



Asthma and Allergy
Foundation of America

January 17, 2020

Susan T. Shero, RN, MS
Executive Secretary
NAEPPCC
NHLBI, NIH
6701 Rockledge Blvd., Room 9182
Bethesda, MD 20892

Subject: Update on Selected Topics in Asthma Management 2020: A Report from the Expert Panel Report-4 (EPR-4) Working Group

Dear Ms. Shero,

Thank you for the opportunity to review and provide feedback on the Expert Panel Report-4, (EPR-4). The Asthma and Allergy Foundation of America's (AAFA) feedback is attached. Additionally, AAFA has signed on to the response letter submitted by Health Resources in Action.

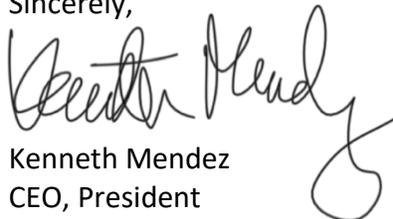
The most significant change in the guidelines is the use of ICS/formoterol as a rescue medication, which puts us in line with GINA guidelines. We ask that you please consider how this recommendation can be highlighted since it will change clinical practice in the United States.

We are concerned that the "conditional" recommendations offer weak guidance that will more than likely not impact clinical practice. Because there is not strong evidence for a recommendation, we ask that the recommendation be removed from the report.

We would like to acknowledge and thank the Workgroup for their hard work on updating the Guidelines. We are looking forward to the final report.

AAFA would welcome the opportunity to discuss our feedback and next steps. Please feel free to contact me at Kmendez@aafa.org or 202-947-1231, ext. 233.

Sincerely,



Kenneth Mendez
CEO, President



Asthma and Allergy Foundation of America

Effectiveness of Indoor Allergen Reduction in Management of Asthma

Comparative Effectiveness Review Number 201

The Asthma and Allergy Foundation of America (AAFA) recommends that Six Priority Action Steps outlined in EPR-3, including “Control environmental exposures that worsen the patient’s asthma” remain a priority in EPR-4. Reducing allergens and irritants in the home is a strategy to address asthma in those who are disproportionately impacted by the disease.

The rates of hospitalizations and deaths due to asthma are both three times higher among African Americans than among whites¹, with Puerto Ricans having the highest rates of asthma attacks and deaths due to asthma.² The percentage of people with asthma taking daily medicine to control asthma is lower among Hispanics (23.2%) and African Americans (25.1%) than among Whites (35.1%).³

Communities of color are disproportionately impacted by asthma and may not have access to allergy testing, or even a medical home. They are more likely to live in substandard housing which has a negative impact on their health⁴. In order to address the social determinates of health, interventions need to happen in the home. Low-cost allergen mitigation strategies are the first line of defense to reduce environmental triggers. *Controlling environmental exposures that worsen the patient’s asthma* is one of the Six Priority Action Steps in EPR-3⁵, and should remain a priority in EPR-4.

Implementation Guidance, page 35, line 1335

In Adults and children with asthma, we recommend skin testing (preferred) or in vitro antigen specific IgE testing to determine allergic sensitization along with thorough history of possible environmental allergens triggers even if testing is negative.

¹ Centers for Disease Control and Prevention. Asthma prevalence, health care use and mortality: United States, 2003-05.

² Heron MP, Hoyert DL, Murphy SL, Xu JQ, Kochanek KD, Tejada-Vera B. Deaths: Final Data for 2006. National vital statistics reports; vol 57 no 14. Hyattsville, MD: National Center for Health Statistics. 2009.

³ Chevarley, F.M. Asthma Preventive Medicine in 2006—Who Takes Them? Statistical Brief #237. March 2009. Agency for Healthcare Research and Quality, Rockville, MD.

⁴ Jacobs DE. Environmental health disparities in housing. Am J Public Health. 2011;101 Suppl 1(Suppl 1):S115–S122. doi:10.2105/AJPH.2010.300058

⁵ . Guidelines for the diagnosis and management of asthma. Bethesda (MD): National Institutes of Health; National Heart, Lung, and Blood Institute; April 1997. NIH publication no. 97-4051.



Since there are disparities in who has access to allergen skin (or in vitro) testing, EPR-4 should include guidance on mitigation strategies to clinicians and families if skin testing is not possible.

What Clinicians Should Discuss with Patients, page 36, line 1359

AAFA surveyed the asthma and allergy physicians that serve on its Medical Scientific Council. One hundred percent (100%) of respondents (n=5) say they “often” or “always” recommend dust mite reduction strategies to their patients who are dust mite sensitive. Clinicians should continue to follow the guidelines in EPR-3 Six Priority Action Steps to help patients reduce environmental factors that trigger asthma.

