

Comparative Analysis of Allergic Rhinitis in Children and Adults

Adriana Izquierdo-Domínguez · Antonio L. Valero · Joaquim Mullol

Published online: 19 December 2012
© Springer Science+Business Media New York 2012

Abstract Allergic rhinitis (AR) is a worldwide health problem that generates a significant healthcare burden in adults, adolescents, and children. Epidemiological studies have indicated that the prevalence of AR has progressively increased over the last three decades in developed and industrialized countries. AR currently affects up to 40 % of the worldwide population, with differences between adults and children and different countries of the World. Although not life-threatening, AR symptoms are frequently bothersome, adversely affecting work and quality of life of the affected patients, and causing a significant burden on both the individual and society. The symptoms have the potential to lead to both physical and mental complications, with sleep-disordered breathing in childhood and adolescence being associated with disorders in learning performance, behavior, and attention. Clinical features and comorbidities are very important for the “allergic march”,

and in both adults and children there is some evidence of association between AR and asthma. ARIA classifications of both symptom duration (intermittent, persistent) and severity (mild, moderate, severe) have been validated in both adult and pediatric populations. Based on the duration and severity of patient’s disease, an appropriate treatment strategy has been issued for both adults and children, which consists of patient’s education, allergen avoidance, and pharmacological as well as allergen-specific immunotherapy treatment. The present review will attempt to compare the characteristics of AR between children and adults, either in the epidemiology, clinical features, impact on QOL, and management of the disease.

Keywords Allergic rhinitis · Adults · Children · Epidemiology · Quality of life · Management · Clinical features · Comparative analysis · Prevalence · Classification · Clinical features · Management · Immunotherapy

A. Izquierdo-Domínguez
Department of Allergology, Hospital Quirón, Barcelona,
Catalonia, Spain
e-mail: adrianaeizquierdo@hotmail.com

A. L. Valero
Department of Pneumology and Respiratory Allergy, ICT, Hospital
Clínic i Universitari, Institut d’Investigacions Biomèdiques August
Pi i Sunyer (IDIBAPS); and CIBER de Enfermedades
Respiratorias (CIBERES), Barcelona, Catalonia, Spain
e-mail: valero@clinic.ub.es

J. Mullol
Rhinology Unit & Smell Clinic, Department of
Otorhinolaryngology, Hospital Clínic i Universitari, Institut
d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS); and
CIBER de Enfermedades Respiratorias (CIBERES), Barcelona,
Catalonia, Spain

J. Mullol (✉)
Rhinology Unit & Smell Clinic, Department of
Otorhinolaryngology, Hospital Clínic, IDIBAPS, Villarroel 170,
08036 Barcelona, Catalonia, Spain
e-mail: jmullol@clinic.ub.es

Introduction

Allergic rhinitis (AR) is a worldwide health problem that generates a significant healthcare burden in adults, children and adolescents. AR is characterized by sneezing, rhinorrhea, nasal congestion and nasal pruritus, which are often accompanied by ocular pruritus/redness and or watery eyes in 60–70 % of patients. Although not life-threatening, AR symptoms are frequently bothersome, adversely affecting work and quality of life of the affected individual, and causing a significant burden on both the individual and society [1]. The symptoms have the potential to lead to both physical and mental complications, with sleep-disordered breathing in childhood and adolescence being associated with disorders in learning performance, behavior, and attention [2].

Similarly to adults, there is evidence of association between AR and asthma in children [3]. Children are vulnerable during

growth and, due to their physical constitution and breathing pattern, they are more susceptible than adults to the effects of air pollution on health [4].

AR can be classified according to the type of exposure to aeroallergens as perennial, seasonal, and occupational. According to ARIA (Allergic Rhinitis and its Impact on Asthma) [5], AR can be classified either based on symptom duration as intermittent (IAR) and persistent (PER) rhinitis, or based on severity through the impairment of four health-related quality of life (HRQL) parameters: sleep, daily activities/sport/leisure, work productivity/school performance, and troublesome symptoms. The disease is mild when there is no impairment of any of these items, whereas it is considered moderate/severe when one or more of these are impaired. Valero et al. have recently proposed [6, 7] a modification of this original ARIA severity classification, by stratifying moderate/severe into separate moderate ([1–3 affected items) and severe (all 4 items affected) categories. The ARIA classifications have also been validated in pediatric population, for both symptom duration [8•] and disease severity [9•].

The present review will attempt to compare the characteristics of AR between children and adults, either in the epidemiology, clinical features, impact on quality of life (QoL), and management of the disease.

Epidemiology

Epidemiological studies have indicated that the prevalence of AR has increased progressively over the last three decades in developed and industrialized countries worldwide. AR currently affects up to 40 % of the worldwide population [5, 10], with 23–30 % of the population affected in Europe [11, 12] and 12–30 % of individuals affected in the USA [13]. The prevalence of seasonal AR is higher in children and adolescents than in adults while perennial rhinitis seems to be more common in adults [14].

Recently, Katelaris et al. [15•] reviewed the prevalence and diversity of AR in different regions of the world in both adults and children. Citations of the prevalence of AR and associated factors were identified using “AR”, “seasonal”, and “perennial” AR as the primary search terms in association with “prevalence” and “incidence”. This covered specific countries and regions, including Africa, Asia-Pacific, Australia, Eastern Europe, Latin America, and Middle East. A total of 3,675 citations were highlighted, covering publications from the period January 1980 to August 2010.

Prevalence in Children

The prevalence of AR in children is very well studied worldwide thanks to the standardized and translated versions of the

International Study of Asthma and Allergies in Childhood (ISAAC) based on written and/or video questionnaires [16–19]. In comparison, there are relatively few studies on the prevalence in adults.

