



Dr. Stukus: Hello, and welcome to Conversations From the World of Allergy, a podcast produced by the American Academy of Allergy, Asthma & Immunology. I'm your host, Dave Stukus. I'm a Board-certified allergist and immunologist and serve as the social media medical editor for the Academy. Our podcast series-- we use different formats to interview thought leaders from the world of allergy and immunology. This podcast is not intended to provide any individual medical advice to our listeners. We do hope that our conversations provide evidence-based information. Any questions pertaining to one's own health should always be discussed with their personal physician. The Find An Allergist search engine <http://allergist.aaaai.org/find/> on the Academy website is a useful tool to locate a listing of board certified allergists in your area. Finally, use of this audio program is subject to the American Academy of Allergy, Asthma & Immunology Terms Of Use agreement which you can find at www.aaaai.org.

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[2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group](#)

Dr. Cloutier: Thank you very much, Dave. I appreciate your invitation.

Dr. Stukus: Yes, I think this is going to be great. And before we discuss the details of the 2020 Asthma Guidelines, I think it would be useful for our listeners to learn a little bit about the background behind the NHLBI Asthma Guidelines. Are you able to offer us just a brief historical overview of what goes into this?

Dr. Cloutier: Certainly. So it's pretty hard to believe, actually, but almost thirty years ago, the first Asthma Guidelines were released by the National Heart, Lung, and Blood Institute. These guidelines were subsequently updated twice, and then, back in 2002, there was an update to them. But this is the first update to the guidelines in the past thirteen years. And what's amazing about the guidelines from a historical perspective is that, in 1991, when we first recognized, in the very first guidelines, that asthma was a chronic inflammatory disease, and recommended corticosteroid therapy for the treatment of asthma, and, since then, we've seen this evolution in terms of our understanding of the disease, our approach to managing asthma, and all of this effort and work has resulted in the Selected Topics Update to the Guidelines in 2020.

Dr. Stukus: This work group that you chaired for the creation of the newest Asthma Guidelines, I notice, is very large and diverse. Can you give us some insight in regards to just the process to select members and what kind of background they come from?

Dr. Cloutier: Certainly. The important thing about the expert panel that wrote these guidelines is that they do represent a diverse group of individuals. So there are asthma contents experts-- both the pediatric as well as adult, emergency care physicians, primary care clinicians, pediatricians, and internists, as well as healthcare policy individuals, and implementation and dissemination individuals. So that what NHLBI did, and, in particular, the NAEPP Coordinating Committee did, was to create a group of people who could address asthma at multiple levels. In addition, I want to mention one other component of the guidelines, and that was patient engagement and involvement. What we did was we held a series of focus groups, interviews, and discussions with a wide-ranging number of individuals representing different aspects of asthma care-- so individuals with asthma, caregivers, etc.-- to discuss various components of the updates and to obtain the patient perspective relative to these updates. And that's especially important given the methodology that we used in developing the guidelines.

Dr. Stukus: That's really fascinating, to include that aspect of it, and I think that lends into the next question that I have for you. I'm sure a lot of listeners weren't aware of that aspect of it and the diverse group of-- and large group of members of the expert panel, but I'm sure a lot of our listeners do have the next question of: why is there such a long lag in between the updates of the NHLBI Asthma Guidelines? It's been thirteen years since the last one was published. I suspect it has something to do with what you just described but take us behind the scenes as to why it takes so long.

Dr. Cloutier: Well, some of it just has to do with funding and resources. The bottom line, right? You need the money and you need the resources to do this. In addition, NHLBI, to their credit, and I think this really is to their credit, wanted to develop a guideline that was heavily and strongly evidence-based, used the best current science, would be guidelines that individuals could trust, and, as such, this sort of process takes a fair amount of time. It takes time to develop, first of all, what areas are you going to look at? What are the important questions you want to ask? And to do that, NBHLBI and the advisory council of the

National Heart, Lung, and Blood Institute, conducted a national needs assessment, and so got input from many, many different groups-- patients, as well as non-profit organizations interested in asthma, professional societies, specialists, primary care clinicians. And so they used that information to decide what areas were they going to update. Once they decided on what areas, the key questions relative to those areas were then developed. What is it that you want to know specifically about that topic? And so all of that was done a priori, as opposed to sort of saying, "Let's look and see what's been published the last couple of years, and let's decide to update in those specific areas." So it's just a different approach. One isn't bad; one isn't good. It's just different. But that takes time. And then you have the Agency for Healthcare Research and Equality, and their evidence practice centers were contracted to conduct the systematic reviews. And the systematic reviews, again, were not timed for a one-year lookback or a two-year lookback, but most of them were from the inception of the database moving forward. So they tried to capture all of the literature related to the specific topics. Then-- go ahead.

