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Cost-effectiveness of pediatric asthma treatments

To the Editor:

In a recently published review, Spahn and Szefer¹ summarized progress made during the past 15 years in the management of childhood asthma and discussed the need to recognize asthma early and to identify the most effective and safe treatment for early and long-term asthma control. Several important new classes of medications are currently being used in the treatment of persistent asthma in children, and their placement in the hierarchy of available asthma medications will evolve as data from controlled clinical trials and real-world experience accumulate. Current guidelines recognize inhaled corticosteroids as the cornerstone of asthma therapy. Inhaled corticosteroids provide greater overall asthma control than nonsteroidal controllers, including cromolyn, theophylline, and leukotriene modifiers. For example, a study by Leflein et al² demonstrated that budesonide inhalation suspension was more effective than nebulized cromolyn sodium and was well tolerated in young children with mild to moderate persistent asthma.

One important issue not discussed by Spahn and Szefer is the cost-effectiveness of competing asthma treatments. Cost-effectiveness studies are a new and rapidly evolving area of interest to health care providers. In light of the substantial morbidity and economic burden of asthma, the "National Asthma Education and Prevention Program Working Group Report on the Cost Effectiveness of Asthma Care"³ has emphasized the need for cost-effectiveness studies of asthma treatments. A recent study by Smith et al⁴ reported that the number of emergency department visits was halved in a group of patients after the start of inhaled corticosteroid treatment, whereas the number of emergency department visits in patients not receiving inhaled corticosteroids nearly doubled. Higher prescription payments for patients using inhaled corticosteroids were offset by reductions in medical visits and other medical costs, resulting in similar Medicaid payments between the groups. Despite the limitations of this study (eg, the retrospective design), it demonstrates the utility of cost analysis to guide treatment decisions. Similarly, a second study reported by Adams et al⁵ demonstrated a significant protective effect of inhaled antiinflammatory therapy on the risk for hospitalization and emergency department visits in children with asthma. In a Swedish study, Andersson et al⁶ further demonstrated that budesonide was more cost-effective than sodium cromoglycate (cromolyn sodium) and resulted in fewer drug switches to maintain asthma control.

Ideally, cost-effectiveness studies should take into consideration the benefits and risks associated with treatments. Spahn and Szefer explained that the Childhood Asthma Management Program (CAMP) Research Group study⁷ was the first prospective, randomized trial specifically demonstrating a reduction in significant asthma exacerbations that lead to hospitalizations, urgent care visits, and prednisone courses. Importantly, safety data from the CAMP study regarding estimated final adult height, bone mineralization, and ocular disorders with budesonide were reassuring.

In summary, given the substantial economic burden of asthma, optimal disease management must now take into consideration the efficacy and the safety of competing asthma treatments as well as their cost-effectiveness. Research regarding the relative cost-effectiveness of inhaled corticosteroid use in children will be especially valuable. As new data from CAMP are published, additional insight into factors to be included in such studies can be ascertained.

Kevin R. Murphy, MD
Midwest Children's Chest Physicians

8552 Cass St
Omaha, NE 68114

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Atopic dermatitis and the clinical effect of house dust mite avoidance

To the Editor:

I have read with great interest the report by Oosting et al.¹ Theirs was a very thoroughly performed prospective investigation of the clinical effect of house dust avoidance strategies on the course of atopic dermatitis (AD).

However, I would like to make 5 remarks:

1. The authors performed a subgroup analysis by dividing the patients into 4 subgroups with low and high Der p1 exposures and low and high AD scores. The authors did not observe significant differences in clinical effect among these 4 groups. Surprisingly, there is no subgroup analysis regarding the outcome of the atopy patch test (APT). It has been proposed that APTs indicate the clinical relevance of house dust mite exposure in AD²; this subgroup analysis would therefore have been interesting. Instead, the authors performed an analysis using the APT as secondary outcome measure. This analysis seems to be less useful: A nickel contact dermatitis is expected to improve when the allergen is avoided, but the patch test reaction is not expected to disappear within 1 year.
2. The authors state that one of their inclusion criterion was a specific IgE (anti-Der p1) value greater than 0.7 kU/L. However, in Table V there are patients (ranges, 0.2-90 and 0.3-90 kU/L) with values below this threshold.
3. The authors state that our previous study on the same topic³ had "low power" inasmuch as only 10 patients in 2 treatment groups were described. This is not true; in our study, 20 patients (not 10 patients) were investigated. Moreover, the study was powerful enough to show a highly significant effect on reduction of allergen levels, though this was not accompanied by a clinical effect.
4. The authors' subgroup analysis (as described above) yielded groups of statistically less than 10 patients (35:4 = 8.75; 38:4 = 9.5). Hence their own analysis, according to their definition, would be of "low power."
5. In conclusion, AD is a heterogeneous disease with (as mentioned above) a number of different subgroups (eg, adult/child-

dren, extrinsic/intrinsic type, house dust mite monosensitization/polysensitization, negative/positive atopy patch test, and low/high antigen exposure).⁴ It is desirable that in the future studies enrolling a statistically reasonable number of patients be performed in order to stratify for all of these different factors.

