Editorial

Allergen immunotherapy: Much more than a shot in the dark

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Allergic rhinitis (AR) is a prevalent disease that can significantly affect the well-being, productivity, and quality of life of children and adults. Allergen immunotherapy has been used to effectively treat AR for more than 100 years and is unique among available therapeutic interventions in its ability to modify AR's course. In addition, there is evidence that it prevents new sensitizations. Thus, it is important to establish whether subcutaneously administered allergy immunotherapy (AIT) is associated with lower health care costs. In this issue, Hankin et al[1] examine its cost benefits in adults and children.

Hankin et al[2,3] have previously addressed this question in Florida Medicaid-enrolled children younger than 18 years, newly diagnosed with AR and not previously exposed to AIT. In the earlier study, only 3% of the children with a new AR diagnosis received AIT, more than half for less than a year, and 84% for less than 3 years. The study compared health care costs and use in the 6 months before and after initiating AIT and found pharmacy, outpatient, and inpatient use and costs reduced in children receiving AIT.[3]

For the current case-control study, the authors again used Florida Medicaid claims data of health care use and costs.[1] The data set included all ages and compared 18-month health care costs of those newly diagnosed with AR who received *de novo* AIT with those who did not. The investigators compared children (younger than 18 years) and adults (at least 18 years) separately and all together. They found that AIT-treated subjects had significantly lower average total health care costs than matched controls, with cost reductions observed within 3 months of starting AIT. The cost reductions (30% in adults, 42% in children) remained significant when each group was analyzed separately. The average 18-month health care cost savings conferred by AIT did not significantly differ between age groups. Although adults were less likely to be diagnosed with AR, they were 1.3 times more likely to initiate AIT.

To be included in the AIT group, patients had to have received at least 2 AIT injections. They were matched with up to 5 controls with newly diagnosed AR who had not received AIT and according to the following variables: age within 6 months of first AR diagnosis; sex; race/ethnicity; illness burden measured by the Charlson Comorbidity Index[4,5]; treatment initiation date; and other allergy-related conditions (asthma, conjunctivitis, and atopic dermatitis). The Charlson Comorbidity Index predicts health care utilization and costs in a primary care patient with a range of comorbid conditions including cardiovascular disease, HIV/AIDS, and cancer. Both the AIT and control groups were also required to have at least 18 months of follow-up.

Hankin et al are to be congratulated for their thorough analysis and for focusing attention on the cost versus benefits of AIT and in so doing raising interesting issues about what we know of the benefits of AIT. Although there were fewer inpatient stays (overall and for children), fewer outpatient visits excluding those for AIT, and lower total health care costs among those receiving AIT, one issue is whether those patients selected for AIT were healthier. Indeed, those receiving AIT had a lower overall disease burden as measured by the Charlson Comorbidity Index; however, they had more upper respiratory tract infections, sinusitis, nasal polyps, and some other respiratory diseases than did the matched controls. Separate from this issue, the matching process resulted in the unintended exclusion of sicker patients in both the AIT-treated and matched control groups. Of 5760 eligible patients, 793 receiving AIT could not be matched with controls and were excluded from analysis. Those AIT-treated patients who were not matched and were excluded were more likely to have comorbid conditions, measured by the Charlson Comorbidity Index, more likely to have asthma, and less likely to have atopic dermatitis or conjunctivitis, when compared with the AIT-treated matched patients included in the analysis. Overall, more eligible adults than children were not matched (21% vs 12%).

It is unclear why a cost benefit of AIT was observed before therapeutic benefit typically occurs—as the authors note, at least 3 years of AIT is recommended by national guidelines.[6] Also, among subjects newly receiving AIT, the median number of administrations over 18 months was 13 and in adults, it was only 6. Nonetheless, cost benefit was seen as early as 3 months. This suggests that either the direct benefit of AIT occurs earlier than expected or in addition to its direct benefit, AIT confers indirect benefit via increased medical supervision. Additional study will be necessary to clarify this interesting observation.

Another thought-provoking finding in both this and in previous analyses by the investigators is that only a very small percentage, less than 3% of newly diagnosed patients with AR, received AIT. This finding suggests that access to AIT may be limited. Furthermore, among those who had at least 2 injections, 31% (2610 of 8370) did not have at least 18 months of enrollment and presumably discontinued AIT, although reasons other than problems of access, such as the possibility that patients moved away and could no longer participate, or that they no longer qualified for Medicaid, cannot be excluded. These same findings also raise the possibility that adherence may be difficult. Although adherence was not addressed in this study, it is another subject for further investigation.

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Total outpatient cost savings over 18 months from the initiation of AIT were nearly 3 times greater in AIT-treated children than in AIT-treated adults. To better understand this dichotomy, it will be important to follow the AIT-treated children and controls as they transition into adulthood. At present, however, the data are inadequate to explain why outpatient cost savings were lower in the adults—that is, whether they had more comorbidities, or less accurate diagnosis, or whether the impact of AR changes as individuals age. In addition, why were adults more likely than children to receive AIT? Was it because adults on the whole tolerate injections better, or were they less responsive to other therapeutic interventions for AR?

Finally, as the authors note, the long-term cost savings beyond 18 months are not captured by this analysis. Patients successfully receiving AIT generally will have lasting benefit for years and in addition may be less likely to acquire new sensitivities that also would have required treatment; therefore, one would expect the cost savings to increase over time, and so a longer comparison is necessary.

In summary, Hankin et al confirm that AIT provides substantial cost savings for children and adults with AR who do not have major non–allergy-related comorbidities, and those are the patients for whom we generally recommend it. Barriers to access and barriers to adherence require study. We also need to understand why the cost-saving benefits of AIT appear so early in the course of therapy. Long-term studies would be beneficial to assess the true cost savings. As the authors note, the generalizability of their analysis may be limited by the geographic restriction and by restriction to Medicaid patients. The Medicaid population, a population rarely used in clinical trials, is an important one to study and to determine how these patients and AIT treatment and costs differ from the general population. Finally, this study prompts similar questions regarding sublingual immunotherapy.

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