Media Briefing on New Asthma Guidelines from the National Asthma Education and Prevention Program
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Unedited Transcript

PRESENTATION

Moderator — Ladies and gentlemen, thank you for standing by. Welcome to the Asthma Guidelines conference call. At this time all participants are in a listen-only mode. Later, we will conduct a question and answer session; instructions will be given at that time. As a reminder, this conference is being recorded. I would now like to turn the conference over to our host, Ms. Diane Striar. Please go ahead.

D. Striar — Good morning. I'm Diane Striar, acting Communications Director for the National Heart, Lung, and Blood Institute at the NIH. I want to welcome you to today's briefing on new asthma guidelines from the National Asthma Education and Prevention Program. The guidelines have been posted online today. We will begin the briefing with a brief statement and introduction from Dr. Elizabeth Nabel, the Director of the National Heart, Lung, and Blood Institute. Dr. Nabel's remarks will be followed by remarks from Dr. William Busse, chair of the Expert Panel convened by the National Asthma Education and Prevention Program. A question and answer session with our assembled experts will conclude today's briefing. Dr. Nabel.

Dr. Nabel

Thank you, Diane, and good morning. We're here today to talk about asthma, a major public health problem in the United States. Asthma affects over 22 million Americans, including 6.5 million children; it's one of the most common chronic diseases in the United States. The new scientific evidence that makes up the guidelines that we're releasing today points to one truth: asthma control is achievable for nearly every patient. With appropriate medical care, healthy environments, and well-informed and empowered patients, asthma can be controlled and patients can lead full, active lives. As health care providers and as patients we really should accept nothing less.

All too often asthma can seriously impact a person's quality of life; children miss school, adults miss work, and many people cut back on their physical activity and other pleasures of life. Unfortunately, without adequate control asthma can also lead to poor lung function. But it really doesn't have to be that way, that's why we're very proud to present the new guidelines today. These new NHLBI guidelines place an even stronger emphasis on asthma monitoring as one of the key components to achieving asthma control. This new approach to asthma monitoring focuses on two related yet distinct aspects of the disease: the level of daily impairment that an asthma patient might be experiencing, that is, what are the symptoms that they might be having on a daily basis; and the second is

the asthma patient's future risks for further asthma episodes, loss of lung function and side effects from medications.

This is an important new distinction that we're making in the guidelines, again, focusing on monitoring of daily impairment and future risks. We know that there can be subtle distinctions, for example, there are some asthma patients who have very few day-to-day effects of asthma, that is, they're not really impacted on a daily basis but yet they still could be at very high risk for frequent episodes of asthma in the future, which could, in turn, ultimately affect their lung function, so we will be highlighting these differences.

In a moment, Dr. Busse, Chair of the Expert Panel that prepared these new asthma guidelines, will describe to you in greater detail how impairment and risk are measured, as well as other key recommendations that are being presented today in the guidelines. I want to emphasize that these guidelines really do represent the best currently available and most up-to-date science. The Expert Panel distilled a large body of recent scientific evidence, and as a result these guidelines now provide critical guidance to asthma patients and their families, as well as physicians, health care providers, and others in the community, including the school community, on how to recognize asthma and manage it.

These guidelines are really just one of very many significant efforts by the National Heart, Lung, and Blood Institute to improve the health and well-being of patients with asthma. As you know, the NHLBI supports a very large research portfolio in asthma, and in fact we spend more than $150 million each year on asthma research. We believe that this investment in asthma research and how the research is translated into the guidelines and guidelines being implemented by physicians and in the community are really paying off. Since the National Asthma Education and Prevention Program was established in 1989 we've seen an increased understanding of the asthma disease process. We've also seen improved approaches to diagnosis and treatment. While more people are being diagnosed with asthma, the rate of people reporting asthma attacks has remained stable and deaths due to asthma have dropped, so that's really good news. More patients are receiving education about how to manage and control their asthma, and fewer asthma patients report that they limit their activity because of asthma, and that's really good news as well.

Our hope today is that these guidelines will help even more asthma patients and their families feel better so they can lead active, full lives, not restrict their activities, sleep through the night, and really maintain normal lung function. The NHLBI is very committed to ensuring that these

updated guidelines are widely implemented, and in order to achieve that goal we've really stepped up our efforts to work very closely with the nearly 40 organizations that comprise the National Asthma Education and Prevention Program. We're also exploring partnership opportunities among the organizations and with private industry.

To achieve the goal of implementation we've also convened a Guidelines Implementation Panel, which will help identify priority actions that we can all use to get these guidelines implemented in patients' lives. That report will be presented on October 17th as part of our Asthma Stakeholder Strategy meeting. One of the goals of that meeting will be to encourage professional societies, community groups and other stakeholders to disseminate and implement these guidelines.

I now would like to introduce Dr. William Busse, Chair of the Department of Medicine at the University of Wisconsin at Madison. Dr. Busse chaired the Expert Panel that prepared these guidelines. Dr. Busse.

Dr. Busse Thank you, Dr. Nabel. As Dr. Nabel indicated, our understanding of the basic mechanisms of asthma has increased greatly in the past years, and this information is rapidly being translated into more effectively treating this disease, particularly controlling airway inflammation. Secondly, we

have effective medications to treat asthma that are safe. Thus, our report builds on an extremely solid foundation, which was laid out in the previous versions of the guidelines.

