

# Severity and impairment of allergic rhinitis in patients consulting in primary care

Jean Bousquet, MD,<sup>a</sup> Françoise Neukirch, MD,<sup>b</sup> Philippe J. Bousquet, MD,<sup>a</sup>  
Pierre Gehano, MD,<sup>c</sup> Jean Michel Klossek, MD,<sup>d</sup> Martine Le Gal, MD,<sup>e</sup>  
and Bashar Allaf, MD<sup>f</sup> Montpellier, Paris, Poitiers, and Lyon, France

**Background:** Allergic rhinitis is a disease impairing quality of life, sleep, and work. A new classification for allergic rhinitis, Allergic Rhinitis and its Impact on Asthma (ARIA), has recently been proposed.

**Objective:** To study the effect of allergic rhinitis using ARIA definitions to determine severity and duration.

**Methods:** A total of 3052 patients consulting general practitioners for allergic rhinitis were studied. Patients were classified according to the 4 classes of ARIA. In all patients, quality of life (Rhinoconjunctivitis Quality-of-Life Questionnaire), sleep (Jenkins questionnaire), and work performance (Allergy-Specific Work Productivity and Activity Impairment questionnaire) were assessed.

**Results:** Mild intermittent rhinitis was diagnosed in 11% of the patients, mild persistent rhinitis in 8%, moderate/severe intermittent rhinitis in 35%, and moderate/severe persistent rhinitis in 46%. The severity of rhinitis has more of an effect on quality of life, sleep, daily activities, and work performance than the duration of rhinitis. In moderate/severe rhinitis, more than 80% of patients report impaired activities, as opposed to only 40% with mild rhinitis.

**Conclusion:** It seems that the term *moderate/severe* should be replaced by *severe*. A study in the general population is necessary, however, to assess the prevalence of the 4 ARIA classes of allergic rhinitis, especially in patients who are not consulting physicians for their symptoms. (J Allergy Clin Immunol 2006;117:158-62.)

**Key words:** Allergic rhinitis, classification, ARIA, intermittent, persistent

The recent Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations have proposed a new classification for allergic rhinitis.<sup>1</sup> Previously, allergic rhinitis was subdivided on the basis of the time of exposure

## Abbreviations used

ARIA: Allergic Rhinitis and its Impact on Asthma

QOL: Quality of life

RQLQ: Rhinoconjunctivitis Quality-of-Life Questionnaire

WPAI-AS: Allergy-Specific Work Productivity and Activity Impairment

into seasonal, perennial, and occupational diseases.<sup>2-4</sup> However, this classification did not appear to be entirely satisfactory for the following reasons: (1) there are many places where pollens and molds are perennial allergens,<sup>5,6</sup> (2) symptoms of perennial allergy may not always be present all year round because of the seasonality of perennial allergens,<sup>7</sup> (3) the majority of patients are sensitized to many different allergens and therefore present symptoms throughout the year,<sup>8</sup> (4) many patients allergic to pollen are also allergic to molds, and it is difficult to define the pollen season,<sup>9</sup> and (5) because of the priming effect on the nasal mucosa induced by low levels of pollen allergens<sup>10</sup> and minimal persistent inflammation of the nose in patients with symptom-free rhinitis,<sup>11,12</sup> symptoms often persist for periods longer than allergen exposure.

Thus, a major change in the subdivision of allergic rhinitis was proposed in ARIA with the terms *intermittent* and *persistent*.<sup>1</sup> It was shown that the classic types of seasonal and perennial rhinitis cannot be used interchangeably with the new classification of intermittent/persistent, because they do not represent the same stratum of disease. There is also evidence that the persistent type describes a distinct group with characteristics that differentiate them from intermittent allergic rhinitis.<sup>13-15</sup> The ARIA guidelines have also proposed a new grading of severity (mild and moderate/severe).

It is now recognized that allergic rhinitis is made up of more than the classic symptoms of sneezing, rhinorrhea, and nasal obstruction. Allergic rhinitis is associated with impairments in how patients function in day-to-day life at home, at work, and in school.<sup>3,16</sup> Patients may also be bothered by sleep disorders, emotional problems, impairment in activities, and social functioning.<sup>17</sup> However, it is not known whether and to what extent quality of life (QOL) scores, work impairment, or sleep can be altered according to the severity and duration of rhinitis.

