comments review, the EPR-3 guidelines were published in 2007.¹ As in the Update on Selected Topics 2002, the EPR-3 included level of evidence

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(A, B, C, or D), but now also included strength of the recommendation that was based upon the EPR expertise that determined whether the clinical practice is “recommended” or “should/may be considered” or “is desirable.”¹ In 2007, the first Guideline Implementation Panel (GIP) was established to review implementation strategies and prepare recommendations, which would enhance dissemination and adoption of the guidelines.^{7,8}

Many organizations suggest that, in general, guidelines should be reviewed for updates at least every 5 years to avoid obsolescence.^{9,10} As such, the NAEPP agreed that the EPR-3 asthma guidelines should be reviewed, but with a focus on selected topics every 2 to 3 years rather than an update of the guidelines in their entirety.⁸ In this way, the NAEPP envisioned that the guidelines would exist as a “living document,” in which the updates reflect priority topics that would be of clinical relevance.

Thus, this next guideline iteration began with NHLBI posting NOT-HL-14-203 “Request for Information (RFI): Topics to be Considered for Systematic Reviews and a Possible Update to Clinical Practice Guidelines for the Management of Asthma” with responses to be received by March 2014. In April 2014, an Asthma Expert Working Group established by NHLBI met to determine if and which topics warranted an update to EPR-3. This Asthma Expert Working Group was composed of members from the 2007 Expert Panel, NAEPP Coordinating Committee, GIP, National Asthma Control Program Projects members, and the public. The need for updates was based primarily upon 2 objectives: (1) whether there was sufficient new evidence to warrant a systematic literature review to inform a revision, and (2) whether there is a potentially high significance or large impact of a topic on asthma management. The Asthma Expert Working Group was asked to identify the 5 highest priority topics and the specific questions that should be asked for each topic for update. The specific questions associated with each topic were identified by the Asthma Expert Working Group using an evidence-based decision-making process, PICO (P, patient population of interest; I, intervention or variable of interest; C, comparison; O, outcome of interest).

In addition to the highest priority topics, the Asthma Expert Working Group also identified topics that should be acknowledged in an update but did not warrant a systematic review because they were either an emerging topic of strong interest with ongoing scientific investigations, but insufficient published literature to support review, or the topic required only a concise amendment to clarify an existing statement due to questions raised in the needs assessment by the Asthma Expert Working Group (Table 1).⁸ The topic areas identified for systematic review were as follows: (1) Role of Adjustable Medication Dosing in Recurrent Wheezing and Asthma; (2) Role of Long-Acting Antimuscarinic Agents (LAMAs) in Asthma Management as Add-on to inhaled corticosteroid (ICS); (3) Role of Bronchial Thermoplasty in Adult Severe Asthma; (4) Role of Fractional exhaled Nitric Oxide (FeNO) in Diagnosis, Medication Selection, and Monitoring Treatment Response in Asthma; (5) Role of Remediation of Indoor Allergens (e.g., House Dust Mites/Animals/Pests) in Asthma Management; and (6) Role of Immunotherapy in Treatment of Asthma.⁸

Systematic reviews and meta-analyses were performed by AHRQ EPCs, which were selected by competitive application. The process for the systematic reviews included the following: (1) Prepare and develop the topic (identify key

TABLE 1. TOPICS FOR ACKNOWLEDGMENT IN AN UPDATE, BUT NOT SYSTEMATIC REVIEW

<i>Emerging topic</i>	<i>Topics for concise amendment</i>
• Asthma heterogeneity • Biomarkers (other than FeNO) • Classifying asthma severity • Biologics • Prevention of asthma onset • Adherence • Step down from combination (ICS plus LABA) therapy • Role of community health workers in asthma management	• Medication charts-removal • Medication charts-addition • Stepwise approach-clarification

ICS, inhaled corticosteroid; LABA, long-acting beta₂-agonist.

questions and inclusion/exclusion criteria; develop the analytic framework); (2) Conduct literature search (identify study eligibility criteria, search for studies, and select evidence for inclusion in analyses); (3) Extract data from published and unpublished studies; (4) Analyze and synthesize studies (assess quality and applicability of individual studies, synthesize quantitative data, and grade strength of evidence); (5) Report systematic review (peer review and public comment and publish final review); and (6) Identify gaps in knowledge and future needs.

The protocols were developed by the EPCs and a Technical Expert Panel (five to eight members with expertise in content and methodology), and consultants selected by the EPC guided the evidence review process. The protocols and summary reports prepared by the EPCs were previously posted for public comment on the AHRQ website. The final documents (Systematic Review of Intermittent Inhaled Corticosteroids and of Long-acting Muscarinic Antagonists for Asthma; The Clinical Utility of Fractional Exhaled Nitric Oxide (FeNO) in Asthma Management; The Effectiveness of Indoor Allergen Reduction and the Role of Bronchial Thermoplasty in the Management of Asthma; and The Role of Immunotherapy in the Treatment of Asthma) will be published in peer-reviewed journals in 2018.

What are the next steps? In August 2015, the NAEPP Coordinating Committee was chartered as a federal advisory committee (governed by the provisions of the Federal Advisory Committee Act, FACA) in accordance with 424B of the Public Health Service Act, 42 U.S.C. 285b-7b, as amended. The NAEPP FACA committee consists of 15 members with diverse expertise and will advise NHLBI and other federal agencies on matters relating to asthma. This committee will continue to partner with major medical associations, voluntary health organizations, and community programs to fulfill the mission of educating patients, health professionals, and the public. Additional working groups may be established by the NAEPP FACA and currently includes the Expert Panel Working Group. The Expert Panel Working Group will update the selected topics of EPR-3 by developing a plan for the guideline update, create a draft guideline update, seek peer and public review, and revise the guideline for publication. These steps are expected to be completed by August 2019. In future issues of this journal, more detailed discussion on the new recommendations will be provided when updates are available.

In summary, the process for updating the EPR-3 guidelines began in early 2014 and is expected to be finalized by August 2019. Peer-reviewed publications of the selected topics will be available in 2018.

Author Disclosure Statement

Kathryn Blake, PharmD served as a paid consultant to the EPC for the topic “Systematic Review of Intermittent Inhaled Corticosteroids and of Long-acting Muscarinic Antagonists for Asthma.” Dr. Blake has also been a member of the NAEPP Coordinating Committee since 2005.

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