In that respect, we have retained the four components of comprehensive asthma management: assessment and monitoring, control of environmental factors, medications, and patient education. But a number of key changes, already indicated to you by Dr. Nabel, have been included, and these are both in terms of medical treatment and fundamental new approaches to overall asthma care, and they are part of the Expert Panel report number three, which will be briefly described below, and then open for questions later. In the original 1991 Expert Panel report goals of asthma treatment were identified. These included: to minimize symptoms, to achieve normal levels of activity, reduce the need for rescue bronchodilators, aim for normal or near normal lung function, and prevent asthma exacerbations or asthma attacks, and do this all in the presence of safety with medication use.

Our update has brought two original concepts of asthma treatment, severity and control, into the guidelines, with very specific changes. First, our report defines asthma severity as the intrinsic intensity of the disease process and the assessment used to initiate treatment. Second, asthma

control, in contrast, refers to the degree to which the manifestations of asthma severity are minimized by treatment and the goals of therapy met. In other words, how responsive is the patient to treatment.

Our report further identifies two domains for both asthma severity and control, and these have already been identified by Dr. Nabel, and they are: current impairment and future risks. Impairment is defined as the current frequency or intensity of symptoms or functional limitations. Impairment is the here and now of the disease. Risk, in contrast, represents another and likely distinct more longitudinal feature of asthma that includes exacerbations or asthma attacks, progressive loss of lung function, and adverse effects from medication.

We feel that impairment and risk are distinct, but linked in our manifestations of both asthma severity and control, and their component factors may respond differentially to treatment. Therefore, in formulating treatment for asthma to achieve optimal control, the domains of both impairment and risk need to be assessed and monitored and are essential for best care of asthma. Asthma also has considerable heterogeneity, a feature of this disease that needs to be considered in its treatment. This heterogeneity is reflected in many aspects, including the age of the patient.

To more fully incorporate this feature of asthma in the formulation of treatment plans, three age bracket categories are now considered: zero to four years, five to eleven years, and greater than 12 years. These age groupings were chosen for a number of reasons, which can be discussed in the question and answer period.

Another new feature of our report is an expansion of the stepwise approach from four to six treatment steps. In persistent asthma, inhaled corticosteroids remain the preferred foundation for anti-inflammatory therapy, with additions of other medications with some revisions but very similar, in many respects, to the previous versions of the guidelines. Two new steps have been added, steps five and six. These treatment steps, which are intended for those patients with the most severe asthma and for patients greater than 12 years of age, consider the addition of omalizumab, a monoclonal antibody directed against IgE, which is important in allergic components and allergic inflammation.

As Dr. Nabel indicated, overall the news is reassuring. Although asthma is a common chronic illness that can pose a serious burden for patients, their families, and their communities, we firmly believe that asthma control can be achieved in nearly every patient with asthma. And I just really want to reemphasize this point—which has already been indicated

by Dr. Nabel—thus, it is our anticipation, expectation and hope that the recommendations in this new report will pave the way to improved control of asthma, prevention of risks, particularly asthma attacks, and represent a continuing effort to finally cure this disease.

My colleagues from the Expert Panel and I will be glad to answer any questions you may have about our report and our new recommendations, and I'd like to turn the briefing back to Dr. Nabel.

Dr. Nabel — Thank you, Dr. Busse. Now, to answer any questions that you might have, we've assembled a group of experts today. These individuals are all members of the Asthma Expert Panel and have extensive clinical experience in taking care of individuals with asthma. In addition to Dr. Busse we have joining us today: Dr. Robert Lemanske, and Dr. Lemanske is Professor of Pediatrics and Medicine at the University of Wisconsin in Madison; Dr. Stuart Stoloff, who is Clinical Professor of Family and Community Medicine at the University of Nevada; and Dr. Homer Boushey, who is a Professor of Medicine at the University of California in San Francisco. So now we'll open up the lines for questions from all of you.

Moderator — Our first question comes from Daniel Denoon from WebMD.

D. Denoon — Hello. Thank you for taking my question. I'd like to ask Dr. Busse and the other experts on the panel precisely what patients will be told. How will these new guidelines look to patients and what will patients notice when they come to their doctor the next time for their next check-up?

Dr. Nabel — Dr. Busse, would you like to address that question.

Dr. Busse — I think they'll notice a number of things that we've tried to stress. I think first they'll notice is how we're assessing how effective our treatment for asthma is. We're not only interested in what's happened to their lung function, which we still are very interested in, but what's going on with the patient; how often are they needing their bronchodilator, how often do they have to limit activities, and how frequently are their normal activities interfered with. But more importantly, the caregiver is going to be interested in other components, in other words, how frequently do they have attacks of asthma. So I think it's a far more encompassing approach to the treatment of asthma and we hope, and I think evidence is beginning to indicate this, but if we use this approach the impairments from the disease are going to be minimized quite considerably. I'm just really wondering if some of the other panel members would like to expand on this.