Single Allergen Mitigation Interventions, page 37, line 1381

There is mixed scientific evidence to support a recommendation against dust mite allergen mitigation interventions. AHRQ’s evaluation of this area was weak and called for more research. There’s no strong evidence to abandon prior practice from EPR-3. We are asking the Workgroup not to abandon the previous guideline without better research.

The studies reviewed in EPR-4 did show there is limited data providing evidence for single use mitigation strategies to reduce allergens. Additionally, many of the studies referenced in the Report looked at individuals who were sensitized to various allergens, but the studies did not demonstrate that the subjects were allergic (i.e., symptomatic when exposed to the allergen). Without knowing if the subjects are truly allergic to the allergen, it is hard to determine if the allergen reduction strategies were effective or ineffective.

Sensitization (i.e., positive skin or blood test) does not equal “allergy,” and there is no way to determine a true “allergy” in those sensitized, which makes finding studies that show an effect problematic. AAFA recommends the use of dust mite reduction strategies (encasings and washing bedding) in those sensitized but acknowledges that some of these patients will not see a benefit. Erring on the side of abatement does not have a negative impact on an individual’s asthma and overall health.

There is still strong scientific evidence to use dust mite covers to reduce emergency room visits, even as a single component intervention. In 2017, Murray et al⁶ “*Preventing Severe Asthma Exacerbations in Children. A randomized Trial of Mite-Impermeable Bedcovers*” concludes that a “simple and relatively cheap intervention of mite allergen—impermeable bed encasings...is effective in reducing emergency hospital attendance with severe asthma exacerbations.”

AAFA surveyed its asthma and allergy patient community to ask those who use protective bed coverings how effective they are in reducing symptoms. Out of the patients who responded

⁶ Murray CS, Foden P, Sumner H, Shepley E, Custovic A, and Simpson A, Preventing severe asthma exacerbations in children. A randomized trial of mite-impermeable bedcovers. *Am J Respir Crit Care Med* 2017;196:150-8



(N=35) 83% stated they used coverings to reduce dust mite exposure, and (n=29) 55% stated the coverings were either very or somewhat effective.

Variability in the quality of bed coverings may also impact reported outcomes. There are currently no federal standards for the permeability of textiles that claim to prevent dust mite transfer. Due to the lack of federal guidelines, the Asthma and Allergy Foundation of America has adopted standards for fabric performance and evaluated the effectiveness of various bedding products to form an effective barrier to the passage of allergen.

Multicomponent Mitigation Interventions, page 38, line 1409

A multicomponent allergen reduction intervention will also address additional triggers in the home, such as irritants like secondhand smoke. Even though inhaled irritants were not in the scope of this Report, reducing irritants as part of the *controlling environmental triggers that worsen the patient's asthma* as recommended in EPR-3 will benefit individuals living with asthma and others that live in the household.

Please see AAFA's original response on the *Effectiveness of Indoor Allergen Reduction in Management of Asthma* previously submitted at the end of this document. We respectfully support and encourage additional research on the effectiveness of single and multicomponent allergen reduction methods.

Intermittent Inhaled Corticosteroids and Long-Acting Muscarinic Antagonists for Asthma

Recommendation #10, Implementation Guidance, page 50, line 1654

AAFA asks the NAEPP to develop a robust educational program for providers and patients, as clinicians and educators will be responsible for helping recalcitrant patients to this major change in medication recommendations and raise their comfort level in using the SMART regimen.

AAFA surveyed its asthma patient community to ask about their comfort regarding taking controller medication as rescue/reliever medication. Out of the patients who responded (n=43), 91% are taking both long-term controller and quick-relief medications. Of those taking both medications, 71% stated they felt not comfortable at all or somewhat uncomfortable using "ICS therapy as rescue medications". While we acknowledge this question was a bit misleading (since the proposed guidelines would use ICS + reliever as the as-needed therapy), it does demonstrate the potential resistance from patients. Clinicians and educators will be responsible for helping patients understand this major change in medication recommendations and help raise their comfort level in taking ICS on an as needed basis with a short acting bronchodilator. And we encourage the NAEPP to develop a robust and comprehensive educational program for both providers and patients around this issue.