Carsten Gutgesell, MD
von-Siebold- Straße 3
D-37075 Göttingen
Germany

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Reply

To the Editor:

In response to Dr Gutgesell's 5 points:

1. The objective of our study¹ was to investigate whether encasings could reduce house dust mite (HDM) allergen in a domestic setting, resulting in an improvement of clinical symptoms of allergic dermatitis (AD) as measured with the Leicester sign score (LSS). Although a positive relation between the distribution pattern of AD (mainly at air-exposed body parts) and the APT score has been reported,² several other authors have reported no relationship between APT score and clinical response^{3,4}; indeed, an inverse relationship was reported by Gutgesell and colleagues themselves.⁵ Therefore, we choose to use the LSS as a primary outcome measure and the APT score with HDM as a secondary outcome measure. Subgroup analysis with positive and negative APT scores did not result in significant differences between placebo and treatment groups in our study.
2. As shown in our article's Table I, the HDM RAST inclusion criterion was (a) a specific IgE of 0.7 kU/L or (b) a skin test index of 0.7. Although there is a high correlation between these 2 tests, differences can occur. Such differences accounted for the lower range of our specific IgE results.¹
3. In the 2001 study of Gutgesell et al,⁶ a lack of clinical effect was shown despite a significant reduction in HDM allergen. In that study, only 10 patients in each treatment group (20 patients in all) were included, and a lack of discriminative power could still account for the lack of significant clinical effect. Because Tan et al⁷ saw a decrease in the LSS score of 20% in the placebo group and 50% in the active treatment group, we calculated beforehand that we needed at least 30 patients in each treatment group. In our study, 73 patients completed the whole study—35 patients in the placebo group and 38 patients in the treatment group. Furthermore, no clinical effect on AD was seen in our study despite a significant reduction in HDM allergen. The power of our study was comparable with that of the study of Tan et al.⁷
4. Because subgroup analysis yielded groups of fewer than 10 patients, the power was indeed low. Accordingly, the data for this analysis were not shown. This was noted in our article.¹
5. We agree with Dr Gutgesell that AD is a heterogeneous disease and that patients with AD can be divided on the basis of differ-

ent characteristics into smaller subgroups. The goal of our study was to select patients who would normally get encasings according to their sensitization to HDM combined with clinical symptoms of AD, allergic asthma, and/or allergic rhinitis in a Dutch setting. Gutgesell proposes several characteristics by which such subgroups can be created. Differentiation on the basis of age (eg, in adulthood and young childhood) seems to be meaningful, inasmuch as it takes into account the immune system's maturation, the variability of which could result in different reactions to environmental allergens.^{8,9} On the other hand, differentiation on the basis of extrinsic AD/intrinsic AD is not meaningful, because by definition patients with the intrinsic type of AD are not allergic; in the Netherlands, they would not get encasings to prevent exacerbation of AD. Differentiation on the basis of monosensitization/polysensitization is likewise not meaningful: Although a significant clinical effect might be proved in future studies, only a small percentage of patients with AD are sensitized to HDM alone and would benefit, and applying rigorous measures for this group alone would probably not be cost-effective (which seems to be becoming a more and more important criterion for therapy). Differentiation on the basis of low/high antigen exposure might be meaningful, but in most domestic environments HDM antigen exposures are found to be below 10 g of Der p 1 + Der f 1 per gram of dust, and reduction of the antigen concentration below this level seems to have had limited or even no clinical effect on allergic rhinitis, allergic asthma or AD in most randomized, double-blind, placebo-controlled studies of 1 year's duration.^{1,7,10-15}

Albert-Jan Oosting, MD, PhD

Marjolein S. de Bruin-Weller, MD, PhD

Carla A.F.M. Bruijnzeel-Koomen, MD, PhD

Department of Dermatology and Allergology

University Medical Center Utrecht

Utrecht

The Netherlands

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