A study was performed with 3052 patients consulting general practitioners for allergic rhinitis to assess the impairment incurred by allergic rhinitis. Patients were

From <sup>a</sup>the University Hospital and Institut National de la Santé et de la Recherche Médicale U454, Montpellier; <sup>b</sup>Institut National de la Santé et de la Recherche Médicale U408, Paris; <sup>c</sup>Assistance Publique des Hôpitaux de Paris-Bichat-Claude-Bernard, Paris; <sup>d</sup>University Hospital La Milettrie, Poitiers; <sup>e</sup>CRO, MAPI SA, Lyon; and <sup>f</sup>Almirall-France, Paris.

Disclosure of potential conflict of interest: B. Allaf is employed by Almirall Pharma. M. Le Gal is a CRO employee who received money from Almirall. The rest of the authors had no conflict to disclose.

Supported by Almirall-France.

Received for publication May 30, 2005; revised September 26, 2005; accepted for publication September 27, 2005.

Available online December 5, 2005.

Reprint requests: Jean Bousquet, MD, Clinique des Maladies Respiratoires, Hôpital Arnaud de Villeneuve, Centre Hospitalier Universitaire, 34295 Montpellier Cedex 5, France. E-mail: jean.bousquet@wanadoo.fr.

0091-6749/\$32.00

© 2005 American Academy of Allergy, Asthma and Immunology

doi:10.1016/j.jaci.2005.09.047

classified according to the 4 classes of ARIA (mild intermittent, mild persistent, moderate/severe intermittent, and moderate/severe persistent).<sup>1</sup> In all patients, QOL was assessed by using the Rhinoconjunctivitis Quality-of-Life Questionnaire (RQLQ),<sup>17</sup> sleep was assessed by using the Jenkins questionnaire, and work performance was measured by using the Allergy-Specific Work Productivity and Activity Impairment (WPAI-AS) questionnaire.<sup>18,19</sup>

## METHODS

### Patients

A total of 3052 patients aged between 18 and 80 years were recruited from 811 general practitioners randomly selected from the national list. All patients fulfilled the following inclusion criteria: (1) patients had allergic rhinitis for at least the past 3 years, (2) the diagnosis of allergic rhinitis was based on symptoms according to criteria proposed in the International Consensus of Rhinitis<sup>2</sup> and 55.4% had a demonstrated diagnosis of allergy using skin prick tests or allergen specific IgE or Phadiatop (Pharmacia Diagnostics, Uppsala, Sweden),<sup>20</sup> and (3) 59.7% of the patients were currently being treated for allergic rhinitis symptoms. Among the treated patients, 82.4% received oral antihistamines, 22.8% intranasal corticosteroids, and 19.4% various other treatments.

The patients were enrolled during a year and were selected from all regions of France to rule out any geographic or seasonal parameter.

### Assessment of classification and severity of rhinitis

Patients were categorized as having intermittent or persistent rhinitis according to the ARIA classification.<sup>1</sup>

### Outcome measures

Quality of life was assessed by the RQLQ.<sup>17</sup> In this questionnaire, patients rate the degree of impairment during the preceding week by responding to each of the 28 items and using a 7-point scale on which a score of 0 indicates no impairment and a score of 6 maximal impairment. The questionnaire provides an overall score and scores in 7 domains: limitation of activities, sleep, non-hay fever symptoms, practical problems, nasal symptoms, eye symptoms, and emotions.

Patients also completed the WPAI-AS questionnaire<sup>18</sup> and the Jenkins questionnaire on sleep.<sup>21</sup>

Patients were asked to fill in the RQLQ and WPAI-AS questionnaire and to send them by mail to the central monitoring office.

### Data analysis

Although some of the variables are normally distributed, others are not. We therefore choose to use nonparametric statistics for all variables. The Kruskal-Wallis test with Bonferroni-Dunn post hoc analysis and  $\chi^2$  were used. Data are expressed in medians and percentiles.

Because allergy was confirmed in only 55.4% of the patients, we conducted a subanalysis and compared the patients with a proven diagnosis of allergy with those without allergy diagnosis. We found no significant difference for sex, age, symptoms, and the RQLQ global score. It was then decided to use the complete database for the report of the data without segregation between patients with a demonstrated allergy diagnosis and those with a probable diagnosis of allergy.