Dr. Nabel Dr. Stoloff, how will you approach this now in your family practice?

Dr. Stoloff Thank you, Dr. Nabel. In my practice we've looked at validated questionnaires, which are very simple to use—the asthma control test being one—five questions, five answers that can be administered in multiple languages in approximately two minutes. And that information really facilitates, we know what the scores mean, we know that if they have less than a certain score that their control of asthma is not present the way it should be, so it helps facilitate a discussion between the patient and the clinician. I think this type of device as one of the composites of looking at control will really facilitate better communication between the clinician and the parent, the family member, and the patient themselves. That's really what we're doing, this is much more encompassing and much more honing down on really finding out what's going on in the life of the patient with asthma.

Dr. Nabel Dr. Lemanske, how about your pediatric practice, how will you use these guidelines in your practice?

Dr. Lemanske I think one of the new advances for the guidelines is clearly this new division by different ages from zero to four, five to eleven, and 12 and above. There are clearly different developmental issues that we deal with

as pediatricians and clinicians in the preschool kids that are much, much different than we deal with in the kids once they enter school, and then obviously during the adolescent period, when there are clearly other issues that we have to be dealing with, with regards to treatment approaches, compliance, etc. I think this new separation into three groupings will give clinicians a much better idea on the very unique things that can happen at different developmental stages in the children and young adults.

Dr. Nabel Thank you. We're ready for our next question.

Moderator Our next question comes from Rob Foreman of *CBS Early Show*.

R. Foreman Good morning. Thank you. Dr. Lemanske, you led into my question perfectly. I'd love some detail, please, on what the differences are among these age groups and why they've been set apart in this way, Dr. Lemanske and everybody, please.

Dr. Nabel Dr. Lemanske, why don't you lead off?

Dr. Lemanske There are actually probably three or four reasons why we chose to do this. The first is that there are certain medications where there's clearly

abundant evidence that they work in kids and adults 12 and above, and the database just is not there for the kids that are younger than age 12.

Second is, for certain medications the information that we currently have suggests that school age children are more likely to respond to low doses of inhaled corticosteroids and really don't appear to need the benefits of combination therapy, as has been demonstrated in the adult population. However, this information needs some further definition, and as a result of this one of the NHLBI sponsored networks for children, the Childhood Asthma Research and Education Network, is currently conducting a protocol to try to determine in children who are on low dose inhaled corticosteroids what's the next best step for them in terms of their care.

Third, the Expert Panel felt that separating, again, the kids into the five to eleven group and the zero to four, I think I've already mentioned, is that there are different developmental stages. And the school component of this we really wanted to emphasize, in terms of the families and the clinicians working with the teachers, the physical education teachers, etc., in a much better team approach in terms of overall care for the kids.

Finally, drug delivery systems are clearly age dependent, as is the ability to monitor pulmonary function as part of this new impairment domain.

And because of these factors we felt that they could potentially affect treatment decisions and it was better for us to divide them and to approach it based on more of a developmental aspect or approach.

R. Foreman If I can follow up, does that mean the child medicating him or herself, or treating him or herself in other ways?

Dr. Lemanske Yes. That will be addressed in terms of the children being able to carry their rescue inhalers at school, have them more available to them; much more comprehensive than we were before. And also the use of asthma action plans, which is a very important aspect of these guidelines, that every patient should have an asthma action plan and these asthma action plans should translate not only into the family situation but into the school situation as well.

Dr. Nabel Thank you very much. Our next question.

Moderator Our next question comes from Denise Grady from *New York Times*.

D. Grady Thank you very much. I also wanted to know anything more you can tell us about these age groups and different responses to drugs. Now, you mentioned that it seems as if some of the younger kids do not need the

combination treatment, and I wondered if you could tell us exactly what you're talking about when you're talking about particular drugs combined. Are these the drugs that combine a bronchodilator and a steroid, are you saying those are the ones they don't need?

Then I'd like to ask one other thing, Dr. Busse mentioned the notion of ultimately curing asthma. Is there really any hope of that? Can you give us some idea what you have in mind when you say that? Thanks.

Dr. Nabel — Why don't we start first with Dr. Lemanske, and Dr. Stoloff maybe you could visit a little bit more then about the medications, and then we'll move on to the last component of the question.

Dr. Lemanske — This is Dr. Lemanske. For combination therapy what I was referring to is the combination of an inhaled corticosteroid with a long-acting beta agonist. There are combination therapies that are currently available in the marketplace, and we really don't have any data with regards to their efficacy that is combination therapy in the zero to four group. For the five-year-olds to eleven-year-olds we have very good data to suggest that children respond very, very well to just low doses of inhaled corticosteroids, what we call monotherapy, that is, they only have one medicine to treat their disease. And really, they don't need, at least in the

data we have available it looks like their response to just inhaled corticosteroids alone is so good that they may not need combination therapy.

In the adult population it seems like combination therapy, in many patients, seems to give them a little bit more advantage than do low doses of inhaled corticosteroids. But because this question isn't completely answered yet, we are, as I stated, doing a prospective one year long clinical trial that will hopefully provide us with the evidence to make a firm statement as to what are some of the differences in response to these different medications between children and adults.