Dr. Stukus: Oh, no. Please. This is fascinating.

Dr. Cloutier: Then that information was used by the expert panel to determine sort of the certainty of the evidence, the quality of the evidence, and to make recommendations. And the process that the expert panel used is a process called GRADE, which stands for grading of recommendations, assessment, development, and evaluation. And what is especially important about using GRADE is that it provides-- it's very strongly evidence-based, but it comes at the recommendations from a patient perspective, which is why those patient focus groups were so very important. Because it's that information that then gets incorporated into making the recommendations. And unlike-- and I think this is true. I could be wrong about that. But unlike any of the other sorts of systems for evaluating evidence, both the benefit as well as the harm of an intervention, as well as patient preferences and beliefs, are incorporated into the recommendations.

Dr. Stukus: Did prior iterations of the Asthma Guidelines from the NHLBI incorporate the GRADE process or is this the first time?

Dr. Cloutier: This is the first time that we have used GRADE.

Dr. Stukus: Now that background is really, really fascinating on so many levels. That just gives tremendous insight as to what a massive operation this is and why it just takes time to do this in the manner that it was done. And this is in comparison to the Global Initiative for Asthma, which is also known as GINA, where they tend to update their asthma guidelines annually. Is there any collaboration between GINA and the NHLBI, or do you operate in different silos in regards to the development of guidelines?

Dr. Cloutier: Well, I think we have different perspectives, and we use different methods and approaches. So GINA really looks at it from a global perspective, whereas the 2020 Asthma Guidelines Update uses a United States perspective. So we have some differences there. We also have some differences in definitions and differences in methodologies. And each of those differences results in different strengths. GINA is able to be very agile. They look at the literature for the past year, year and a half, decide what new work has been published in the area of asthma, and then update their document with that new

information. They are not a guideline, per se, and I think they actually go out of their way to say that they're not a guideline. Whereas this approach was not meant to be all-encompassing, which is a weakness of the NAEPP Asthma Guidelines. It is a selected topics update, and it's based upon areas where there were felt to be significant advances that warrant a very careful and systematic review. So they have different uses, different backgrounds, different methodologies. I-- well, I'm going to leave it at that.

Dr. Stukus: No, it's great. Because they are very different in many ways, and I love how you phrase this of, you know, it's not right or wrong. It's just a different way of approaching things. You gave us such great background into this iteration, the 2020 Asthma Guideline Update, incorporating systematic reviews and really taking a deep, deep dive into specific topics. And I would love to hear-- how the heck did you decide what areas to focus on and which questions to try and answer?

Dr. Cloutier: Yes, so all of that work-- all of the work relative to the conflicts and the key questions was actually determined before the expert panel was configured. And, again, deciding what topics to update was based on a national needs assessment. And there were, in this needs assessment-- there were eighteen topics that came up for thought relative to revising. Eleven of them were decided not to be included in the update either because there was no new or significant information available in the specific area or the topic was considered important, but not enough new evidence, and specifically this addresses the issue of biologics and biologic therapy. So when the needs assessment was conducted and completed, and the decision was made relative to the topics chosen, there was only one asthma biologic available on the market, and that was omalizumab. And it was felt that the asthma biologics were just, at the time-- and this is back, now, in 2015, were, at the time, not ready for updating. No one predicted-- in that group, no one predicted that there would be such an explosion of asthma biologic therapy in the interim period. And when the expert panel met, we discussed at great lengths our desire, our strong desire, to include asthma biologics. But to do that and to use the GRADE methodology would have required a new systematic review and all of the sort of steps beyond that systematic review and would have delayed the release of these guidelines for probably another year. And so the decision was made to not include the biologics. And I think, again, it was a reasonable decision to make at the time, but clearly it's an important gap in the update.

Dr. Stukus: So, in essence, you're at the mercy of the peer-reviewed, published evidence to date when you decide on what topic to investigate. For the listeners out there who have not participated in this sort of analysis before, it can be a never-ending process, right? Where, once you get started, new publications come out, and new publications come out, and new questions get raised, but, at some point, you just have to commit to it and get the work done. Do you think that's a fair assessment?

Dr. Cloutier: Yes, absolutely. What we did was-- the expert panel itself updated the systematic reviews through October of 2018. So this update includes that literature through October of 2018.

Dr. Stukus: Okay. Well, with that tremendous background, if it's okay with you, I'd really like to take a deep dive into each of the areas to allow for you to provide some context and practical advice surrounding each one of them. And I would say let's just go in order of the guidelines and start with the

role of immunotherapy in the treatment of asthma. But before we even get into that, help us understand: how do inhalant allergens and allergies actually relate to asthma?