The effect of treatment was also studied. There was no effect of treatment regarding sex, age, symptoms, and the RQLQ global score. We then decided to use the complete database for the report of the data without segregation between treated and untreated patients.

Because there was an imbalance among the number of patients in the 4 ARIA classes, the  $\beta$  error was calculated.

## RESULTS

### Demographic characteristics of the patients

The demographic characteristics of the patients are presented in Table I. Except for age, there was no difference in sex ratio, socioeconomic status, or smoking between the 4 ARIA classes.

### Repartition of patients in the 4 ARIA classes

Two hundred thirty-three patients (7.6%) could not be classified and were excluded from the analysis. Mild intermittent rhinitis was diagnosed in 112 patients (4%), mild persistent rhinitis in 85 (3%), moderate/severe intermittent rhinitis in 1183 (42%), and moderate/severe persistent rhinitis in 1436 (51%).

Patients with moderate/severe intermittent rhinitis had a significantly ( $P < .01$ ) shorter number of symptomatic days per week and a significantly shorter duration of consecutive symptomatic weeks ( $P < .01$ ) than those with persistent rhinitis (Fig 1). Patients with persistent rhinitis usually had symptoms every day of the week.

### Nonnasal symptoms

Nonnasal symptoms are presented in Table I. Ocular symptoms, loss of smell, and headache were similar in mild intermittent or persistent rhinitis, and only conjunctivitis was significantly more severe in moderate/severe intermittent or persistent rhinitis. Asthma prevalence increased from mild rhinitis (15.1% and 16.5%) to moderate/severe persistent rhinitis (22.8%; Table I).

### QOL

Most patients were able to fill in the RQLQ questionnaire. The rate of response to the different domains ranged from 85.5% to 92.0%. Overall and individual domain scores in the RQLQ were significantly different in the 4 ARIA classes (Table II). Patients with mild intermittent and persistent rhinitis had similar total and specific QOL scores. However, the lack of difference between these 2 groups may be related to the low number of subjects because of an insufficient power of the test. Patients with moderate/severe rhinitis had a significantly higher score. Patients with moderate/severe persistent rhinitis had a significantly higher score than those with moderate/severe intermittent rhinitis.

### Sleep

Most patients were able to fill in the Jenkins questionnaire. The overall assessment in this questionnaire was significantly different in the 4 ARIA classes (Table III). Patients with mild intermittent and persistent rhinitis had similar scores. However, the lack of difference between these 2 groups may be related to the lower number of subjects because of an insufficient power of the test. Patients with moderate/severe intermittent or persistent rhinitis had a significantly higher global score.

### Work productivity

Most patients were able to fill in the WPAI-AS questionnaire. There was no loss of work days incurred by