Dr. Nabel — Dr. Boushey or Dr. Stoloff, anything to add to that comment?

Dr. Stoloff — I would add the other point that Rob was talking about, Dr. Lemanske was, in zero to four they don't talk to you a great deal so you're looking at what we call "predictive indicators" in that age group that will assist the clinician in making a diagnosis of asthma and determining if they need to take maintenance medication, the medicine that they need to take every day, what we call controller medication. We've looked at the data by the networks, by members within the networks in their institutions, and we now have information of how we can predict, especially in young children

three years of age and younger who wheeze frequently, what their probable risk is that the wheeze, even though it's caused by viral infections, may in fact represent asthma and should receive continuous daily medication. That helps us divide in that population, very young population, those children who should receive medication daily then, as Dr. Lemanske alluded to in the zero to four.

The other point that I just want to quickly make is in the past year or so there's federal legislation passed allowing children to carry their medications, their rescue inhalers to school to assist so they don't have asthma attacks of such severity that would result in them having to leave the school. That type of education this document continues to pass on, and that's why we want schools and teachers and physical education teachers and nursing and ancillary staff to understand how to assist children when they have an episode at school. That's why written asthma action plans need to be made available for all children with asthma, as well as all adults, so people know what to do when they're well as well as when they begin to have difficulty.

Dr. Nabel Dr. Boushey, anything to add?

Dr. Boushey I think it's sort of a spin-off of this change in how we're presenting asthma control in two domains, how people are doing now, how they're feeling and how they're functioning, that's one domain of asthma control; and then the second, of risk of severe attacks.

We're now entering the time when asthma attacks requiring hospitalizations peak, every year it's in September and October, and that's driven by viral respiratory infections in school age children. What we think has been going on is that people have been believing that because their symptoms aren't very active—over the summer they're not exposed to a lot of viral infections—that they don't need to take their asthma medications because their current symptoms and impairments are mild. But we know that that doesn't necessarily mean their risk of a severe attack is low. So by emphasizing that we have to consider risk of attacks as part of the picture, that's the way to encourage use of medication regularly, especially as return to school approaches, and we hope this will reduce this year-after-year peak in hospitalizations of asthma among children in September and October.

Dr. Nabel Dr. Busse, maybe I can ask you to return to the question earlier about the potential for a cure of asthma.

Dr. Busse Thank you, Dr. Nabel. It certainly is the goal of anybody that takes care of patients with asthma who is involved in the research of asthma to have this as a goal for all the obvious reasons; it affects so many individuals and the morbidity is very significant, and it's a lifelong illness for many individuals. I think one has to be optimistic with the advances that are occurring, as far as basic research is concerned, that we've been able to identify a number of factors which are very important in leading to the disease, first of all, expressing itself, and secondly, becoming persistent.

And as we begin to get these factors better understood we're beginning to understand what are the factors that can control it. I think with new techniques and tools and drug development and interruptions of those processes, again, I think one has to be very optimistic that this will eventually occur. The timeline on this, however, I think is still not fully defined, but the advances are occurring rapidly and I think that this is a goal we all have to keep in mind all the time when we're dealing with patients with asthma.

Dr. Nabel Thank you. Next question.

Moderator Our next question comes from Allison Aubrey with NPR. Please go ahead.

A. Aubrey — Hello. Thanks for taking my question. You talked a little bit about this five to eleven group in medications and the evidence to date does not answer the question fully about whether the combination therapy might work. But what about the other newer medications, how do they fit into the guidelines, for instance, the leukotriene modulators like Singulair or some of the newer, longer acting beta agonists?

Dr. Nabel — Dr. Boushey, could I ask you to address that first, and then Dr. Lemanske.

Dr. Boushey — The guidelines haven't changed greatly the place of the leukotriene antagonist, there's been some tinkering with that in the children's group, but there is a new medication now recognized in the guidelines and that's this monoclonal antibody directed against IgE. IgE is the antibody responsible for allergies and allergic asthma, so you can think of a monoclonal antibody against IgE as an anti-missile missile, and it's an engineered antibody to neutralize an antibody in the body. This is developed by Genentech, and it works, and it works to reduce responses to allergens and has been shown to reduce the frequency of attacks of asthma in people with severe asthma not well controlled even by high dose inhaled corticosteroids or combination treatment, or even by taking oral corticosteroids with all their attendant side effects.

Because of the emergence of the efficacy of this new, I guess you have to call it an immune modulator, it's an antibody that alters immune function, because it's effective in preventing exacerbations it now is placed in the guidelines for people at the higher steps of severity, the steps we call four and five, it's now recommended. But only for people over 12. It isn't proven safe and effective in children under 12 yet sufficiently to have FDA approval. It appears to work in that population, but the FDA needs more evidence before it will approve it for that group.

D. Grady And what is it called?

Dr. Boushey The trade name is Xolair. The generic name is omalizumab.

D. Grady And you mentioned about Singulair, the recommendations or guidelines haven't changed, so what are the recommendations? Where does it fit into the step guidelines for the five to twelve ...?

Dr. Boushey I'm going to refer that to Dr. Lemanske, since he's a pediatrician and knows this better than I.

