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Preface to outcome measures in allergic rhinitis

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Allergic rhinitis represents a global health care problem, affecting an estimated 10% to 25% of the population,^{1,4} with higher figures from some countries, in which approximately 40% of children have symptoms compatible with allergic rhinitis.^{5,6} Allergic rhinitis has been calculated to affect 20 to 40 million individuals within the United States annually.^{7,8} The effect of the disease is often underestimated. Because rhinitis is not life-threatening and the nose can be bypassed, so to speak, by oral breathing, the disease is often trivialized. Quality of life evaluation reveals, however, that allergic rhinitis has a significant effect on well-being beyond the presence of nasal symptoms.⁹ Allergic rhinitis has been found to impair work and school performance¹⁰⁻¹³ as well as learning ability and is a major cause of lost school attendance and work absenteeism.¹⁴ It has been calculated that in 1 year in the United States, there are a staggering 811,000 missed workdays, 4,230,000 reduced productivity days, and 824,000 school absences caused by rhinitis.¹⁴ Thus, there

are not only personal health costs but also direct and indirect costs of the disease in health-economic terms.

Allergic rhinitis is 1 of the 10 top conditions that commonly lead to consultation in managed care populations in the United States.¹⁵ For 1996, it was calculated that the direct financial cost of rhinitis in the United States exceeded \$3 billion, and there were additional costs of \$4 billion for its effect on concomitant conditions such as asthma and otitis.¹⁶ The relevance of rhinitis to the health care costs of these comorbid conditions has been illustrated by a study of direct medical costs of illness in US children with and without asthma.¹⁷ Children with asthma had 3.1 times as many prescriptions, 2.2 times as many emergency department visits, and 1.9 times as many ambulatory care visits as children without asthma. Further analysis of the data, however, revealed that only 26% of these additional costs were related to asthma-specific medical care and that a substantial part of these additional costs were related to upper airways illness such as rhinitis. Consistent with these findings, a population-based study of asthma costs identified that the yearly medical charges were, on average, 46% higher for patients with asthma and concomitant rhinitis than for patients with asthma alone.¹⁸ A more recent study has also identified that allergic rhinitis in patients with asthma almost doubles the annual medical resource utilization and costs and is associated with increased use of asthma-related medications.¹⁹ The presence of allergic rhinitis, once other factors had been controlled for, was associated with an increase in annual costs of more than \$350 per person. Rhinitis commonly coexists with asthma and may be overlooked if the individual is not assessed as a whole, and it is probable that a substantial amount of these additional costs may be saved with appropriate management of rhinitis. In populations in whom the treatment of rhinitis has been the focus of attention, this has been found to lead to reduced antibiotic prescribing, reduced consultations, and improved asthma control.^{15,20,21}

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In treating rhinitis, in addition to economic endpoints, there must also be personal endpoints. Classically, rhinitis is evaluated subjectively on the basis of patients' symptom reporting. The draft guidance provided by the US Food and Drug Administration, Allergic Rhinitis: Clinic Development Programs for Drug Products (www.fda.gov/cder/guidance/2714.htm) recommends the use of rating scale self-assessment by patients as the primary outcome, with an overall summed symptom score of individual symptoms of nasal itch, sneeze, rhinorrhea, and congestion to provide a composite single symptom score. Both an instantaneous symptom score (ie, an evaluation of symptom severity immediately before the next dose) and a reflective symptom score (ie, an evaluation of symptom severity after a predefined period such as 12 hours) are suggested. The basis for the indication that subjective symptom reporting is the most appropriate endpoint is that such an approach is the best-validated method and that alternatives are less substantiated.

This dependency on subjective evaluation of symptom severity contrasts with evaluation in many disease areas, in which only objective criteria would be accepted. It is a reflection not only of the lesser validation of objective approaches for clinical trial evaluation but also of the failure of any single objective parameter to encompass adequately the spectrum of manifestations of rhinitis. It is appreciated, however, that such subjective reporting may be influenced by factors other than disease severity and that the personal response to illness and an individual's perception of disease severity will vary within a population and will be modified by past experience as well as current events.

This supplement, enabled by an unrestricted educational grant from AstraZeneca, assesses a range of additional outcome measures that could be used in the objective evaluation of rhinitis severity, considering their applications and limitations. Where possible, each approach has been considered not only in relationship to disease expression but also to provide a more critical evaluation, encompassing considerations such as the repeatability of measurement, confounding factors, variables that affect measurement and, where available, comparisons with other nasal outcomes. In addition to outcome measures, considerations are given to trial design, adverse effects evaluation, and special disease situations such as pediatric nasal disorders and nasal polyposis.

The application of objective methods of evaluation to rhinitis should provide a more critical appraisal of the effect of treatment, provide a greater understanding of the spectrum of activity of current therapeutic approaches in managing the patient with rhinitis, and help guide future developments, focussing on therapeutic need, in this disease. Ideally, pulling together an evaluation of the range of potential approaches for the objective monitoring of rhinitis will stimulate further thought and consideration of the application of objective monitoring in the evaluation of the patient with rhinitis. It is hoped that this supplement will stimulate the more widespread exploration and evaluation of the use of objective monitoring in clinical trials in rhinitis.

We thank all of the participants in this supplement who generously gave up time to attend a workshop to discuss issues related to the monitoring of rhinitis and to make a special effort to prepare articles and apply their expertise to address the goals of the meeting and make this a successful project. These contributions have been grouped by theme into sections relating to subjective outcomes and adverse event monitoring in rhinitis, assessment of nasal mucosal inflammation, and assessment of nasal physiology and patency, and a final section on clinical trial design, challenge models, and adaptation to children, nasal polyps, and classes of medications. The components of these sections are attributed to identify the individual contributions, because within the unified themes, not all of the components may reflect the views of all of the authors. However, the synthesis has allowed easy assimilation of the different approaches within an area, an appreciation of their individual strengths and weaknesses, and an understanding of the complementary nature of different measures. Finally, we thank AstraZeneca, without whose support this supplement would not have been possible.

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