The ISAAC phase-I [16] demonstrated major worldwide variations in the prevalence of symptoms of asthma, rhinoconjunctivitis, and eczema in children [20, 21]. More than 700,000 children were included in the study: 257,800 from 6 to 7 years old and 463,801 from 13 to 14 years old. Substantial worldwide variation was found in the prevalence of reported symptoms of rhinoconjunctivitis, with up to 25-fold variations in the 13 to 14 year olds [20]. For both age groups, the lowest prevalence values were found in parts of Eastern Europe and in Southern and Central Asia. In the older age group, low prevalence values were found in China and Portugal.

The ISAAC phase-II involved a more detailed protocol to assess possible etiological factors in 9- to 11-year-old children. Standardized modules were used, which included examination of dermatitis, skin prick testing, bronchial challenge, blood sampling for genetic analyses, and dust sampling. The prevalence of rhinoconjunctivitis symptoms widely varied worldwide (1.5–24.5 %) and the population attributable fraction (PAF) varied from 0 to 71 % for a positive prick test to seasonal allergens and from 0 to 41 % to perennial allergens. The estimated PAF for sensitization to seasonal and perennial allergens was higher for centers in affluent (36 and 25 %, respectively) than in non-affluent (1.3 and 12.6 %, respectively) countries. Atopy only accounted for a limited proportion of the reported rhinitis symptoms, particularly in less affluent countries [17].

The ISAAC phase-III has involved repeating the phase-I survey after 5–10 years to examine trends in the prevalence of the three conditions and to include new centers to expand the coverage of world prevalence maps for these conditions [18]. For both age groups, the findings for time trends in the prevalence of symptoms of rhinoconjunctivitis, where both phase-I and phase-III have been completed and have been reported in the previous publications [22, 23]. The average overall prevalence of current rhinoconjunctivitis symptoms in ISAAC phase-III was 14.6 % for the 13- to 14-year-old children (range 1.0–45 %). A variation in the prevalence of severe rhinoconjunctivitis was observed between centers (range 0.0–5.1 %) and regions (range 0.4 % in Western Europe to 2.3 % in Africa), with the highest prevalence being observed mainly in the centers from middle and low income countries, particularly in Africa and Latin America [24].

The prevalence of AR in some regions (Africa, Asia-Pacific, Australia, Eastern Europe, Latin America, Middle East, and Turkey) has predominantly been investigated in children, with studies indicating wide inter- and intraregional variations ranging from 2.9 % in 10- to 18-year-old children in Turkey to 54.1 % in 13- to 14-year-old children

in Nigeria [15•]. Moreover, the prevalence of AR has markedly increased over the last decade particularly in some of the more affluent African countries, China-Taiwan, and several Middle East countries. The great AR diversity in these regions is in contrast to the lower diversity seen in western populations (USA and Europe) where the disease tends to be more uniform [15•]. The prevalence and severity of allergic diseases change with age, and marked sex differences exist for the predictive role of specific IgE or the severity of allergic disease at 10 years [25].

Prevalence in Adults

Although there are some reports from other regions, no suitable studies in adults showing AR prevalence in Africa, Latin America, or the Middle East were found. In Australia, a longitudinal study has investigated the prevalence of self-reported AR in a population-based cohort of adults, using a questionnaire in a stratified random sample. The authors demonstrated that the prevalence for hay fever (19.2 %) in 1968 doubled to 41.3 % in 1991–1993 [26].

The prevalence of confirmable adult AR in Europe ranged from 17 % in Italy to 28.5 % in Belgium [27]. In this study, the prevalence of AR was 24.5 % in France, 21.5 % in Spain, 20.6 % in Germany, and 26 % in the UK. European prevalence studies demonstrated a mean age from 31.3 to 42.7 years old for these countries, IAR prevalence ranged from 72 % in Belgium to 19.2 % in Germany, while PER ranged from 53.8 % in the UK to 21 % in Spain.

Cingi et al. [28] assessed the prevalence of AR in the Turkish adult population across seven distinct geographical regions, using a custom-designed questionnaire with a particular emphasis on descriptive parameters. After adjusting for survey errors, data from 4,125 volunteers indicated that the prevalence of self-reporting AR and physician-diagnosed AR ranged from 16.3 to 15.7 %, respectively. Among Turkish regions, the prevalence ranged from 27.5 % in Anatolia to 23.4 % in the Marmara region.

In Asia and Pacific, a few studies have reported the prevalence of AR in adults. A population-based study assessing self-reported AR by validated questionnaires and via telephone-based interviews in over 38,000 subjects from 11 major cities in China recently demonstrated that the prevalence of AR, once adjusted for age and gender, was highly variable ranging from 8.7 % in Beijing in east China to 24.1 % in Urumqi in west China [29]. Importantly, this study further demonstrated that 74.4 % of subjects with self-reported AR were diagnosed with intermittent AR and 25.6 % with persistent AR.

In Latin America, a cross-national survey has described the symptoms, impact, and treatment of AR in subjects ≥ 4 years old [30]. In total, 22,012 households across Latin

American countries were screened for children, adolescents, and adults with AR diagnosis. A total of 1,088 adults and 457 children and adolescents were included and the sample was probability based to ensure valid statistical inference in relation to the population. Approximately 7 % of the Latin American population was diagnosed with AR, with two out of three respondents stating that their allergies were seasonal or intermittent in nature. Nasal congestion was the most common and bothersome symptom of AR. Sufferers indicated that their symptoms affected productivity and sleep and that they had a negative impact on quality of life. Findings from this cross-national survey on AR have confirmed a considerable negative impact on daily quality of life and work productivity in Latin America [30].

The epidemiological data and characterization of AR has also been reviewed for the USA where chronic rhinitis symptoms are among the most common problems reported to physicians. AR prevalence range from 9 to 42 % with an estimated prevalence of 19 million people. In comparison, the prevalence of mixed rhinitis stands at approximately 26 million while total AR ("pure" and "mixed" combined) concerns 58 million people [31].