Dr. Lemanske One of the problems that we have had in making recommendations is that there are fewer studies that directly compare one drug versus another.

Most of these drugs have been approved by the FDA based on their safety and efficacy in comparison to placebo, so when you're trying to say you should say one medicine at a given step versus another what you really need is the evidence to make that kind of a statement, in terms of one being preferred versus one not being as preferred.

We now have some data that we have generated in the Childhood Asthma Research and Education Network and published in the kids that are five to eleven grouping, where we directly looked at the efficacy and safety of a low dose of inhaled corticosteroid versus a leukotriene receptor antagonist. And for the majority of patients, for the majority of outcomes, all the outcomes actually that we looked at, the response was better with the inhaled corticosteroid than it was with the montelukast. The importance of those findings is that now when we come to the step where we're trying to make recommendations in terms of which controller should we use at which particular juncture we can feel pretty confident now that the inhaled corticosteroid recommendation as the preferred treatment is based on solid grounds.

D. Grady Could I ask one more question about on these guidelines? When you were breaking out this five to eleven group, what is the message to patients or to parents of patients about when you're breaking out, talking about written

asthma plans, you mentioned that already about school, about self-monitoring and also about patient education, what do you really mean by patient education? Are there just a few quick things patients need to know? There's certainly lots of information, but if you had to prioritize three things every asthma patient should know between five to eleven what would they be?

Dr. Nabel Dr. Stoloff, would you like to address that?

Dr. Stoloff Yes ... Number one, recognize when your symptoms are getting worse. Number two, recognize what to do when your symptoms are getting worse, to use your rescue inhaler. And number three, recognize when in spite of using your rescue medication you need additional medication and your clinician, your physician needs to be contacted.

D. Grady Thank you.

Dr. Nabel Thank you.

Dr. Stoloff And Susan Jansen, a professor in the School of Nursing here at UCSF, would emphasize that it's not enough to transmit knowledge, you have to transmit skills, and there's more emphasis on making sure people know

how to use inhalers. It's not intuitive, necessarily, to use an inhaler properly and to know how to monitor your peak flow and to know what to do and have the skills to do it. So it's transmitting skills as well as knowledge that's necessary.

M I'll add one other thing. Our education section of this document is not just one section, education is the key component throughout the entire document. We are encouraging clinicians each time they see patients to provide them placebo devices, especially for the rescue medication, and ensure that the patient can use the medication properly or the device properly.

Dr. Lemanske This is Dr. Lemanske. I just would like to add something. The other thing in this five to eleven group that is potentially different is that the dynamic between the patient and the family really begins to change. In the zero to four group, obviously the parents are taking care of the children, making sure hopefully they're getting the medicines, that they're delivering them in the proper way, etc. In the five to eleven group, this is when the parents begin to try to get their kids a little bit more independent, so when we see them in clinics the kids are telling us that they're taking their medicine, the parents are saying they're not, and vice versa. So it's a whole different approach to try and gauge control and gauge whether or not we're giving

the right kinds of medications and the right amounts of medications. And of course once the kids get to be 12 and above, at least during puberty, you get into a whole different set of dynamics with regards to adherence, which are different, again, than what we see in the adult population.

So there are different issues that we have to deal with in these different age groups and it made a lot more sense to us that rather than grouping in the old guidelines between zero and four, and five and above, to recognize the fact that there clearly are developmental distinctions that we need to be thinking about.

Dr. Nabel — Terrific. Thank you. Next question, please.

Moderator — Our next question comes from Dennis O'Brien with *Baltimore Sun*. Please go ahead.

D. O'Brien — Thank you. You mentioned that when school starts kids basically think they're okay, so they stop taking their medications and you have a lot of asthma attacks in September and October. Does that happen in the adult population at any given season, or is there a comparable problem with adults?

Dr. Boushey This is Homer Boushey at UCSF. Oh yes, most asthma exacerbations are associated with viral respiratory infections. The most common cause of attacks of asthma requiring emergency visits or hospitalization is infection with the common cold virus, and it, in the Northern Hemisphere, has a kind of seasonal distribution. It's here all the time, but it peaks between Labor Day and Thanksgiving, and 85% of respiratory infections are cold viruses, rhinovirus, common cold viruses, and then starting after Thanksgiving many other winter viruses that can also worsen asthma come on. So the greatest peaks are in children because they get together in classrooms, and this emphasis on hand washing and sneezing into the crook of the elbow, these are actually good recommendations in reducing transmission. But all the same, that's a way where these viruses are exchanged, and then they're brought back into the general community. There is a peak in hospitalizations in adults as well starting in the fall. It's not as sharp or as clear as in children, but it is reflective there too.

Rob Lemanske is a great expert on viral respiratory infections and how they cause asthma exacerbations, so maybe you want to comment here, Rob.

