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Guest Editorials

Allergy and immunology practice parameters and guidelines
The new normal

It's spring break, and you're seeing a college student who has a history of moderate-to-severe spring and summer rhinoconjunctivitis. Skin testing shows remarkable wheal and flare reactions to tree and grass pollens. In addition to recommending aeroallergen avoidance measures, which initial treatment has the highest likelihood of helping this patient: intranasal corticosteroid monotherapy or intranasal corticosteroid combined with intranasal antihistamine? Previous practice parameters tended to outline treatments with good evidence of effectiveness, but they rarely provided specific recommendations for these types of questions.

A Turning Point

The allergic rhinitis parameter update that appears in this issue of the *Annals*[1] marks a turning point for the Joint Task Force on Practice Parameters (JTFPP). Previous parameters tended to cover an entire condition from diagnosis to treatment, whereas the new guidelines will focus on a few important questions for each topic with the goal of answering them based on a rigorous systematic review of the medical literature. To express the answers as clearly as possible, we have adopted the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) framework[2] with the support of the American Academy of Allergy, Asthma & Immunology (AAAAI) Board of Directors and the ACAAI Board of Regents. Although this will result in smaller, more focused parameters, we anticipate that the results will prove to be as useful to the allergy-immunology community as the previous, more inclusive parameters have been.

Formation of the JTFPP

Of the many individuals who have contributed to the success of the JTFPP, there are 2 who merit special mention.

In 1987, during his AAAAI presidency, Albert Sheffer accurately perceived the challenges our specialty would face in future years and set wheels in motion that led to the formation of the JTFPP in 1989. In his memoirs, Henry Kissinger pointed out, "All great leaders walk alone. Their singularity springs from their ability to discern challenges that are not yet apparent to their contemporaries."[3] The formation of the JTFPP occurred before the managed care era,[4] in which our diagnostic and therapeutic interventions would require justification to payers, and long before the current transition from volume-based to value-based reimbursement.[5]

Richard Nicklas served as co-chair of the JTFPP representing the AAAAI from its inception until July 2016. During this time, the JTFPP published 50 practice parameters focused on topics central to the practice of our specialty, including but not limited to allergen immunotherapy, anaphylaxis, atopic dermatitis, drug allergy, exercise-induced bronchospasm, food allergy, immunodeficiency, rhinitis, sinusitis, stinging insect hypersensitivity, and urticaria and angioedema.

The JTFPP developed parameters that served to establish boundaries of appropriate patient care for conditions within the spectrum of allergy and immunology, with the goal of encouraging improved outcomes for patients with allergic and immunologic disorders. Management practices associated with improved outcomes, such as routine assessment of control in patients with asthma, were encouraged,[6] whereas management practices not associated with improved outcomes, such as extensive and routine diagnostic testing in patients with chronic urticaria with an otherwise unremarkable history and physical examination, were discouraged.[7]

The Need for Change

The earliest practice parameters consisted of a series of recommendations, each followed by a narrative text with citations to support them. Starting in 2005 with the food allergy parameter,[8] it became clear that we needed a way to describe the quality of the evidence each recommendation was based on because that would influence its validity. To do this, each reference was graded and the grades of the underlying references were used to categorize the strength of evidence for each recommendation. The classification system for evidence and the strength of recommendation based on that evidence are presented in Table 1. This system for making recommendations had some shortcomings. A therapeutic intervention reported to be efficacious in a randomized controlled trial (RCT) was awarded a Level "A" recommendation, whereas a therapy for which an RCT had not been published could not be categorized as Level "A," although it also might be effective. It became clear that the quality of evidence supporting a recommendation did not necessarily correspond with how important it was to follow that recommendation. For this reason, another system was added that specified how important it was that the recommendation be followed (Table 2).

More recently, concerns have been raised about how the evidence supporting each recommendation is identified. Previous parameters were developed without a rigorous, systematic review of the literature, implying that bias could have been introduced by not considering all evidence bearing on a particular recommendation. In addition, the process by which evidence was obtained

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Table 1
Classification of Level of Evidence and Strength of Recommendations Traditionally Used for Our Practice Parameters

Category of evidence	
Ia	Evidence from meta-analysis of randomized controlled trials
Ib	Evidence from ≥1 randomized controlled trial
IIa	Evidence from ≥1 controlled study without randomization
IIb	Evidence from ≥1 other type of quasi-experimental study
III	Evidence from nonexperimental descriptive studies, such as comparative studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities or both
Strength of recommendation	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated recommendation from category I evidence
C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
LB	Laboratory based

and appraised and the course taken moving from evidence to recommendations were not transparent. The recommendations made in our parameters often were based on consensus rather than strictly based on evidence, with no clear information provided describing how a consensus was reached. The JTFPP has taken strides to improve the development process and presentation of management recommendations, such that our parameters are increasingly based on evidence, more transparent, and consistent with Institute of Medicine (IOM) criteria for guidelines.[9] In addition, more details describing the development process are provided in the preface of our parameters, including potential conflicts of interest and how these are resolved in the context of guideline development. Although evidence-based medicine principles such as number-needed-to-treat calculations, likelihood ratios, and systematic reviews were used in several parameters,[6,7,9] others lacked this type of rigor. The new generation of guidelines will consistently achieve this degree of transparency and rigor.