**TABLE I.** Demographic characteristics of the patients

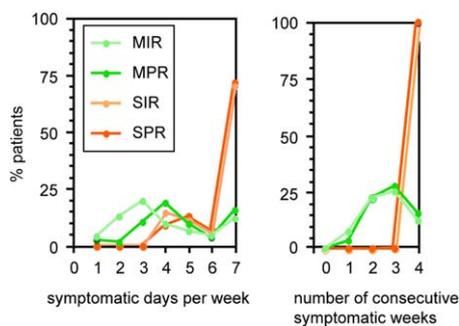
	All patients	Mild intermittent (MI)	Moderate-severe intermittent (SI)	Mild persistent (MP)	Moderate-severe persistent (SP)	P value*	Bonferroni-Dunn post hoc analysis			
							MI/SI	MI/MP	MP/SP	SI/SP
Number	3052	109	1177	86	1439	NA				
Percent		3.9	41.9	3	51.2					
Age, y	39 (30-51)	41 (31-55)	40 (30-51)	43 (31-56)	39 (29-50)	.03	NS	NS	NS	NS
Male subjects (%)	45.3	42.6	46.0	45.2	45.0	NS	NS	NS	NS	NS
Socioeconomic status (%)						NS	NS	NS	NS	NS
Farmer	2.9	3.7	3.6	1.2	2.3					
Craftsman, shopkeeper	6.1	7.3	6.7	3.5	5.6					
Worker	7.2	5.5	6.9	10.5	7.5					
Executive, intellectual, employee	51.6	52.3	50.3	44.2	53.0					
Unemployed	23.1	27.5	23.5	30.2	22.1					
Other	9.1	3.7	9.0	10.4	9.5					
Smokers and exsmokers	33.1	25.9	34.4	38.8	32.3	NS	NS	NS	NS	NS
Number of symptomatic days per week	7 (4-7)	3 (3-5)	4 (3-6)	7 (6-7)	7 (6-7)	<.001	<0.01	<0.01	<0.01	NS
Duration of rhinitis, y	7 (4-10)	6 (3-15)	5 (3-10)	7 (4-15)	8 (4-12)	<.001	NS	NS	NS	<0.01
Allergy diagnosis†	55.4	38.9	47.8	51.2	62.9	<.001	NS	NS	NS	<0.01
Diagnosed asthma, %	19.9	16.5	17.0	15.1	22.8	.0011	NS	NS	NS	NS
Conjunctivitis, %	46.5	31.2	41.1	38.4	52.5	<.001	<0.01	NS	<0.01	<0.01
Loss of smell, %	47.2	21.1	48.2	33.7	49.3	<.001	<0.01	NS	<0.01	NS
Headache, %	49.7	27.5	48.6	38.4	52.9	<.001	<0.01	NS	<0.01	NS

NA, Not applicable; NS, not significant.

Results are given in percentages or medians and 25-75 percentiles.

\* $\chi^2$  and Kruskal-Wallis test used for qualitative and quantitative variables.

†Allergy diagnosis made by skin prick tests and/or serum specific IgE.



**FIG 1.** Duration of symptoms in the week and number of weeks with symptoms depending on the ARIA class. *MIR*, Mild intermittent rhinitis; *MPR*, mild persistent rhinitis; *SIR*, moderate/severe intermittent rhinitis; *SPR*, moderate/severe persistent rhinitis.

rhinitis (data not shown). The overall assessment of work and individual scores in the WPAI-AS questionnaire were significantly different in the 4 ARIA classes (Table III). Patients with mild intermittent and persistent rhinitis had similar scores. However, the lack of difference between these 2 groups may be related to the lower number of subjects because of an insufficient power of the test. Patients with moderate/severe intermittent or persistent rhinitis had significantly higher scores only for loss of work productivity.

## DISCUSSION

In this study, performed in general practices on a large number of patients with allergic rhinitis, it was found that almost 93% of the subjects had moderate/severe rhinitis according to the ARIA classification. The severity of the rhinitis was having more of an effect on QOL, sleep, daily activities, and work performance than the duration.

One of the problems of the study is the imbalance between the number of patients with mild and moderate/severe rhinitis. This result was surprising because patients were seen in primary care. This suggests that patients consult a physician for allergic rhinitis only when they have severe symptoms. An important question to be addressed is the prevalence of severe allergic rhinitis in the general population and among subjects with symptoms of rhinitis who do not consult a physician.<sup>22</sup> Recently, Bachau and Durham<sup>14,15</sup> found that, in the general population, the majority of patients with allergic rhinitis have mild rhinitis.

The imbalance between groups led us to calculate the  $\beta$  error for some parameters. It was found that the power of the statistical analysis was insufficient to make a definite conclusion for the groups of patients with mild intermittent and mild persistent rhinitis. However, an alternative explanation would be that using the ARIA mild intermittent and mild persistent rhinitis definitions may not identify groups that have clinical meaningful outcome differences between them.