Dr. Lemanske I think Dr. Boushey has really nicely outlined these seasonal peaks that we see in asthma exacerbations, in that we have very good epidemiologic

evidence that these are related to viral respiratory tract infections, primarily the rhinovirus, of which there are now known over 130 different what we call “serotypes” or strains. So just getting one cold virus doesn’t mean you won’t get another one for the rest of your life, you have many possibilities of getting repeated colds, as we all have known for many years, but now we have the techniques available to be able to define these different viruses. And what many of us are interested in is to determine if there are certain types of cold viruses which are more likely to cause these asthma exacerbations. And if we can determine that, then obviously we can, from a molecular standpoint, hopefully begin to direct therapy at these different specific viruses that might be helpful to patients with asthma. We also have some data from a number of different ... studies that children who wheeze very early on with the rhinovirus, the common cold, particularly in the first ... of life, are these kids who really then are the most likely to go on to develop childhood asthma. So wheezing with these viruses, not only early in life, is a marker for potentially going on to getting asthma, but once asthma is there getting these infections can clearly cause some significant exacerbations that can lead to increased morbidity in the asthmatic individual.

Dr. Boushey To get back to the question, we do know that taking an inhaled corticosteroid is not only effective for improving pulmonary function and

reducing symptoms, but also for preventing attacks. And if a person only takes their inhaled steroid when they're having symptoms and stops taking it in early August because they're feeling pretty well, they can still be at great risk of bad exacerbations or attacks from a viral infection. That's why we want people to think not just of your symptoms of asthma, but the risk asthma is associated with of attacks from exposure to viruses or high doses of allergens in the future. So if people will remember to take their inhaled corticosteroids, under the advice of their physician, because they're at risk we hope to reduce these peaks of exacerbations in the fall.

Dr. Busse This is Dr. Busse. I just wanted to expand on the areas that both Dr. Lemanske and Dr. Boushey have commented on. As Dr. Boushey indicated, if you take your medications currently you many times can reduce the frequency or the intensity of these asthma exacerbations from a cold. However, many people will still get an attack of asthma with a cold even though they're on their medications, and this is why one needs to be very alert to this factor in controlling the disease. I think the second aspect that it's very important that patients and physicians understand is that sometimes the reason that we don't get as good control with asthma from respiratory infections is that the mechanism may be very different with colds than it is with other forms of asthma. I think the last thing that is also very important, these are viral respiratory infections and they're not

bacterial infections, and the way to treat them is to really accentuate the treatment for asthma, not necessarily the use of antibiotics.

Dr. Nabel — Thank you all. We'll move on now to the next question.

Moderator — Our next question comes from Jennifer Corbett with *Dow Jones*. Please go ahead.

J. Corbett — Thanks. Hello, I have two questions. One quick question, somebody mentioned that there's an ongoing trial to look at the treatment options in I guess it sounds like the kids. I'm wondering when those results might be available. The other question I have is, you mentioned the newest part of this are the recommendations to assess the future risk, and I'm wondering if somebody can describe how clinicians assess the future risk.

Dr. Nabel — I'll ask Dr. Lemanske to address the first question regarding ongoing studies in children, and then Dr. Stoloff, if you could address the question about assessment of risk.

Dr. Lemanske — Sure. Thank you, Dr. Nabel. This is Dr. Lemanske. The study that I briefly mentioned before is a trial that's being conducted and supported by the National Heart, Lung and Blood Institute by the Childhood Asthma Research and Education Network, or CARE Network. The research

question we're attempting to answer in this trial is, we're taking children who are on low doses of inhaled corticosteroids who are not adequately controlled with that particular medication and we're asking the question, if that should occur in a patient, in a child, what would be the next best step to do, to increase the dose of the inhaled corticosteroid, number one; number two, to keep the dose the same and to add a long-acting beta agonist; or number three, to keep the dose the same and add a leukotriene receptor antagonist?

Each of the children enrolled in the trial will get all three of these treatments over a year long period of time, not a year long but the treatment term will be 16 weeks and the total enrollment for the child will be a year. I think the reporter asked about when the trial will be completed, we have about a third of the children enrolled at this point and we anticipate that the trial will be done in approximately a year. By the time we get the data together and take a look at it, I would say we hopefully will have the results available to the public within 18 months to 24 months.

Dr. Nabel — Terrific. I'm going to ask Dr. Stoloff and then Dr. Boushey to comment on assessment of risk.

Dr. Stoloff Thank you, Dr. Nabel. This is Dr. Stoloff. Assessment of risk, number one, you go back to previous history of risk, so you will ask about emergency room visits, unscheduled visits to the office or urgent care, or hospitalization. Near fatal asthma would be someone who unfortunately not only was hospitalized, but ended up in an intensive care unit and had to be intubated.

Then one of the keys is lung function. There are studies, especially in children, both from this country and in foreign countries, in which they've looked at the level of the lung function, how much airway obstruction in a person who appears well, and then look at the following year, and we've identified the lower the lung function, where it isn't normal, the higher their risk of having a worsening event, what we call an exacerbation, an asthma attack. So the history of what's gone on in the previous year, what's gone on in the last month or months, as well as combined with lung function affords the clinician an opportunity to have an assessment of risk of, number one, an attack; number two, of where the lung function will be; and then number three, from talking about the risk of an adverse or a side effect from medication is evaluating the patient as well as taking a history. At that point, I'll pass it on to Dr. Boushey.