Dr. Cloutier: So clearly-- and, Dave, you're the expert on this. But clearly there are individuals who, upon exposure to different inhalants, develop an allergic response, that is a response mediated by allergen-specific IgE and often eosinophilic inflammation. And for these individuals, after sensitization to a specific aero-inhalant, subsequent exposures can result in symptoms of rinoconjunctivitis, but also symptoms associated with asthma, such as coughing, wheezing, or shortness of breath. And so, for some individuals, not all, but some individuals-- and, in fact, you might say many individuals-- aero-allergens may play a role in their asthma.

Dr. Stukus: And along those lines, help us better understand the role of immunotherapy, and are there various types of immunotherapy that were evaluated specifically as part of the systematic review?

Dr. Cloutier: So immunotherapy-- and I am clearly not an expert in immunotherapy-- but immunotherapy is one of the few therapeutic options that actually is capable of modulating the IgE response. And the 2020 Asthma Guideline Update looked at two different forms of immunotherapy, namely subcutaneous immunotherapy, in which small amounts of an allergen to which an individual is sensitized and symptomatic upon exposure-- an individual is exposed to increasing amounts of that allergen through allergy shots and, as a result of that, increasing exposure develops tolerance to the specific allergens. And the second type, which also works in a similar way, is sublingual therapy. And sublingual therapy is exactly as it sounds. It's either in a tablet form or in drop form for individuals who are sensitized to specific allergens.

Dr. Stukus: I think it's fantastic that both subcutaneous and sublingual immunotherapy were evaluated as part of the review. And help us out. So what did you find? What are the take-home messages regarding immunotherapy and asthma according to the 2020 Asthma Guidelines?

Dr. Cloutier: So what the guidelines recommend is that, in individuals who are five years and up who have mild to moderate allergic asthma, subcutaneous immunotherapy is recommended. It is a conditional recommendation. I'll explain that in a minute. In addition to, or as an adjunct to standard pharmacotherapy. There are some important sorts of-- not caveats but some important considerations relative to subcutaneous immunotherapy. So the first is that it's really recommended in individuals who are sensitized either by allergy skin tests or by allergen-specific IgE to a specific allergen. It's recommended that therapy be implemented both during the initiation phase as well as during the build-up phase and the maintenance phase. Be administered when their asthma is under control, so you don't-- and the reason of this-- it's just in place to decrease the risks of adverse effects, most of which occur within thirty minutes after administration. It's recommended that it be administered in the clinician's office and not at home. And there is a suggestion that individuals receiving this therapy should have access to subcutaneous epinephrine. The latter is an opinion of the expert panel.

Dr. Stukus: Okay. So bottom line: for those folks who are deemed allergic and that their allergies are contributing to their asthma, immunotherapy has been observed to be an effective treatment option. Is that an accurate summary?

Dr. Cloutier: It is an accurate summary, but I want to make sure that people understand that it is a conditional recommendation. And what I mean by that is: a conditional recommendation is one for which, at the level of a patient, a patient may say the potential benefits of immunotherapy, which are not large, by the way-- there are small benefits-- are greater than the potential harm, which, while frequent in this case, are not severe, but can be life-threatening, so there is risk. And, again, remember how I talked about GRADE having sort of that balance? This is part of the balance of the benefits-- small benefits, some harms-- and that, in making the decision to recommend immunotherapy to a patient, it's part of what the guidelines stress as shared decision-making. It's important for patients in whom you're considering referring for immunotherapists that they understand what the benefits might be, what the risks might be, and what the patient's burdens might be, because it's important that you come in regularly for this therapy. And that all of those things, not just the science of immunotherapy but all of those things, are balanced and measured and enter into the equation for a decision of what to do.

Dr. Stukus: I think that's a very important perspective, and I'm so glad that you offered some context and put that in that frame of reference for people to understand. And, just to clarify, being somewhat facetious here, are there guideline police that will come and take you away in handcuffs if you don't do everything that's exactly written per the guidelines? Or is there, obviously, room for interpretation?

Dr. Cloutier: Well, obviously, yes. That's a very important point. A very important point. And it's one that the guidelines make throughout. There are only a couple of recommendations in the entire guidelines that were considered strong recommendations. That is to say they were based on high certainty of evidence, like a lot of data in thousands of individuals, that this is treatment of choice. So they have high certainty. It's a strong recommendation for it. Most patients are going to want it. Very few are not. And, as a clinician, this is something you should be doing. Most of the recommendations are conditional, and that is to say they are based upon, really, the balance between benefits, harms, burdens, costs, equity, feasibility. All of these things should enter into a decision of whether to implement a specific therapy in a specific individual or not. And what the guidelines now give to the clinician is they give them all of that information to now be able to use with an individual patient. And that's the real strength of it. And so it's incredibly transparent how decisions and recommendations were made, what were sort of the balance of forces that were used. And that, to me, is the real strength of using the GRADE approach for clinicians because it now-- there's not this sort of veil of secrecy or behind the wall is the information. It's all there for clinicians to use with their patients.