**TABLE II.** Results of RQLQ

	Mild intermittent (MI)	Moderate-severe intermittent (SI)	Mild persistent (MP)	Moderate-severe persistent (SP)	Kruskal-Wallis	Bonferonni-Dunn post hoc analysis			
						MI/SI	MI/MP	MP/SP	SI/SP
Number of patients*	109/84	1177/874	86/64	1439/1092		NS	NS	NS	NS
Global score	1.7 (1.1-2.4)	2.7 (2.1-3.4)	2.1 (1.5-2.6)	3.0 (2.3-3.6)	<0.001	<0.01	NS	<0.01	<0.01
Activities									
Sleep	1.0 (0.3-2.0)	2.3 (1.3-3.7)	1.3 (0.7-2.0)	2.7 (1.7-4.0)	<0.001	<0.01	NS	<0.01	<0.01
General problems	1.3 (0.6-2.1)	2.1 (1.4-3.0)	1.4 (0.9-2.3)	2.3 (1.6-3.3)	<0.001	<0.01	NS	<0.01	<0.01
Practical problems	3.0 (1.7-4.0)	3.7 (3.0-4.7)	3.0 (2.0-4.3)	4.0 (3.3-5.0)	<0.001	<0.01	NS	<0.01	<0.01
Nasal problems	2.7 (1.7-3.7)	3.5 (2.7-4.2)	3.2 (2.2-3.7)	3.7 (3.0-4.5)	<0.001	<0.01	NS	<0.01	<0.01
Ocular problems	0.5 (0.0-1.5)	2.0 (0.7-3.2)	1.2 (0.0-2.5)	2.0 (0.7-3.5)	<0.001	<0.01	NS	<0.01	NS
Emotions	1.5 (0.5-2.5)	2.5 (1.7-3.5)	1.7 (0.7-2.7)	3.0 (2.0-3.7)	<0.001	<0.01	NS	<0.01	<0.01

NS, Not significant.

Results are expressed in medians and 25-75 percentiles.

\*First number: total number of patients; second number: number of patients with an evaluable RQLQ.

**TABLE III.** Results of the Jenkins questionnaire on sleep and WPAI-AS questionnaire

	Mild intermittent (MI)	Moderate-severe intermittent (SI)	Mild persistent (MP)	Moderate-severe persistent (SP)	Kruskal-Wallis	Bonferonni-Dunn post hoc analysis			
						MI/SI	MI/MP	MP/SP	SI/SP
Number of patients*	84	894	66	1107					
Loss of work productivity (%)† (N=1397)	20 (10-30)	40 (20-70)	20 (0-40)	40 (20-62)	<0.001	<0.01	NS	<0.01	<0.01
Loss of school productivity (%)† (N=379)	10 (0-30)	40 (20-72)	20 (0-30)	40 (20-70)	<0.001	<0.01	NS	NS	NS
Loss of daily activities (%)† (N=2217)	20 (10-40)	50 (30-70)	30 (15-40)	50 (30-70)	<0.001	<0.01	NS	<0.01	NS
Global Jenkins score	4 (1-7)	6 (4-9)	4 (2-8)	7 (4-11)	<0.001	<0.01	NS	<0.01	<0.01

NS, Not significant.

\*Number of patients with evaluable WPAI-AS and Jenkins questionnaires.

†WPAI-AS questionnaire.

The diagnosis of rhinitis may be determined by using scores,<sup>23,24</sup> but it appears that simple diagnostic criteria can be used to diagnose the common nasal allergies with a very high certainty.<sup>25</sup> In the current study, allergy was tested in 55.4% of subjects and, because this study examined outcomes in primary care settings (rather than in specialty practices), the lack of objective testing for allergy in many patients reflects actual practice. We analyzed separately patients with and without an objective analysis of allergy, and we found no significant difference for RQLQ. Thus, we did not differentiate both patient groups in the analysis.

Severity of rhinitis can be classified by using symptom scores for all symptoms of rhinitis or QOL.<sup>17</sup> In the current study, patients were classified according to the ARIA criteria, which combine symptom scores and the effect of rhinitis on daily activities and sleep.<sup>1</sup> Patients were included over a period of 1 year to overcome the possible seasonal differences. However, in this study, it was found that patients with intermittent and persistent rhinitis are distributed in both seasonal and perennial rhinitis groups. These results confirm the study of Demoly et al<sup>13</sup> and Bachau and Durham<sup>14,15</sup>

showing that seasonal and perennial rhinitis are not synonymous with intermittent and persistent rhinitis.