Dr. Boushey Nice summary, Stuart. When a patient comes in, the clinician, by these guidelines, should be assessing current impairment. And as Stuart also said, we've proposed, in the guidelines, these models of questionnaires that have been validated that take very little time but ensure that you've asked about interruptions of sleep, inability to work or go to school, frequency of symptoms, and frequency of need for albuterol, a rescue medication. The second focus is on estimating risk of events in the future, particularly exacerbations. The strongest predictor, as Stuart said, is to have a history of having them.

The next best validated predictor is the level of lung function. Measuring spirometry, a very easy test, is not universally done, especially in primary care offices, although now the new devices that are made are easy to use and provide validated methods, so we're encouraging greater use of spirometry in the assessment of patients with asthma, both at the initial assessment and to determine whether they're well controlled, because, as several people have said today, even if a person has few symptoms they still may be at high risk. One of the ways of identifying a person being at high risk is their lung function is poor, and you want to encourage that patient to stay on their controller medications and be sure they have the written action plan, what to do if they develop symptoms of worsening asthma.

There are people who have normal pulmonary function and no symptoms who still have severe attacks, this is an especially difficult group, and the guidelines refer to some of this very interesting research on measuring the amount, say, of nitric oxide in the air they exhale, that's a very easy test to do, or the number of eosinophils in their sputum. These also appear to be markers of risk of bad attacks in the future. So we have some methods now, history of previous exacerbations and pulmonary function, and we're getting better at it with these new methods, like measuring sputum, eosinophils, or exhaled NO, and identifying these people who face high risk, even though they feel like they're doing okay, over the last several weeks before they saw their physician.

Dr. Nabel Terrific. Thank you very much. We'll move on to the next question.

Moderator Our next question comes from Dianne Debrovner with *Parents Magazine*. Please go ahead.

D. Debrovner I assume that most children with asthma are treated by their primary care physician, their pediatrician, or their family practitioner, who obviously are hard-working and busy. I'm wondering if there's some top priorities in terms of ways in which asthma specialists could help pediatricians do

things a little bit differently. Are there some medication dosing habits that you would suggest that they re-think, or that they need to be spending a little bit more time on inhaler education? What would be some priorities for primary care physicians in particular?

Dr. Nabel I guess I'll ask Dr. Stoloff, who is a primary care physician, to address that first. And then ask any of the three of you who might want to expand ...

Dr. Stoloff Thank you, Dr. Nabel. I'm actually a solo family physician in Carson City, Nevada, where I've been for over 29 years, and the main thing I used to do was deliver babies, so I'm well aware of the difficulties and the time constraints in practice, as other members of our panel are from different aspects. I think that, number one, what we're doing in this document, and that we're using our previous documents to expand upon, is providing better ways within the time constraints to assess as well as monitor infants, children and adults, questionnaires that can easily be utilized within a matter of minutes and are validated and help provide information on the level of impairment, limitations.

Number two, we're further expanding and reiterating on the need to have individuals show that they can use their medications properly, these inhalers, since everyone with asthma, whether they have intermittent or

daily, what we call "persistent asthma" they need to know how to use their rescue medication, albuterol and other agents, properly in the devices, or for the parent to know how to use it properly in children who cannot self-administer. So I think that really what this is doing is we're trying to put into a concise way within the time constraints of the individual in practice, that they can give good care in a very chronic disease.

Dr. Boushey This is Homer Boushey. The question had to do with how can a specialist help the primary care physician, what would be the key messages? Is that right?

D. Debrovner Yes.

Dr. Boushey And you're quite right, over 70% of people with asthma, or by the way, COPD, get their care from a primary care physician, not from a specialist. In the specialty community some of us do believe that we have an obligation to help the primary care physician deliver the best care under the real demanding conditions of primary care practice. Dr. Stoloff joined a group with the American Thoracic Society in studying ways of introducing spirometers into primary care practices, so people can use them readily and easily and interpret the results accurately, because we do think that's important.

The message, when I speak to primary care physicians, is that the prescription and use of inhaled corticosteroids is impeded by popular myths making people fearful of inhaled corticosteroids. People are confused about the distinction between an anabolic steroid, as athletes take them, or systemic corticosteroids that can cause very serious side effects, and inhaled corticosteroids, of which very small amounts are absorbed into the bloodstream, that really are quite safe, even safe in growing children, and their effects on growth are transient. The evidence is that children achieve absolutely the predicted height, no different from their non-asthmatic siblings or their predicted height from their parents, and that inhaled corticosteroids, and we've had large studies of them, inhaled corticosteroids are effective and they are safe and we should be comfortable prescribing them and encouraging their use, because they're so effective in treating asthma.

Dr. Lemanske This is Dr. Lemanske. I'd just like to add something to the comments of my colleagues. As a specialist, one of the, I think, simple messages that we could hopefully get to our primary care colleagues is since asthma is a chronic disease probably one of the most important things about dealing with it is to see the patients on a regularly scheduled basis, not just when they're sick but when they're doing hopefully okay. And this is especially

important in the framework that we have now with regards to control, to be able to assess their current degree of symptoms and impairments, as well as looking over a period of time in terms of what their relative risks would be based on their previous performance, if you will, during certain seasons, or of previous control during certain seasons, etc., so just basically to see the people more often. This is a chronic disease, and emphasize that instead of doing crisis management all the time to really try to get the disease under control over a long, long period of time.