Classification of Rhinitis

Most epidemiologic data concern seasonal AR. Using questionnaires, the prevalence of seasonal AR widely ranges from 1 to 40 %, while perennial rhinitis varies from 1 to 13 % [5]. Using the ARIA classification, the prevalence of AR has been found to be around 25 % in adults, with 71 % being intermittent and 29 % persistent [27]. The studies and their characteristics between children and adults are shown comparatively in Table 1.

Classification in Children

Two recent studies compared the prevalence of severity using both original (o-ARIA) and modified (m-ARIA) ARIA classifications [8•, 9•]. The first validation of o-ARIA in a pediatric population was performed in 1,275 children recruited from 271 Spanish centres. Almost 60 % of patients suffered from intermittent rhinitis and, according to severity, moderate/severe intermittent (52.1 %) or persistent (37.6 %) were more frequent than mild intermittent (7.1 %) or persistent (3.2 %). When patients were classified according to the allergen seasonal pattern (classical), 60.7 % of patients suffered from seasonal rhinitis. And when both classifications were compared (o-ARIA vs. classical), a significant difference was observed between them ($p < 0.0001$) indicating that these two classifications analyze different disease characteristics and so cannot be interchanged [8•].

Table 1 Prevalence of allergic rhinitis according to the different classifications in both children and adults from Spain

	Children (%)	Adults (%)
Classical classification	Jáuregui et al. 2011 (ref. 8•)	del Cuvello et al. 2010 (ref. 32)
Seasonal	60.7	61.2
Perennial	39.3	35.1
o-ARIA classification	Jáuregui et al. 2011 (ref. 8•)	del Cuvello et al. 2010 (ref. 32)
Duration of symptoms		
Intermittent	59.5	51.1
Persistent	40.5	48.5
Disease severity		
Mild	10.3	66
Moderate / severe	89.7	34
m-ARIA classification	Montoro et al. 2012 (ref. 9•)	Valero et al. 2007 (ref. 6)
Duration of symptoms		
Intermittent	59.5	64
Persistent	40.5	36
Disease severity		
Mild	10.1	17
Moderate	59.5	57
Severe	30.4	26

o-ARIA original ARIA severity classification, *m-ARIA* modified ARIA severity classification

In children, the validation of the m-ARIA severity classification was performed in 1,269 patients from 271 Spanish centers. When using o-ARIA classification, 10.1 % of patient had mild and 89 % moderate/severe AR, while the m-ARIA criterion was able to discriminate between moderate 59.5 % and severe 30.4 % AR patients [9•].

Classification in Adults

In Spain, the validation of ARIA duration and severity classifications was studied in the ADRIAL cohort where 3,529 AR patients were included. Half (51.5 %) of the patients had intermittent and half (48.5 %) persistent AR while, using the classical allergen exposure classification, patients were grouped as seasonal (61.2 %), perennial (35.1 %), and occupational (3.7 %). Concerning to severity, 66 % of patients were classified as mild and 34 % as moderate/severe [32]. Given that most of the AR patients were moderate/severe, there was an unmet need to differentiate between these two severity categories. In the first study, where m-ARIA was validated in 141 non-treated patients with moderate/severe AR, 36 % were persistent and 64 % intermittent while 57 % were moderate and 26 % severe [6].

Clinical Features

Typical AR symptoms include anterior rhinorrhoea, sneezing, nasal obstruction, and nasal itching [5]. Most patients with rhinitis have eye symptoms such as ocular itching or watery eyes. The total loss of smell (anosmia) is infrequent in AR, but mild hyposmia is not rare. Guilemany et al. found that patients with persistent AR had a moderate loss of smell (BAST-24) with higher severity in those with self-reported hyposmia [33]. Snoring, sleep disruption, postnasal drip, or chronic cough, in particular if chronic rhinosinusitis is present, can also be accompanying symptoms [34, 35].

Clinical Features in Children

AR is part of the “allergic march” during childhood [36], IAR, however, is unusual before 2 years of age. Furthermore, AR is the most prevalent chronic allergy during school-age years [37]. Children with moderate/severe AR may develop noisy breathing, repeated throat clearing, snoring, and a reduction in sense of smell. Children may also have facial manifestations of obstructed breathing, including a gaping mouth, chapped lips, hypertrophied gingival mucosa, a long face, dental malocclusions, and allergic shiners. They may also show signs of itching (e.g., an allergic salute or an allergic transverse nasal crease) [38] or have malaise and disturbed nocturnal sleep with subsequent daytime fatigue. Co-morbidities associated with AR in children include asthma, atopic dermatitis/eczema, allergic conjunctivitis, chronic rhinosinusitis, and otitis media. In the two studies which utilized either the validated o-ARIA or the m-ARIA in children, the most frequent comorbidities were conjunctivitis (53.6 %), asthma (49.5 %), and atopic dermatitis (40 %), while the most frequent sensitizing allergens were pollens (53.5 %) and house dust mites (43.5 %) [8•, 9•].

The differential diagnosis of AR in preschool children includes infectious rhinitis (usually viral), foreign bodies, anatomical variations including unilateral choanal atresia, benign tumors including dermoid cysts and meningoencephalocele, cystic fibrosis and related diseases [39], mucociliary dyskinesia [40], or nasal obstruction induced by adenoid hypertrophy. In older children, facial trauma (septal hematoma, fractured nasal bones, and synechiae), cerebrospinal fluid rhinorrhoea, nasal glioma, and rhinitis medicamentosa due to an abuse of topical decongestants should also be considered. Nasal polyps are uncommon in children and, if observed, the diagnosis of cystic fibrosis must be considered.

Clinical Features in Adults

Studies using the ARIA classification show that over 50 % of patients sensitized to pollen suffer from PER [5, 12], and that, in the general population, a large number of HDM sensitized patients have mild IAR [12]. Despite some reservations, the

prevalence of IgE sensitization to indoor allergens (i.e. HDMS and cat allergen) is positively correlated with asthma and its severity. *Alternaria* [41] and insect (dust mites and cockroach) [42, 43] have also been found to be linked with asthma and its severity as well as with rhinitis. Multiple sources of indoor environmental allergens may have a synergistic effect on atopic co-morbidities [44].