It has been recognized for many years that seasonal and perennial allergic rhinitis impair QOL,<sup>16,17</sup> and this study confirms these data in patients with both intermittent and persistent rhinitis. The results of RQLQ are similar to previous studies performed with patients with allergic rhinitis in France<sup>26</sup> and show that all patients with allergic rhinitis consulting in primary care have a significantly greater score than normal subjects of a similar age.<sup>27</sup> For all of the outcome measures studied, rhinitis severity was more important than duration. These results should be taken into consideration within the update of the ARIA guidelines in 2006. It is surprising that treatment for rhinitis has no effect regarding symptoms and RQLQ global score. Many patients with allergic rhinitis do not have well controlled disease despite treatment following guidelines. These patients still have moderate to severe symptoms and, as shown by this study, a QOL similar to untreated patients with symptoms of the same severity.

Sleep was also impaired in patients with allergic rhinitis. Many other studies have shown that allergic rhinitis impairs sleep,<sup>28,29</sup> and one of the RQLQ items is

sleep.<sup>17</sup> However, no other study exists assessing sleep disturbances in such a large number of patients, and there was no clear correlation with disease severity and/or duration. Although in the ARIA, classification sleep impairment should place the patients in the moderate/severe category, some patients with mild disease and supposedly no sleep impairment also have sleep disturbances. Sleep was impaired in intermittent and persistent rhinitis, and rhinitis severity was more important than duration.

Loss of smell was common, as previously reported in allergic rhinitis.<sup>30,31</sup> In the current study, hyposmia was associated with the severity of the disease.

Although it is commonly accepted that work is impaired by allergic rhinitis,<sup>3,32-34</sup> no large study exists in general practices assessing the effect of nasal symptoms on work performance. Daily activities and work productivity were also impaired in patients placed in all 4 ARIA categories, but again, rhinitis severity was more important than duration. The number of adolescents was low, and school performance may not have been accurately assessed in the current study.

This study showed that approximately 90% of patients with allergic rhinitis consulting general practitioners have moderate/severe symptoms that are impairing daily activities, sleep, and work. It seems therefore that the term *moderate/severe* should be replaced by *severe*. A study in the general population is required, however, to assess the effect of allergic rhinitis.