Dr. Boushey Good point.

Dr. Nabel Excellent. I think we have time for two more questions. I'll ask that we keep both the questions and the answers succinct. Next question, please.

Moderator A follow up question comes from Rob Foreman with *CBS Early Show*. Please go ahead. Mr. Foreman, your line is open.

R. Foreman I'm sorry, I had the mute on. Thank you. We've spoken tangentially but haven't really addressed the ultimate lung damage that people with asthma can suffer, and I guess two parts to the question. How much does the episodic or chronic control prevent the longer term damage? And can you

please define what some of the longer term damage is, and if the episodic has to be supplemented to prevent the long term.

Dr. Nabel — Dr. Boushey, could you please address that?

Dr. Boushey — It's a very good question. Studying older people with asthma, over age 50—I'll try to be brief, sorry—we know that people who have had asthma for many years may have irreversible airflow obstruction, their lung function is as if they had smoked a pack a day since they were 18-years-old, and they've never smoked and never been in a dusty occupation. It's not a big group, but it's definitely there, so some patients with asthma develop irreversible progressive narrowing of the airways. It's a common belief, but it's not yet proven, that good asthma control, especially controlling the inflammation of asthma with an inhaled corticosteroid, reduces the risk of this developing. But to be perfectly honest, we're not sure even of that, it's just the best we can do and it makes sense, but that has not been proven, that good control will prevent this. It happens in a sub-group, and there are so many other reasons for achieving good control we're sure people should do it, and it's a question that remains outstanding. Bill, I think you should comment too, Dr. Busse.

Dr. Busse I think, Homer, you summarized that very, very nicely. Again, it's not like emphysema, but it's part of asthma. And again, some of the concepts are not fully defined, but there is evidence emerging saying that maybe each time you have one of these severe exacerbations it's what's leading to the progressive loss of lung function, and it may fit with the greater focus on trying to prevent future risks.

Dr. Nabel Excellent. Thank you. I think we'll take our last question now.

Moderator Our last follow up question comes from Denise Grady with *New York Times*. Your line is now open.

D. Grady Thank you. This is, I think, a quick question, and it's because we have not yet seen the guidelines. I just wondered if you could give us an idea of whether or not there is any more role for cromolyn with any patients in either inhalers or nebulizer?

Dr. Nabel Dr. Lemanske.

Dr. Lemanske Thank you, Dr. Nabel. This is Dr. Lemanske. We still have cromolyn in the guidelines with regards to chronic therapy. There are clearly medications that we have available to us that are going to be more

effective than either cromolyn or nedocromil. The place that I would use cromolyn or nedocromil therapy would be for prevention of exercise induced asthma. This class of medication is probably not as effective as albuterol is, or the beta agonists, but in certain patients it can be very effective and very helpful in trying to prevent the exercise induced asthma from developing, so that's kind of where we have put the focus on that class of medication.

Dr. Boushey If a child's doing well on cromolyn, though, Rob, it's still in the guidelines as an alternative to inhaled corticosteroid treatment. If the child is doing very well, don't necessarily change the child's treatment.

Dr. Lemanske That's exactly right, you don't try to fix something that isn't broken.

Dr. Boushey There you go.

Dr. Lemanske So it's still there, but we have studies to show that the ... trial, for example, comparing long term use of inhaled corticosteroids with a cromolyn-like molecule and nedocromil, showing that for most of the outcome measures, if not all of the outcome measures that were looked at, the inhaled corticosteroid was clearly more effective. So that's the position we've taken with the medications.

D. Grady And what about cromolyn use in adults, any of you?

Dr. Stoloff This is Dr. Stoloff. I think that cromolyn use, that there are better medications where the data is much more apparent, much more robust, that shows over time people with other medications which are in fact easier to use, less frequency of use on a daily basis, will provide better control and better ability to decrease, therefore, both their impairment and their future risk. So we have preferred therapy and alternative therapy, there is no position in the document where cromolyn or chromones are put as preferred therapy. Inhaled corticosteroids are the foundation of care, both in infants, in children, in pregnant women, in adults, and in the older population.

Dr. Nabel Thank you very much. That was our final question. I simply want to thank all of you for calling in today. We know that you have a vital role in communicating these health messages to the public, and we appreciate your work and we thank you very much for the service that you provide.

For any of you who called in late, there will be a re-broadcast of this teleconference. It will be available for 24 hours. A transcript of the call will also be posted on our NHLBI Web site. That can be found at

www.nhlbi.nih.gov, and then simply click on Newsroom. Any reporters who have additional questions or who would like to arrange an interview with any one of us panelists please feel free to call our NHLBI communications office, and that number is 301-496-4236. Thank you again very much for your participation.

Moderator — Ladies and gentlemen, this conference will be available for replay after 2:30 p.m. today through August 31st at midnight. You may access the AT&T TeleConference Replay System at any time by dialing 1-800-475-6701 and entering the access code 882901. International participants dial 320-365-3844.

That does conclude our conference for today. Thank you for your participation and for using AT&T Executive TeleConference. You may now disconnect.