The GRADE Approach

As presented in Table 3, the GRADE approach has some clear advantages.[2] The GRADE system classifies recommendations in a binary fashion as strong or weak and quality of evidence as high, moderate, low, or very low. An RCT begins with a high level of confidence in the quality of the evidence, but the GRADE system entails an analysis of possible limitations in each RCT that can lead to a downgrading of quality based on a critical appraisal of aspects of the RCT[10] that includes questions such as:

Table 2
Revised Classification of Level of Evidence and Strength of Recommendations Used More Recently for Our Practice Parameters

Recommendation rating scale		
Statement	Definition	Implication
Strong recommendation (StrRec)	A strong recommendation means the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent (Grade A or B)*. In some clearly identified circumstances, strong recommendations might be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate (Mod)	A recommendation means the benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (Grade B or C)*. In some clearly identified circumstances, recommendations might be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Clinicians also should generally follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Weak (Weak)	An option means that the quality of evidence that exists is suspect (Grade D)* or that well-done studies (Grade A, B, or C)* show little clear advantage to one approach vs another.	Clinicians should be flexible in their decision making regarding appropriate practice, although they can set bounds on alternatives; patient preference should have a substantial influencing role.
No recommendation (NoRec)	No recommendation means there is a lack of pertinent evidence (Grade D)* and an unclear balance between benefits and harms.	Clinicians should feel little constraint in their decision making and be alert to new published evidence that clarifies the balance of benefit vs harm; patient preference should have a substantial influencing role.

Category of evidence	
Ia	Evidence from meta-analysis of randomized controlled trials
Ib	Evidence from ≥1 randomized controlled trial
IIa	Evidence from ≥1 controlled study without randomization
IIb	Evidence from ≥1 other type of quasi-experimental study
III	Evidence from nonexperimental descriptive studies, such as comparative studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities or both
Strength of recommendation	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated recommendation from category I evidence
C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
LB	Laboratory based
NR	Not rated

*Strength of recommendation as defined in the lower panel of Table 2.

Table 3
Advantages of the GRADE System for Classification of Level of Evidence and Strength of Recommendations

Separation between quality of evidence and strength of recommendation
Ability to downgrade or upgrade evidence based on methodologic criteria
Consideration of the relative importance of various outcomes to patients
Assessment of values and preferences in association with making recommendations
Clear understanding of the implications of "strong" and "weak" recommendations

Abbreviation: GRADE, Grades of Recommendation, Assessment, Development, and Evaluation.

- ☐ Was assignment of subjects randomized?
- ☐ Was there concealment of randomization?
- ☐ Except for the experimental intervention, were the groups of subjects treated equally?
- ☐ Were subjects, study personnel, and outcome adjudicators "blinded" to treatment?
- ☐ Were subjects analyzed in the groups to which they were randomized?
- ☐ Was follow-up complete?

When major methodologic shortcomings are identified, the quality of evidence can be lowered. Alternatively, observational studies begin at a low level of quality but can be upgraded based on consideration of factors such as effect size or whether there is a remarkable dose-response gradient. The GRADE approach entails a transparent process, in which there is a clear separation of evidence from recommendations. For instance, using the GRADE system we can make a strong recommendation when an intervention offers benefit that outweighs considerations of harm, burden, or cost—such as epinephrine administration for acute anaphylaxis—despite the absence of an RCT demonstrating efficacy. We can stipulate in the context of moving from evidence to recommendations, as we did in our current allergic rhinitis guideline,[1] that based on the balance of the potential for benefit compared with the potential for harm or burden and consideration of cost, use of combination intranasal corticosteroid and intranasal antihistamine, compared with intranasal corticosteroid monotherapy, is associated with a weak recommendation. With a strong recommendation, the decision-making process is more straightforward: most patients should receive (or not receive) the recommended management. A weak recommendation is a navigational signal for clinicians indicating that treatment decisions can vary based on patient circumstances and implies further research is very likely to have an important impact on our confidence in the estimate of effect and can change the estimate. This evidence-based management recommendation means that for our college student seen at spring break, it is important to carefully consider the potential for benefit, compared with the potential for harm and burden, cost, and patient circumstances, and invite our patient to express her values and preferences and participate in the medical decision-making process. Our patient will consider what the advantages are for combination therapy compared with intranasal corticosteroid monotherapy. The allergy-immunology clinician can serve a vital role in guiding this patient to a decision that is in her best health care interest.

The allergic rhinitis guideline appearing in this issue of the *Annals*[1] will be accompanied by a companion synopsis of our management recommendations for pharmacotherapy of allergic rhinitis that will appear in the *Annals of Internal Medicine.* In addition to these documents, we plan to publish a more traditional "practice parameter" on allergic rhinitis that you can expect to see in the *Annals of Allergy, Asthma, and Immunology* in the next several months.

We welcome feedback regarding our first GRADE-based guideline. Our transition to use the GRADE framework for our guidelines is consistent with recommendations from the IOM[9] and reflects our desire to engage in a process of continuous performance improvement in developing future iterations of our "guidelines" and "parameters." We hope that you will find them useful.

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Could calcium channel blockers treat 2 illnesses with 1 pill?

Ever since Middleton's[1] suggestion that excessive permeability of airway cells to calcium ions might play a role in the underlying mechanism of bronchial hyperresponsiveness (BHR) and asthma, researchers have questioned whether calcium channel blockers (CCBs) might be efficacious in the treatment of this illness. Their potential utility makes a great deal of sense, because cytoplasmic calcium is involved in bronchoconstriction, mast cell mediator release, vagal reflex stimulation, airway mucous gland secretion, chemotaxis of eosinophils, and possibly even smooth muscle remodeling.[2,3] Despite this theoretical possibility, multiple studies of the efficacy of CCBs in asthma

Disclosures: Dr Oppenheimer is a consultant for GlaxoSmithKline, Teva, DBV, Kaleo, and Church & Dwight; is on adjudication committees for Quintiles, PRA, and ICON; is associate editor of the *Annals of Allergy* and *Allergy Watch*; is chief editor of *Medscape* (pulmonary); and a reviewer for *UptoDate*. Dr Kelly has nothing to disclose.