Dr. Stukus: That's great. And you know with asthma, as you know better than anybody, there's such a heterogeneous condition, and there are so many options available for treatment and for medications and things on those lines. I think that's a good spot to sort of transition to the next section, if we may, where the asthma guidelines discuss the use of intermittent inhaled corticosteroids and long-acting muscarinic antagonists for treatment of asthma. Before we get into what the guidelines actually recommend and some of the nuance involved with that, just give us some background as to what these medications do for people who have asthma. What effect do they have inside the airways?

Dr. Cloutier: So inhaled corticosteroids are anti-inflammatory agents. They certainly reduce the inflammatory response. They prevent the development of airway inflammation and treat it, whereas the

LAMAs, or long-acting muscarinic antagonists, are anticholinergic drugs, and, again, result in bronchodilation through their anticholinergic effects.

Dr. Stukus: Okay. And before we talk about specific use of these medications, can you just give us a brief sort of description? I'm asking a lot here, and I realize this before it even comes out of my mouth. But in regards to our understanding of asthma phenotypes and endotypes and sort of that individualized approach to management and why therapy can differ and response to therapy can differ among individuals with asthma.

Dr. Cloutier: Well, that's a big question. I think we should think about sort of currently where we are and where I think we're going to go with this therapy. Currently where we are is we think about asthma treatments in terms of asthma severity, which the update does not address, but pulls through the definitions related to asthma severity from 2007. But we think about that therapy in the step diagrams in which each subsequent step is asthma of a greater intensity or a greater severity, so that, currently, our therapy is guided by severity, and it's also guided by age, since asthma-- and we looked at three different age groups, namely zero-to-four, five-to-eleven, twelve-and-older therapy. And so, in making the recommendations, the recommendations in the update are laid out by age and they're laid out by asthma severity in the step diagrams, which many of your listeners hopefully are familiar with. But I think the eventual downside of this approach is that one size does not fit all, say, six-year-olds with moderate persistent asthma. I think as we move forward into an era of personalized medicine into an era where we really look at asthma as one size does not fit all, so that there are different endotypes. Remember how, back in 1991, we thought of asthma as being really a single disease. Well, we now recognize that it's many, many different-- there are many different aspects or even different diseases lumped under the category of asthma. And, as time moves forward, I think we will get increasingly more able to recognize that there are certain groups of people for whom certain therapies are more likely to be effective or beneficial than other therapies. I'm going to give you one example, and it's something you haven't come to yet, but, for example, in FeNO, in fractional exhaled nitric oxide, a new biomarker for asthma. Individuals who have an exhaled breath nitric oxide level of greater than fifty parts per billion you can predict are going to be responsive to corticosteroids. So that if you've got someone in whom you're uncertain about the disease, whether they have asthma or not, and they have an elevated level of exhaled nitric oxide, you could predict that they are likely to respond to corticosteroid therapy. And it is that sort of greater granularity in choosing our therapies that I think we're going to see over the next ten to fifteen years.

Dr. Stukus: Yes, I agree. I think the age of personalized medicine has been upon us for a little while, but we're just now starting to get to the really fun part of really tinkering with the use of biomarkers and things like that. So let's go back to the 2020 Asthma Guidelines. What are the key messages regarding inhaled corticosteroids and long-acting muscarinic antagonists?

Dr. Cloutier: I think this area represents the biggest change in the guidelines. In the 2007 guidelines, there was some discussion about intermittent inhaled corticosteroid therapy, and the thought was this area is just sort of emerging. It's not there. There's not enough science in the area. Well, since that time there have been some very significant advances and clinical trials in examining inhaled corticosteroid therapy. So just to sort of quickly do the key highlights by age and by severity, by the way. In children