## REFERENCES

- Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108(suppl 5):S147-334.
- International Consensus Report on Diagnosis and Management of Rhinitis. International Rhinitis Management Working Group. *Allergy* 1994; 49(suppl 19):1-34.
- Dykewicz MS, Fineman S. Executive Summary of Joint Task Force Practice Parameters on Diagnosis and Management of Rhinitis. *Ann Allergy Asthma Immunol* 1998;81:463-8.
- van Cauwenberge P, Bachert C, Passalacqua G, Bousquet J, Canonica GW, Durham SR, et al. Consensus statement on the treatment of allergic rhinitis. *European Academy of Allergology and Clinical Immunology. Allergy* 2000;55:116-34.
- Bucholtz GA, Lockey RF, Wunderlin RP, Binford LR, Stablein JJ, Serbousek D, et al. A three-year aerobiologic pollen survey of the Tampa Bay area, Florida. *Ann Allergy* 1991;67:534-40.
- D'Amato G, Ruffilli A, Sacerdoti G, Bonini S. Parietaria pollinosis: a review. *Allergy* 1992;47:443-9.
- Platts-Mills TA, Hayden ML, Chapman MD, Wilkins SR. Seasonal variation in dust mite and grass-pollen allergens in dust from the houses of patients with asthma. *J Allergy Clin Immunol* 1987;79:781-91.
- Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: clinical presentation and medical history. *Thorax* 1991;46:895-901.
- Bruce CA, Norman PS, Rosenthal RR, Lichtenstein LM. The role of ragweed pollen in autumnal asthma. *J Allergy Clin Immunol* 1977;59:449-59.
- Connell JT. Quantitative intranasal pollen challenges, 3: the priming effect in allergic rhinitis. *J Allergy* 1969;43:33-44.
- Knani J, Campbell A, Enander I, Peterson CG, Michel FB, Bousquet J. Indirect evidence of nasal inflammation assessed by titration of inflammatory mediators and enumeration of cells in nasal secretions of patients with chronic rhinitis. *J Allergy Clin Immunol* 1992;90:880-9.
- Ciprandi G, Buscaglia S, Pesce G, Pronzato C, Ricca V, Parmiani S, et al. Minimal persistent inflammation is present at mucosal level in patients with asymptomatic rhinitis and mite allergy. *J Allergy Clin Immunol* 1995;96:971-9.
- Demoly P, Allaert FA, Lecasble M, Bousquet J. Validation of the classification of ARIA (allergic rhinitis and its impact on asthma). *Allergy* 2003;58:672-5.
- Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J* 2004;24:758-64.
- Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy* 2005;60:350-3.
- Leynaert B, Neukirch C, Liard R, Bousquet J, Neukirch F. Quality of life in allergic rhinitis and asthma: a population-based study of young adults. *Am J Respir Crit Care Med* 2000;162:1391-6.
- Juniper EF, Thompson AK, Ferrie PJ, Roberts JN. Validation of the standardized version of the Rhinoconjunctivitis Quality of Life Questionnaire. *J Allergy Clin Immunol* 1999;104:364-9.
- Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics* 1993;4:353-65.
- Meltzer EO, Casale TB, Nathan RA, Thompson AK. Once-daily fexofenadine HCl improves quality of life and reduces work and activity impairment in patients with seasonal allergic rhinitis. *Ann Allergy Asthma Immunol* 1999;83:311-7.
- Crobach MJ, Kaptein AA, Kramps JA, Hermans J, Ridderikhoff J, Mulder JD. The Phadiatop test compared with RAST, with the CAP system; proposal for a third Phadiatop outcome: "inconclusive." *Allergy* 1994;49:170-6.
- Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. *J Clin Epidemiol* 1988;41:313-21.
- Sibbald B, Rink E. Labelling of rhinitis and hayfever by doctors. *Thorax* 1991;46:378-81.
- Ng ML, Warlow RS, Chrisanthan N, Ellis C, Walls RS. Preliminary criteria for the definition of allergic rhinitis: a systematic evaluation of clinical parameters in a disease cohort (II). *Clin Exp Allergy* 2000;30:1417-22.
- Annesi-Maesano I, Didier A, Klossek M, Chanal I, Moreau D, Bousquet J. The score for allergic rhinitis (SFAR): a simple and valid assessment method in population studies. *Allergy* 2002;57:107-14.
- Crobach MJ, Hermans J, Kaptein AA, Ridderikhoff J, Petri H, Mulder JD. The diagnosis of allergic rhinitis: how to combine the medical history with the results of radioallergosorbent tests and skin prick tests. *Scand J Prim Health Care* 1998;16:30-6.
- Bousquet J, Lund VJ, Van Cauwenberge P, Bremard-Oury C, Mounedji N, Stevens MT, et al. Implementation of guidelines for seasonal allergic rhinitis: a randomized controlled trial. *Allergy* 2003;58:733-41.
- Bousquet PJ, Fabbro-Peray P, Janin N, Annesi-Maesano I, Neukirch F, Daures JP, et al. Pilot study assessing the impact of smoking on nasal-specific quality of life. *Allergy* 2004;59:1015-6.
- Olsen KD, Kern EB, Westbrook PR. Sleep and breathing disturbance secondary to nasal obstruction. *Otolaryngol Head Neck Surg* 1981;89:804-10.
- Craig TJ, Teets S, Lehman EB, Chinchilli VM, Zwillich C. Nasal congestion secondary to allergic rhinitis as a cause of sleep disturbance and daytime fatigue and the response to topical nasal corticosteroids. *J Allergy Clin Immunol* 1998;101:633-7.
- Simola M, Malmberg H. Sense of smell in allergic and nonallergic rhinitis. *Allergy* 1998;53:190-4.
- Rydzewski B, Pruszczyk A, Sulkowski WJ. Assessment of smell and taste in patients with allergic rhinitis. *Acta Otolaryngol* 2000;120:323-6.
- Blanc PD, Trupin L, Eisner M, Earnest G, Katz PP, Israel L, et al. The work impact of asthma and rhinitis: findings from a population-based survey. *J Clin Epidemiol* 2001;54:610-8.
- Demoly P, Allaert FA, Lecasble M. ERASM, a pharmacoepidemiologic survey on management of intermittent allergic rhinitis in every day general medical practice in France. *Allergy* 2002;57:546-54.
- Bachert C, Bousquet J, Canonica GW, Durham SR, Klimek L, Mullol J, et al. Levocetirizine improves quality of life and reduces costs in long-term management of persistent allergic rhinitis. *J Allergy Clin Immunol* 2004;114:838-44.