Recommendation #12, page 54, line 1774

It is critical that the Workgroup provides guidance on how clinicians can provide education to patients on using ICS/formoterol as both a daily control and quick-relief therapy, or the Single Maintenance and Reliever Therapy (SMART). AAFA surveyed its asthma patient community to ask about their comfort regarding taking controller medications as rescue medication. Out of the patients who responded (n=43), 91% are taking both long-term controller and quick-relief medications. Of those taking both medications, 71% stated they felt not comfortable at all or somewhat uncomfortable using “ICS therapy as rescue medications”. Similar to our concerns for recommendation #10 (and with the same limitations regarding the survey question), we are concerned that patients will be resistant to SMART therapy due to many years of being educated on the difference between controller and reliever medications. Now with SMART therapy they will have to become comfortable using a single device for both control and relief.



Previously Submitted Comments

Comments on Allergen Reduction Section of Draft Asthma Guidelines

Table i. Recommendation #5

Current recommendation as written is unclear when stating “no specific identified triggers or exposures.” As written, this recommendation could be misread and seems to contradict. Lines 546-557 “Assess Environmental Factors and Provide Education (all steps)”. Lines 547-549 are clear and specific: “Environmental control is a cornerstone of asthma management. Some individuals may have an allergic component to their asthma, therefore, it is important to take a history of environmental allergen exposure and consider testing for specific allergen sensitization, when appropriate. Clinicians are encouraged to determine which allergens individuals are exposed and sensitized to and then consider interventions to mitigate those allergens.”

Consider changing language in Recommendation #5 and include guidance from lines 547-557 as follows:

In adults and children with asthma *who have had skin testing (preferred) or in vitro antigen specific IgE testing and the testing results show no specific allergic sensitization, identified trigger, or exposures*, we conditionally recommend against allergen mitigation intervention as part of routine asthma management. *If the individual has not been tested, we recommend skin testing (preferred) or in vitro antigen specific IgE testing to determine allergic sensitization as cornerstone of asthma management to determine which allergens individuals are exposed and sensitized to and then consider interventions to mitigate those allergens.*

Or consider adding more specific guidance: in “Allergen Reduction” section:

- In Adults and children with asthma, we recommend skin testing (preferred) or in vitro antigen specific IgE testing to determine allergic sensitization along with thorough history of possible environmental allergens triggers even if testing is negative.

Then continue with Recommendation #5 as edited below:

- In adults and children with asthma *who have had skin testing (preferred) or in vitro antigen specific IgE testing and the testing results show no specific allergic sensitization, identified trigger, or exposures*, we conditionally recommend against allergen mitigation intervention as part of routine asthma management.

Table i. Recommendation #8

Delete and keep 2007 EPR-3 guideline. There’s still strong scientific evidence to use dust mite covers to reduce emergency room visits. In 2017. Murray et al²² “Preventing Severe Asthma Exacerbations in Children. A randomized Trial of Mite-Impermeable



Bedcovers” concludes that a “simple and relatively cheap intervention of mite allergen—impermeable bed encasings...is effective in reducing emergency hospital attendance with severe asthma exacerbations.” There’s mixed scientific evidence to support a recommendation against dust mite allergen mitigation intervention. The Agency for Healthcare Research and Quality’s (AHRQ) evaluation of this area was weak and called for more research. There’s no strong evidence to abandon prior practice from EPR-3. Don’t abandon previous guideline without better research.

The literature to support dust mite intervention for asthma control is extensive.¹⁴⁻²⁰

Nonintervention studies show correlations between antigen levels and clinical markers of disease severity.⁴ Custovic et al¹ described a correlation between mite exposure, methacholine reactivity, and decreased FEV₁ in adults. Chan-Yeung et al² noted that dust mite-sensitive asthmatic children showed a positive relationship of mean daily symptom score to total mite allergen level and a negative relationship of daily mean PEFr to dust mite level. Sensitization to dust mites has been associated with acute childhood asthma requiring emergency treatment.⁴

Australian investigators have Reported that changes in allergen concentration in bedding were significantly correlated with bronchial hyperresponsiveness to histamine and to symptom scores.¹⁶ European investigators have documented the value of impermeable mattress covers combined with use of filters in improving bronchial hyperresponsiveness.¹⁷

These more recent studies reinforce other trials from the last decade. Murray and Ferguson¹⁹ studied asthmatic children in dust-free bedrooms that included impermeable covers for pillows, mattress, and box spring; no carpets; and limited toys. Children living in these special rooms compared with children living in standard bedrooms showed fewer days of wheezing, fewer days requiring medication, and fewer days with abnormal peak flow rates. Walshaw and Evans²⁰ evaluated adult asthmatic subjects and compared those living in bedrooms with special bed covers, weekly laundered bedding, and cleaned or removed carpeting and upholstery with those living in standard bedrooms. Patients with aggressive environmental control had significant improvement in the FEV₁ /forced vital capacity ratio, PEFr, and bronchial hyperresponsiveness (histamine), but not FEV₁, compared with the standard group.

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