zero to four-years old who have intermittent asthma, and so they wheeze at least three times or less only in response to respiratory tract infections, the new guidelines recommend, at the start of a respiratory tract infection, adding a seven- to ten-day course of daily inhaled corticosteroids. The old guidelines said use short-acting beta-agonists as needed. New guidelines say, for that specific group, zero to four, wheezing only during respiratory tract infections, begin them on a seven- to ten-day course of inhaled corticosteroids every day. In children five to eleven years of age, now looking at moderate persistent asthma and keeping with the theme of intermittent corticosteroid therapy, SMART therapy is now recommended. SMART stands for single maintenance and reliever therapy. So for those children, five to eleven, with moderate persistent asthma, daily and as-needed combination low-dose inhaled corticosteroids and formoterol or a medium-dose inhaled corticosteroid and formoterol. Now, formoterol is specifically recommended because it is a short-acting beta agonist and it can be used more than twice a day. So for those individuals, they might take-- for example, they might take a daily inhaled corticosteroid/formoterol combination maybe twice a day, and then for rescue therapy they would use that same inhaler up to-- and it depends upon the age-- maybe twelve puffs a day. And the guidelines sort of lay out the detail of in what age range up to what maximum number of puffs each day. And so this is a reflection of the fact that-- sorry. I should say the reason for this recommendation is it actually has been shown to improve asthma outcomes and to decrease the total inhaled corticosteroid and total daily cumulative steroid exposure by these children. So remember one of our concerns always about corticosteroids has been any effects it might have on growth. Well, here is now an approach to therapy that will both decrease the total exposure and, at the same time, improve asthma outcomes for those children. So that's the rationale for that approach. Now in ages twelve or older, there are recommendations across sort of mild persistent asthma, moderate persistent asthma, and moderate to severe persistent. Again, in moderate persistent, that same approach, a daily and as-needed combination, low-dose or medium-dose inhaled corticosteroid/formoterol, preferably in a single inhaler for both maintenance therapy-- so maybe like twice a day-- as well as rescue therapy as needed is recommended. But now in adolescents and adults, in mild persistent disease, there are two equivalent therapies that can be used. One is the current one, which is the low-dose inhaled corticosteroid and as-needed short-acting beta-agonist, and the other is as-needed concomitant inhaled corticosteroids and short-acting beta-agonists. So in that therapy, individuals, when they begin having asthma symptoms, would use their inhaled corticosteroid as well as a short-acting beta-agonist for their treatment. Mild persistent. Now when you move up to moderate to severe persistent asthma, you have individuals who are already on daily and as-needed inhaled corticosteroid therapy/formoterol, and for those individuals the response is inadequate. Well, what the guidelines recommend in moderate to severe persistent asthma is the addition of a long-acting muscarinic antagonist. So for those individuals they would be on both sort of a daily sort of medium to even a high-dose inhaled corticosteroid and a LABA. And it doesn't have to be formoterol. It could be any of the LABAs plus a LAMA plus as-needed short-acting beta-agonist. So the idea is this. We are now moving toward more intermittent therapy, using it when patients are symptomatic. Sometimes using it both for maintenance as well as for reliever therapy, sometimes just using it in the really mild cases, just as needed. And the LAMAs or the long-acting muscarinic antagonists really are add-on therapy. They're adding on when the ICS LABA-- long-acting bronchodilator-- when that is inadequate therapy. So it's a lot-- it's a big change.

Dr. Stukus: Yes. It's a paradigm shift compared with the prior recommendations. We've all had conversations with families about, "You need to take this medication, morning and night, every single day, even when you don't feel well, because that's the best way to use it," and then non-adherence is rampant. And it is, as you mentioned at the start, I mean, talk about patient preference and meeting the patient where they are to help them with self-management. This is empowering, in many ways. But the question I have for you now is: how on earth can we help both clinicians and patients understand why things have changed? What kind of key message can we send as we try to adapt to the new recommendations?

Dr. Cloutier: Well, again, this is where the shared decision-making comes into place. And that is-- we need to understand-- and, unfortunately, this takes time, but we need to understand where our patients are in terms of therapy. For some of them-- and this is what we learned in focus groups-- some patients actually prefer daily therapy. They actually prefer that. They want to know when to take it. Whereas others like-- and really like-- this idea of I just take it when I need it, because the reality is that's what they've been doing anyway. They use it when they need it. And we now sanction that behavior. And that's the good part of that. And so the guilt that they feel, and sort of the denial that they may give us in terms of what treatment they're actually using, that sort of whole area, that burden has been lifted, but it has been replaced by a different burden. It is going to be a burden, and it's going to be a burden in-- think about the child who's five to eleven years of age, and this is what I think about all the time. Does the child decide when to use as-needed therapy? Does the parent or caregiver? How do they make the decision? How does the school nurse make that decision when the school nurse sees the child? Or when they're away at Grandma's house for the weekend or night. These are things that we're going to have to work on. And, again, NHLBI has been just aggressively working on materials for clinicians to use in their office. Sort of guideline helpers. And the guidelines themselves do this, as well. There's a whole section on implementation guidance for every recommendation. Really the who, how, what, where, and why, and what to talk to patients about and how to come to these decisions, these particular decisions. So I think there is going to be sort of a real paradigm shift, and I think some of the low-level fruit's going to be the easiest one to implement-- those patients who aren't taking the daily therapy anyway and who are going to be the early adopters and quickly embrace as-needed therapy. And they're actually going to do quite well with that, and that's going to be fabulous. And then there are those who are going to hold on to sort of regular therapy. But remember, in moderate persistent asthma, they're still on daily therapy. The difference lies in the fact that they're going to use that inhaled corticosteroid as needed in combination with formoterol when they need it. So I think it's going to make them less reliant upon the shorter-acting bronchodilators and improve their outcome measures. And we know it will improve asthma options.