In adults, co-morbidities and/or complications can be conjunctivitis, chronic rhinosinusitis, nasal polyps, chronic cough, laryngitis, and gastro-esophageal reflux. Rhinitis is a risk factor for asthma both in adults [45] and in children [46]. However, in adulthood, the development of asthma is usually independent of allergy [47], whereas in childhood it is often associated with allergy [46]. In the Spanish ADRIAL study [32], asthma was the only co-morbidity whose incidence increased in correlation to AR severity, with this being more frequent in patients with persistent (41.6 %) rather than intermittent (31.5 %) AR, while asthma prevalence was higher in moderate/severe (41.1 %) compared to mild (34.1 %) AR. Conjunctivitis ranged from 51 to 55.6 % among the different severity categories but without statistical significance [32].

Quality of Life

Quality of life (QoL) impairment varies principally depending on the individual's standards regarding "personal well-being", a concept which includes a large set of physical and psychological characteristics, and entails assessing problems in relation to social context and lifestyle. The pathophysiology and symptoms of AR often disrupt sleep, leading to fatigue, irritability, memory deficits, daytime sleepiness, and depression. The total burden of this disease goes beyond impairment of physical and social functioning and has also a financial impact [48]. Nasal obstruction, the most common and troublesome symptom of the disease, deeply affects QoL, especially by reducing the "restoring power of the sleep" [48]. Poor quality sleep causes daytime sleepiness, fatigue, and significant impairment in learning, cognition, and professional performance.

There are multiple generic and specific questionnaires for the evaluation of QoL in children and adults which are summarized in Table 2. Generic questionnaires measure physical, mental, and psychosocial function in all health conditions irrespective of the underlying disease, which can be compared to the general population. Specific questionnaires are used to evaluate allergic disease and have been designed to assess the impact of their disease, rhinitis, or conjunctivitis in different aspects (domains) of their daily life.

Quality of Life in Children

Although not life-threatening, AR can have a significantly detrimental effect on children's QoL [49]. Pediatric

questionnaires (PedsQL) are available, and these have demonstrated an impaired QoL in adolescents with rhinitis [50]. Also, the Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ) has been developed in children to encapsulate problems related to the eyes, ears, nose, lungs, skin, emotions, and everyday activities [51]. Impairment in PADQLQ is directly related to the level of allergen exposure and allergic airway inflammation [51].

In children with uncontrolled AR, learning problems occur during school hours either by direct interference or indirectly through nocturnal sleep loss and secondary daytime fatigue [5]. Seasonal AR may be associated with a reduced ability to learn and with achievement in academic examinations [52]. Children with AR tend to be shy, depressed, anxious, or fearful [48]. The Pediatric Allergies in America survey emphasizes that congestion is the most impactful symptom in children [53].

It has been shown that adolescents with rhinoconjunctivitis suffer similar QoL problems to adults, but have fewer sleep problems and more difficulties in concentrating (particularly with school homework). In addition, children are concerned about practical issues such as carrying or taking the medication, but do not report interference with daily activities or emotional disorders as adults [54, 55].

Quality of Life in Adults

The Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) has been tested in adult patients with seasonal and perennial AR as well as those with intermittent and persistent AR. RQLQ has also been adapted and translated to different cultures and languages [56–58]. Two newly developed instruments to measure health-related quality of life (HRQoL) in Spanish AR patients have shown good reliability, validity, and sensitivity to change: ESPRINT-28 and ESPRINT-15 [59]. Valero et al. [60] compared the psychometric properties of the ESPRINT-15, the short form questionnaire, with those of the Mini-Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) and demonstrated that questionnaires performed well in psychometric terms.

Postulation reference values improve the interpretability and magnitude of the differences found among groups of patients and reinforce their usefulness where providing those values as stratified by gender, type of AR, and symptom severity [61]. The questionnaires were used to compare QoL according to the clinical severity of AR [7] and to assess changes in HRQoL, after 4 weeks of treatment with antihistamines [62]. Furthermore, m-ARIA severity classification clearly discriminates the impact of AR in all domains of ESPRINT-15 as well as categorize symptom scores [63].

In a recent review on the consequences of sleep disturbances, adults become less efficient and more subject to work-related accidents [48]. Thus, the disrupted sleep

Table 2 Summary of Quality of Life Questionnaires in children and adults with allergic rhinitis

Name	Author	No. items	Target population
Adolescent Rhinoconjunctivitis QoL Questionnaire (adolRQLQ)	Juniper et al. 1994 (ref. 54)	25	Adolescents (12–17 years)
Rhinitis QoL Questionnaire (RhinQLQ)	Juniper et al. 1991 (ref. 56)	24	Adults
Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)	Juniper et al. 2000 (ref. 57)	28	Adults
Mini Rhinoconjunctivitis Quality of Life Questionnaire (miniRQLQ)	Juniper et al. 2000 (ref. 57)	14	Adults
Nocturnal Rhinitis QLQ	Juniper et al. 2003 (ref. 58)	16	>12 years
Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ)	Juniper et al. 1998 (ref. 55)	23	Children (6–12 years)
ESPRINT-28	Valero et al. 2007 (ref. 59)	28	Adults
ESPRINT-15	Valero et al. 2007 (ref. 60)	15	Adults

associated with nasal congestion is an important therapeutic target [48].

The socioeconomic burden of AR is significant, including the cost of treatment, reduced productivity, and the use of inappropriate therapies [64]. In the USA, it is estimated that more than US\$6 billion were spent on prescription medications for AR in 2000 [65].