Dr. Stukus: Yes. That's the crux of the matter, right? You translate evidence into practice. And that's why I'm so thankful to have you on to give us such a contextual appreciation for why these changes are occurring and the recommendations are now different. So hopefully people will start to appreciate this and play around with it a little bit and see that their patients are going to do quite well. Let's shift gears back to indoor allergens, or allergens, I should say, because that's the next topic in the 2020 Asthma Guidelines. The next key area really focuses on the effectiveness of indoor allergen reduction measures in the management of asthma, which kind of ties in with the first topic very naturally. But you know, just real basically, what are the major indoor allergens that we're talking about here?

Dr. Cloutier: We're talking about dust mite. We're talking about animal dander. We're talking about environmental tobacco smoke, which the update does not address. And we're talking about pests, cockroaches and rodents.

Dr. Stukus: And should clinicians or patients with asthma just automatically assume that they have indoor allergies and start taking allergy medicine and making changes inside their home, or should they actually be evaluated to see if they are sensitized and allergic before making any changes?

Dr. Cloutier: Yeah, this is an important sort of aspect of the new guideline. So, the assessment of allergy exposure was recommended in the 2007 Guidelines and the assessment continues. So, it is important for clinicians to assess environmental exposures on behalf of their patients with asthma. They need to assess it. Routine, that is, or global allergen mitigation strategies are not recommended however as part of routine asthma care. Rather-- and this is the important part-- rather, strategies are recommended for individuals who are exposed to a particular allergen and who demonstrate sensitization either by allergen specific IGE, or allergy skin testing, or have symptoms upon exposure. So, for people who don't have access to allergy skin testing, if every time the child goes to grandma's house-- and I don't mean to <claps>-- it's grandma's house-- but every time they go to grandma's house, they-- and she has a cat, there's a problem, the family probably should not get a cat. So, it's either evidence of sensitization or symptoms upon exposure. And a history of exposure. And that's important. And a history of exposure. For those individuals, the evidence is pretty clear that single component <coughs>, excuse me, single component mitigation strategies are not effective. Let me give you a couple of examples. Air purifiers, filtration systems. Just simply putting an air filter, or a filtration system in your house for the treatment of dust mite is not effective. Nor are impermeable pillow and mattress covers. Single strategies, by and large, are not effective. When you are going to use-- I know, this is going to be a big thing-- when they are used, or when you're thinking about using them, multi-component strategies are most effective. So, for example, the HEPA system, *plus* impermeable pillows and mattress covers, *plus* cleaning activity are conditionally recommended. So, again, multi-component strategies can be used and may be effective. Having said that, though, the benefits are small. A lot of it had to do with many of the studies were small, there was a lot-- there was no placebo group, and so there was a lot of risk of bias in the studies, and the benefits were not really standardized and so it was difficult to sort of sort through them. So, there were a lot of problems with those particular studies. But the one exception to that is integrated pest management. Which has been shown to have-- when used as a single component strategy, even though it is multiple-component, but integrated pest management, which reduces both infestation, as well as kills existing critters, integrated pest management is, again, conditionally recommended. It has a small benefit in terms of symptoms for individuals, again, who are exposed, and either have symptoms or are sensitized. It does, however, have a burden to families and so it is a conditional recommendation for its use.

Dr. Stukus: That's a lot to unpack! <laughs>

Dr. Cloutier: Uh huh, I know it is!

Dr. Stukus: Yeah, and we won't spend too much time on it, but I just want to clarify for our listeners and kind of put it more in context here. You know, I meet families every day, before they even see me, or

before they're even evaluated to see if they have allergies, they are told to remove all their carpeting. They're told to take down their curtains, they're told to spend thousands of dollars on air purifiers for every room throughout the house. They're told to find new homes for their pets. And you know, that's just blanket recommendations made to these families. And if I'm hearing you correctly, it sounds like you're actually saying, based upon the evidence that we need to not only evaluate exposure to these and then see if we can identify some causative effect of exposure, and with their asthma symptoms, and then even then we can actually recommend targeted intervention strategies. Am I accurately capturing that, of like you're basically saying we need to be thoughtful about what we recommend to families? <laughs>

Dr. Cloutier: Absolutely. Absolutely. Now I'm going to throw another monkey wrench into that, because I think that is what the recommendations are saying. And that is in the focus groups with patients, many of them said, "Well, I'm going to do this anyway. Because they're actually looking for something, "What can I do to make it better?" But at the same time, you know, some of these interventions are burdensome to families. They have a cost associated. For example, air purifiers have not just an initial cost, but also an ongoing cost. And so, we need to be thoughtful about what interventions we recommend. And we have to be realistic about what outcomes, measures, or benefit might accrue to the patient. And again, and the caregiver and the family. And so, this is all part of that sort of shared decision making, and sort of thoughtful approach. And I know that many individuals distribute dust mite impermeable pillow and mattress covers. And individuals might place them on the bed, but one of the things that one of the expert panel members actually said, "But, you know, dust and dust mites collect on the surface of those allergen impermeable pillow and mattress covers. So, they've got to be cleaned. And failure to clean them, any potential benefit you might have had of using them as part of sort of a multi-component strategy will be lost unless they're maintained." So, it all comes down to this-- you must, you should be exposed to it. You should have some demonstration of response to it, either by testing, or by symptoms. And then use a multi-component strategy. Unfortunately, the way the studies were designed that looked at some of these multi-component strategies, they used different combinations of strategies, different outcome measures. And so, it wasn't possible in sort of sorting through the various studies-- and there were a lot of studies, sorting them through to say, "Well, these two or these three are the most effective combinations." And that's where we need to go in terms of this research.

Dr. Stukus: Yeah, that's great background. You remind me of the old joke of, you know, "What does the family do when their allergist tells them to get rid of their dog? They find a new allergist." <laughs> So, you know, shared decision-making absolutely has to be at the heart of all of this stuff.

Dr. Cloutier: Mm hm.

Dr. Stukus: That's great, I'm glad this was addressed in the new asthma guidelines. Well, let's move on to the fourth area, which discusses the effectiveness and safety of bronchial thermoplasty in the management of asthma. And I have no doubt that some of our listeners are asking themselves, "What the heck is bronchial thermoplasty?" So, can you offer us some background?

Dr. Cloutier: Sure, so we know that there is hypertrophy of muscle around the airways in individuals who have asthma. And what bronchial thermoplasty does is it gently and carefully sort of burns away some of

that muscle. So, it's done via bronchoscopy, so it's minimally invasive. It's done over three sort of sessions. And so, they use heat to sort of melt away-- maybe melt away is a better way to describe it-- melt away some of that smooth muscle. And as a result of that, airway resistance is markedly decreased, or caliber is increased. And there have now been three sort of major studies of bronchial thermoplasty. All have followed up of a year, and some of them have follow-up over three to five years. And for some individuals, with asthma that's just-- they're not able to control, it has a benefit. But the risks, and again, this is the value of grade-- but the risks are moderate. And you can imagine there are both short-term complications, so bleeding, atelectasis, being sort of-- asthma exacerbation, are part of that. And there may be some long-term complications of it. And so, the guidelines recommended that this should not be a standard therapy. So, there are recommendations, conditional recommendations against that particular therapy. So, having said that, however, again, here comes that sort of patient contribution, I'll call it. And that is for individuals who, for whom therapy just isn't working or they have a lot of side effects, who say, "You know, I'll take-- it's okay to have these immediate harms, like worsening symptoms. And also, to have some of the unknown sort of long-term side effects." For those individuals, the potential benefits, those individuals might consider bronchial thermoplasty. Again, a shared decision between the clinician and the patient in terms of what's going on with them, and where their preferences and beliefs lie. But when used, because this is such a new therapy, and there are so many questions about this therapy, guideline panel wanted to ensure that individuals receiving this therapy should be enrolled in patient registries or as part of clinical trials, so that we can get the information that we need to determine sort of the balance between benefits and risks.

Dr. Stukus: And with this procedure, I mean, you gave us a great overview and background regarding it. Is that something that people get admitted to the hospital overnight in order to have it done? Is it readily available at any doctor's office? Where's this being done right now?

Dr. Cloutier: No, this is being done in large centers with interventional pulmonologists. So, you need special training to administer this, this is a special piece of equipment that is used in order to this. You can imagine there is a tremendous art to this procedure, as well as the finance.

Dr. Stukus: Oh, absolutely. Well, with that, let's move on to the last area. And this discusses something you mentioned actually previously, which is the clinical utility of fractional exhaled nitric oxide in asthma management. Tell us again, what is fractional exhaled nitric oxide and what does it measure?