In a survey on the AR burden in Europe, Canonica et al. [1] showed a significant health problem because of the high burden of symptoms and their impact on general well-being as well as HRQoL. In a similar survey in Spain, AR represented a significant health problem with an important impact on HRQoL, with most of the patients (83.1 %) reporting that AR symptoms have some impact on daily activities [66].

Management of AR

The management of AR is well established, and many guidelines have been issued for adults and children. The classification of AR aids in the establishment of an appropriate initial treatment strategy based on the duration and intensity of the patient's symptoms and lifestyle limitations [5].

The management of AR encompasses patient education, pharmacotherapy, and allergen-specific immunotherapy. Surgery may be used as an adjunctive intervention in a few selected patients [5].

Education. Patients should be educated regarding the avoidance of inhalant allergens and irritants. In children, current evidence suggests that environmental control measures (single or multifaceted) may be associated with a minor beneficial effect on asthma control. However, no conclusive evidence exists regarding rhinitis or eczema [67]. In adults, multifaceted avoidance measures might be helpful for some patients after environmental advice. For occupational diseases, either rhinitis or asthma, complete avoidance of work allergens is recommended when the subject is sensitized to occupational agents [68].

Pharmacotherapy. A number of studies and guidelines provide a good level of evidence and recommendations for oral and local H₁ antihistamines, intranasal corticosteroids, leukotriene antagonists, local chromones, oral and intranasal decongestants, short courses of oral corticosteroids in severe cases, and intranasal anticholinergics. Second generation H₁-antihistamines and intranasal corticosteroids are recommended for the treatment in both adults and children. In children, no growth retardation has been observed in 1-year follow-up studies with fluticasone propionate or mometasone furoate [69, 70]. Montelukast is also recommended for seasonal AR with asthma in patients over 6 years old.

A recent ARIA publication provides levels of evidence and recommendations on the treatment of adults and children with AR [71••]. It can be concluded that the management of AR is similar, with some minor differences, between both children and adult populations. Clinical recommendations were performed to improve their usefulness following the systematic approach developed by the GRADE working group [72, 73]. According to GRADE, the quality of evidence was categorized in four levels (high, moderate, low, and very low), whereas for strong and conditional recommendations the terms “recommends” and “suggest” were respectively used. Understanding the interpretation of these two levels of strength of recommendation is essential for clinical decision-making. The summary of these ARIA recommendations [71••] is shown in Table 3.

Specific Immunotherapy. Several guidelines and indications for specific immunotherapy with inhalant allergens have been published over the last few years by ARIA, the World Health Organization, and the European Academy of Allergology and Clinical Immunology. They all highlight that allergen-specific immunotherapy may alter the natural course of allergy diseases, reduce the development of asthma, and reduce the development of new sensitizations, beyond its ability to diminish rhinitis symptoms. ARIA [5, 71••] recommends subcutaneous immunotherapy is effective in both adults and children for both pollen and mite allergies. ARIA also recommends sublingual immunotherapy for pollen allergy in adults,

Table 3 ARIA recommendations for the management of allergic rhinitis in children and adults (Data from Brozek et al. [71••])

	Children with AR			Adults with AR		
	Recommends	Suggests	Quality of evidence	Recommends	Suggests	Quality of evidence
Pharmacologic Treatment						
Oral new generation H ₁ -antihistamines (no sedation / no cytochrome P450 interaction)	YES	–	L	YES	–	L
Oral new generation H ₁ -antihistamines (some sedation / cytochrome P450 interaction)	–	YES	L	–	YES	L
Oral old generation H ₁ -antihistamines	NO	–	L	NO	–	L
Intranasal H ₁ -antihistamines (SAR)	–	YES	VL	–	YES	L
Intranasal H ₁ -antihistamines (PER)	–	NO	VL	–	NO	VL
Oral vs. intranasal H ₁ -antihistamines (new generation)	–	YES (IAR and PER)	VL	–	YES (SAR and PER)	VL
Antileukotrienes (SAR and PER)	–	YES	H (SAR) L (PER)	–	YES (SAR) NO (PER)	H
Oral H ₁ -antihistamines Vs. antileukotrienes	–	YES (PER)	L	–	YES (SAR)	M
Intranasal corticosteroids	–	YES	M	YES	–	H
Intranasal corticosteroids vs. oral H ₁ -antihistamines	–	YES	L (PER) VL (SAR)	–	YES	M (PER) L (SAR)
Intranasal corticosteroids vs. intranasal H ₁ -antihistamines	–	–	N/A	YES	–	H
Intranasal corticosteroids vs. antileukotrienes	–	–	N/A	YES	–	L
Oral corticosteroids	–	–	N/A	–	YES (short course)	VL
Intramuscular corticosteroids	–	–	N/A	NO	–	L
Intranasal chromones	–	–	N/A	–	YES	M
Intranasal H ₁ -antihistamines vs. intranasal chromones	–	–	N/A	–	YES	L
Intranasal ipratropium bromide	–	–	N/A	–	YES	M
Intranasal decongestants	–	NO	VL	–	YES (very short course)	VL
Oral decongestants	–	–	N/A	–	NO	L
Combination of oral descongectant and H ₁ -antihistamines vs. H ₁ -antihistamines alone	–	–	N/A	–	NO	M
Intraocular H ₁ -antihistamines	–	–	N/A	–	YES	L
Intraocular chromones	–	YES	VL	–	YES	VL
Allergen-specific immunotherapy						
Subcutaneous specific IT (AR without asthma)	–	YES	L	–	YES	M (SAR) L (PER by HDM)
Subcutaneous specific IT (AR and asthma)	–	YES	M	–	YES	M
Sublingual specific IT (AR without asthma)	–	YES (by pollen) NO (by HDM)	M (by pollen) VL (by HDMs)	–	YES	M (by pollen) L (by HDM)
Sublingual specific IT (AR and asthma)	–	YES	L	–	YES	L

Table 3 (continued)

	Children with AR			Adults with AR		
	Recommends	Suggests	Quality of evidence	Recommends	Suggests	Quality of evidence
Local nasal specific IT	–	YES (by pollen)	VL	–	YES	L
Alternative treatment						
Homeopathy	–	NO	VL	–	NO	VL
Acupuncture	–	NO	VL	–	NO	VL
Butterbur	–	NO	VL	–	NO	VL
Herbal medicines	–	NO	VL	–	NO	VL
Physical techniques and others (phototherapy)	–	NO	VL	–	NO	VL

H high, *M* moderate, *L* low, *VL* very low, *IT* immunotherapy, *AR* allergic rhinitis, *SAR* seasonal allergic rhinitis, *PER* persistent allergic rhinitis, *HMDs* house dust mites, *N/A* not available, *vs.* versus, preferred the first

although this form of immunotherapy is not approved for use in the US. In children, considerable progress has been made in obtaining clinical evidence for allergen-specific immunotherapy in paediatric respiratory allergy [74]. After 100 years of immunotherapy, we now have accrued enough data to demonstrate immunotherapy's efficacy [75, 76].

Conclusions

- Regarding AR prevalence, more studies are needed worldwide in the adult population to compare epidemiological data with studies done in children and adolescent patients. There is a wide range of impact and some imbalance, depending on the study area in both pediatric and adult populations.
- A number of validated questionnaires have measured the impact of AR regarding the quality of life in both adults and children. Nasal congestion is the most bothersome symptom both in children and adults, and AR affects both children's school performance and adults' work productivity.
- The clinical characteristics of both AR adult and children populations are similar in terms of symptoms, although demonstrating some differences in comorbidities. There is, however, a strong association between AR and asthma for both age populations.
- Finally, the management of AR is similar, with some minor differences, for both child and adult AR patients.

Disclosure Dr. Valero has served on boards for Stallergenes, Meda Pharmaceuticals, FAES, and ESTEVE; has received grant support from Uriach; and has received payment for development of educational presentations (including service on speakers bureaus) from FAES, Stallergenes, Novartis, and Pfizer.

Dr. Mullol has served on boards for Uriach, Meda Pharmaceuticals, Johnson & Johnson, FAES, and Hartington Pharma; has received grant support from GlaxoSmithKline, Uriach, FAES, and Merck Sharp & Dohme; and has received payment for development of educational presentations (including lectures and service on speakers bureaus) from Uriach, Hartington Pharma, FAES, Novartis, Boehringer-Ingelheim, ESTEVE, Merck Sharp & Dohme, and PIERRE-FABRE.

Dr. Izquierdo-Dominguez reported no potential conflicts of interest relevant to this article.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC. A survey of the burden of allergic rhinitis in Europe. *Allergy*. 2007;62 Suppl 5:17–25.
2. Nathan RA. The burden of allergic rhinitis. *Allergy Asthma Proc*. 2007;28:3–9.
3. Morais-Almeida M, Gaspar A, Pires G, Prates S, Rosado Pinto J. Risk factors for asthma symptoms at school age: an 8-year prospective study. *Allergy Asthma Proc*. 2007;28:183–9.
4. Annesi-Maesano I, Hulin M, Lavaud F, et al. Poor air quality in classrooms related to asthma and rhinitis in primary schoolchildren of the French 6 cities study. *Thorax*. 2012;67:682–8.
5. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008. *Allergy*. 2008;63 Suppl 86:8–160.
6. Valero A, Ferrer M, Sastre J, et al. A new criterion by which to discriminate between patients with moderate allergic rhinitis and patients with severe allergic rhinitis based on the allergic rhinitis and its impact on asthma severity items. *J Allergy Clin Immunol*. 2007;120:359–65.
7. Valero A, Ferrer M, Baró E, et al. Discrimination between moderate and severe disease may be used in patients with either treated or untreated allergic rhinitis. *Allergy*. 2010;65(12):1609–13.