Dr. Cloutier: So, it measures exactly what it says. If you breathe through a tube and you exhale, there is amounts of nitric oxide in the exhalant, which can be measured. And in individuals who have airway inflammation, in particular, these levels are elevated, and inhaled corticosteroids reduce these levels in the exhaled breath. And so, the question is, is it useful in various aspects of asthma management. And so, the guidelines looked at it in terms of diagnosis and said, "Yes, it's a conditional recommendation that can be used in asthma diagnosis, but in individuals in whom the diagnosis is uncertain." So, it's not a first line. It's not something you would just measure and say, "Aha! You have asthma!" i.e. it's not diagnostic of asthma. Rather, it's an adjunct test to be used with history. Physical exam, spirometry testing with bronchodilator responsiveness. And when you've done it in that way you could still be uncertain as to the diagnosis, then exhaled, FENO, may be useful in helping you to make that diagnosis. It's also in the same

way, it can be helpful in monitoring therapy, and response to therapy over the long term, over the long haul. Particularly when again history, physical exam, spirometry testing. It's not clear if the asthma is under control, is being well-managed, or not well-managed. So, it's an adjunct test, not the hoped-for, single stand on its own test. It's also not recommended to assess asthma control. So, there are other measures that are better at assessing asthma control. Nor does it predict future exacerbations. So, the evidence just does not support that. And nor does it assess exacerbation severity. So, it's an adjunct test when the asthma diagnosis is uncertain, and as a test that you use frequently as part of a whole asthma management system of monitoring disease when sort of things are not clear.

Dr. Stukus: Can somebody have asthma, and even severe asthma, and yet still have a normal level of exhaled nitric oxide?

Dr. Cloutier: Yeah, this is one of the big problems with-- one of the sort of limitations of FENO testing. And that is there are so many things which can affect the FENO levels. Things like comorbid conditions. So, you could not have asthma, but have allergic rhinitis or conjunctivitis, and you might have an elevated level of FENO, or allergic-- so you could have allergies and not asthma and have elevated FENO. You could have obesity is another marker. You could have asthma beyond corticosteroids and have a normal or low level of FENO. So, the interpretation of the result has to be done carefully, and in the context of a variety of comorbid conditions.

Dr. Stukus: And you know, you just talked about bronchial thermoplasty really only being done with highly specialized training and in academic centers and things like that. Is that the same for FENO? Is that something that's readily available, or do you really have to go only to the specialized specialists?

Dr. Cloutier: Well, it depends. And what it depends upon is the testing itself is quite easy. And children, five and over, can actually do this test. So, it's a pretty easy test to perform. As I mentioned, the interpretation is difficult, and so you have to carefully interpret it. It can be done in primary care offices, but it-- but in most primary care offices, it's not going to be cost effective, because you do have to replace the cartridges, and the cartridges have a cost associated with them. And so, in addition to the initial outlay of the equipment. So, I think this is where establishing partnerships and relationships between primary care clinicians and specialists is really especially important. And this is where it can be so very useful in improving our management of asthma. And in sort of using this particular test in disease management.

Dr. Stukus: Okay.

Dr. Cloutier: But again, the cost may limit its availability in primary care settings.

Dr. Stukus: Sure, sure, okay. Well, Dr. Cloutier, this has been a thorough, very thorough, and very informative discussion and I'm so thankful that you came on to discuss, you know, just really the tip of the iceberg in regards to the new asthma guidelines. But if I may, I would love for you to offer some words of wisdom and advice on how clinicians should utilize these new guidelines in their practice. You know, what can we do with this new information?

Dr. Cloutier: To me, the most important sort of aspect of management is the delivery of consistent messages to patients. And so, as the new guidelines are released, I would like to urge that clinicians, that particularly primary care clinicians, but also my specialty colleagues, to work to develop a consensus approach to asthma management within their practice. In this way, they can look at some of the new materials that are coming out, sort of the decision-aids, and they can create sort of this consistent messaging, and similar, not identical, but similar approach to managing asthma in their patients. And using the same terminology and words with patients. I think this will go such a long way in helping patients to better manage and take control of their asthma.

Dr. Stukus: That's great. And I like that you reinforced again, we're not in this all alone. We don't have to sit down and read it cover to cover and memorize it, and then try to spit out a bunch of words that don't make any sense to us or our patients. Use the decision tools, use the materials that'll be pushed out by NHLBI and made available to all of us, and I think it's going to take some time to kind of get comfortable with it, but I agree 100 percent, we need to be consistent with the words that we use and the messaging that we send. Now, you know, along those lines, it was really just an absolute pleasure to have you as a guest today, and I can't thank you enough for your time. You've been more than generous with your time today. And I could talk to you for another hour about this. But I will direct all of our listeners to the journal of allergy and clinical immunology website, where you can have free open access to the complete asthma guidelines, which you can find at www.JACOnline.org. And with that, Dr. Cloutier, I'm happy to offer you the opportunity to share any last words.

Dr. Cloutier: Thank you very much, Dave, for giving me this opportunity. I really appreciate it.

Dr. Stukus: Oh, well, it's our pleasure, thank you! We hope you enjoyed listening to today's episode. Please visit www.aaaai.org to obtain CME credit, as well as show notes, and any pertinent links from today's conversation. If you liked the show, please take a moment to subscribe to our podcast through Apple Podcasts, Google Podcasts or Spotify, so you can receive new episodes in the future. Thank you again for listening.