8. • Jáuregui I, Dávila I, Sastre J, et al. Validation of ARIA (Allergic Rhinitis and its Impact on Asthma) classification in a pediatric population: the PEDRIAL study. *Pediatr Allergy Immunol.* 2011;22:388–92. *This article shows the validation of ARIA classification in children with allergic rhinitis.*
9. • Montoro J, Del Cuvillo A, Mullol J, et al. Validation of the modified allergic rhinitis and its impact on asthma (ARIA) severity classification in allergic rhinitis children: the PEDRIAL study. *Allergy.* 2012;67(11):1437–42. *This article shows the validation of the modified ARIA severity classification in children with allergic rhinitis which discriminates moderate from severe disease among untreated patients.*
10. Bousquet J, Bodez T, Gehano P, et al. Implementation of guidelines for allergic rhinitis in specialist practices. A randomized pragmatic controlled trial. *Int Arch Allergy Immunol.* 2009;150(1):75–82.
11. Bachert C, van Cauwenberge P, Olbrecht J, van Schoor J. Prevalence, classification and perception of allergic and non allergic rhinitis in Belgium. *Allergy.* 2006;61:693–8.
12. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J.* 2004;24:758–64.
13. Nathan RA, Meltzer EO, Derebery J, et al. The prevalence of nasal symptoms attributed to allergies in the United States: findings from the burden of rhinitis in an America survey. *Allergy Asthma Proc.* 2008;29:600–8.
14. Jessen M, Malm L. Definition, prevalence and development of nasal obstruction. *Allergy.* 1997;52 Suppl 40:3–6.
15. • Katelaris CH, Lee BW, Potter PC, et al. Prevalence and diversity of allergic rhinitis in regions of the world beyond Europe and North America. *Clin Exp Allergy.* 2012;42:186–207. *This manuscript presents the latest prevalences of allergic rhinitis in developed countries and in both children and adults.*
16. Asher MI, Keil U, Anderson HR, et al. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J.* 1995;8:483–91.
17. Weiland SK, Björkstén B, Brunekreef B, et al. Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC II): rationale and methods. *Eur Respir J.* 2004;24:406–12.
18. Ellwood P, Asher MI, Beasley R, Clayton TO, Stewart AW, the ISAAC Steering Committee. The International Study of Asthma and Allergies in childhood (ISAAC): phase three rationale and methods. *Int J Tuberc Lung Dis.* 2005;9:10–6.
19. Ait-khaled N, Odhiambo J, Pearce N, et al. Prevalence of symptoms of asthma, rhinitis and eczema in 13- to 14- year- old children in Africa: the International Study of Asthma and Allergies in Childhood Phase III. *Allergy.* 2007;62:247–58.
20. Strachan D, Sibbald B, Weiland S, et al. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: The International Study of Asthma and Allergies in Childhood (ISAAC). *Paediatr Allergy Immunol.* 1997;8:161–76.
21. Williams H, Robertson C, Stewart A, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol.* 1999;103:125–38.
22. Asher MI, Montefort S, Björkstén B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and eczema in childhood: ISAAC phases one and three repeat multicountry cross-sectional surveys. *Lancet.* 2006;368:733–43.
23. Björkstén B, Clayton T, Ellwood P, Stewart A, Strachan D, the ISAAC Phase Three Study Group. Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. *Pediatr Allergy Immunol.* 2008;19:110–24.
24. Ait-Khaled A, Pearce N, Anderson HR, Ellwood P, Montefort S, Shah J, ISAAC Phase Three Study Group. Global map of the prevalence of symptoms of rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC) phase three. *Allergy.* 2009;64(1):123–48.
25. Lødrup Carlsen KC, Söderström L, Mowinckel P, et al. Asthma prediction in school children; the value of combined IgE antibodies and obstructive airways disease severity score. *Allergy.* 2010;65:1134–40.
26. Hopper JL, Jenkins MA, Carlin JB, Giles GG. Increase in the self-reported prevalence of asthma and hay fever in adults over the last generation: a matched parent-offspring study. *Aust J Public Health.* 1995;19:120–4.
27. Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy.* 2005;60:350–3.
28. Cingi C, Topuz B, Songu M, et al. Prevalence of allergic rhinitis among the adult population in Turkey. *Acta Otolaryngol.* 2010;130:600–6.
29. Zhang L, Han D, Huang D, et al. Prevalence of self-reported allergic rhinitis in eleven major cities in China. *Int Arch Allergy Immunol.* 2009;149:47–57.
30. Neffen H, Mello JF, Sole D, et al. Nasal allergies in the Latin American population: results from the Allergies in Latin America survey. *Allergy Asthma Proc.* 2010;31 Suppl 1:S9–S23.
31. Settiple RA, Charnock DR. Epidemiology of rhinitis: allergic and nonallergic. *Clin Allergy Immunol.* 2007;19:23–34.
32. Del Cuvillo A, Montoro J, Bartra J, et al. Validation of ARIA duration and severity classifications in Spanish allergic rhinitis patients—the ADRIAL cohort study. *Rhinology.* 2010;48(2):201–5.
33. Guilemany JM, Garcia-Piñero A, Alobid I, et al. Persistent allergic rhinitis has a moderate impact on the sense of smell, depending on both nasal congestion and inflammation. *Laryngoscope.* 2009;119(2):233–8.
34. Hadley JA, Schaefer SD. Clinical evaluation of rhinosinusitis: history and physical examination. *Otolaryngol Head Neck Surg.* 1997;117:S8–S11.
35. Irwin RS. Silencing chronic cough [see comments]. *Hosp Pract.* 1999;34:53–60. quiz 129–30.5.
36. Kulig M, Klettke U, Wahn V, Forster J, Bauer CP, Wahn U. Development of seasonal allergic rhinitis during the first 7 years of life. *J Allergy Clin Immunol.* 2000;106:832–9.
37. Selnes A, Nystad W, Bolle R, Lund E. Diverging prevalence trends of atopic disorders in Norwegian children. Results from three cross sectional studies. *Allergy.* 2005;60:894–9.
38. Berger WE. Allergic rhinitis in children: diagnosis and management strategies. *Paediatr Drugs.* 2004;6:233–50.
39. Steele RW. Rhinosinusitis in children. *Curr Allergy Asthma Rep.* 2006;6:508–12.
40. Noone PG, Leigh MW, Sannuti A, et al. Primary ciliary dyskinesia: diagnostic and phenotypic features. *Am J Respir Crit Care Med.* 2004;169:459–67.
41. Zureik M, Neukirch C, Leynaert B, Liard R, Bousquet J, Neukirch F. Sensitisation to airborne moulds and severity of asthma: cross sectional study from European community respiratory health survey. *BMJ.* 2002;325:411–4.
42. Rosenstreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma [see comments]. *N Engl J Med.* 1997;336:1356–63.
43. Lewis SA, Weiss ST, Platts-Mills TA, Burge H, Gold DR. The role of indoor allergen sensitization and exposure in causing morbidity in women with asthma. *Am J Respir Crit Care Med.* 2002;165:961–6.
44. Chen WY, Tseng HI, Wu MT, et al. Synergistic effect of multiple indoor allergen sources on atopic symptoms in primary school children. *Environ Res.* 2003;93:1–8.
45. Shaaban R, Zureik M, Soussan D, et al. Allergic rhinitis and onset of bronchial hyperresponsiveness: a population-based study. *Am J Respir Crit Care Med.* 2007;176:659–66.

46. Rochat MK, Illi S, Ege MJ, et al. Allergic rhinitis as a predictor for wheezing onset in school-aged children. *J Allergy Clin Immunol.* 2010;126:1170–5–e2.
47. Shaaban R, Zureik M, Soussan D, et al. Rhinitis and onset of asthma: a longitudinal population-based study. *Lancet.* 2008;372:1049–57.
48. Camelo-Nunes I, Sole D. Allergic rhinitis: indicators of quality of life. *J Bras Pneumol.* 2010;36(1):124–33.
49. Gentile D, Shapiro G, Sloner D. Allergic rhinitis. In: Leung D, Sampson H, Geha R, Szefer S, editors. *Pediatric allergy. Principles and practice.* St. Louis: Mosby; 2003. p. 287–97.
50. Hallstrand TS, Curtis JR, Aitken ML, Sullivan SD. Quality of life in adolescents with mild asthma. *Pediatr Pulmonol.* 2003;36:536–43.
51. Roberts G, Mylonopoulou M, Hurley C, Lack G. Impairment in quality of life is directly related to the level of allergen exposure and allergic airway inflammation. *Clin Exp Allergy.* 2005;35:1295–300.
52. Walker S, Khan-Wasti S, Fletcher M, Cullinan P, Harris J, Sheikh A. Seasonal allergic rhinitis is associated with a detrimental effect on examination performance in United Kingdom teenagers: case-control study. *J Allergy Clin Immunol.* 2007;120:381–7.
53. Meltzer EO, Blaiss MS, Derebery MJ, et al. Burden of allergic rhinitis: results from the Pediatric Allergies in America survey. *J Allergy Clin Immunol.* 2009;124:S43–70.
54. Juniper EF, Guyatt GH, Dolovich J. Assessment of quality of life in adolescents with allergic rhinoconjunctivitis: development and testing of a questionnaire for clinical trials. *J Allergy Clin Immunol.* 1994;93(2):413–23.
55. Juniper EF, Howland WC, Roberts NB. Measuring quality of life in children with rhinoconjunctivitis. *J Allergy Clin Immunol.* 1998;101:163–70.
56. Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. *Clin Exp Allergy.* 1991;21:77–83.
57. Juniper EF, Thompson AK, Ferrie PJ, Roberts JN. Development and validation of the mini rhinoconjunctivitis quality of life questionnaire. *Clin Exp Allergy.* 2000;30(1):132–40.
58. Juniper E, Rohrbaugh T, Meltzer EO. A questionnaire to measure quality of life in and adults with nocturnal allergic rhinoconjunctivitis. *J Allergy Clin Immunol.* 2003;111:484–90.
59. Valero A, Alonso J, Antepara I, et al. Development and validation of a new Spanish instrument to measure health-related quality of life in patients with allergic rhinitis: the ESPRINT questionnaire. *Val Health.* 2007;10(6):466–77.
60. Valero A, Alonso J, Antépara I, et al. Health-related quality of life in allergic rhinitis: comparing the short form ESPRINT-15 and MiniRQLQ questionnaires. *Allergy.* 2007;62(12):1372–8.
61. Valero A, Baró E, Sastre J, et al. Reference values for facilitating the interpretation of the ESPRINT-15 questionnaire (Spanish version). *J Investig Allergol Clin Immunol.* 2009;19(5):396–403.
62. Valero A, Izquierdo I, Giralt J, et al. Rupatadine improves nasal symptoms, quality of life (ESPRINT-15) and severity in a sub-analysis of a cohort of Spanish allergic rhinitis patients. *J Investig Allergol Clin Immunol.* 2011;21(3):229–35.
63. Valero A, Muñoz-Cano R, Sastre J, et al. The impact of allergic rhinitis on symptoms, and quality of life using the new criterion of ARIA severity classification. *Rhinology.* 2012;50(1):33–6.
64. Sardana N, Craig T. Congestion and sleep impairment in allergic rhinitis. *Asian Pac J Allergy Immunol.* 2011;29:297–306.
65. Derebery J, Meltzer E, Nathan RA, et al. Rhinitis symptoms and comorbidities in the United States: Burden of rhinitis in America survey. *Otolaryngol Head Neck Surg.* 2008;139:198–205.
66. Mullol J. A survey of the burden allergic rhinitis in Spain. *J Investig Allergol Clin Immunol.* 2009;19(1):27–34.
67. Marinho S, Simpson A, Custovic A. Allergen avoidance in the secondary and tertiary prevention of allergic diseases: does it work? *Prim Care Respir J.* 2006;15:152–8.
68. Filon FL, Radman G. Latex allergy: a follow up study of 1040 healthcare workers. *Occup Environ Med.* 2006;63:121–5.
69. Fink RS, Pierre LN, Daley Yates PT, Richards DH, Gibson A, Honour JW. Hypothalamic-pituitary-adrenal axis function after inhaled corticosteroids: unreliability of urinary free cortisol estimation. *J Clin Endocrinol Metab.* 2002;87:4541–6.
70. Sastre J, Mosges R. Local and systemic safety of intranasal corticosteroids. *J Investig Allergol Clin Immunol.* 2012;22(1):1–12.
71. •• Brozek JL, Bousquet J, Baena-Cagnani CE, Global Allergy and Asthma European Network, Grading of Recommendations Assessment, Development and Evaluation Working Group, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin Immunol.* 2010;126(3):466–76. *This manuscript shows the GRADE-based ARIA recommendations on the prevention and treatment of adults and children with allergic rhinitis, with and without comorbid asthma.*
72. Schünemann HS, Jaeschke R, Cook DJ, et al. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *Am J Respir Crit Care Med.* 2006;174:605–14.
73. Brozek JL, Baena-Cagnani CE, Bonini S, et al. Methodology for development of the Allergic Rhinitis and its Impact on Asthma guideline 2008 update. *Allergy.* 2008;63:38–46.
74. Calderon M, Gerth van Wijk R, Eichler I, et al. Perspectives on allergen-specific immunotherapy in childhood: An EAACI position statement. *Pediatr Allergy Immunol.* 2012;23:300–6.
75. European Declaration on Immunotherapy: Combating Allergy Beyond Symptoms. <http://eaaci.net/eaacimedia/1663-eaacipresents-the-european-declaration-on-allergen-immunotherapy>.
76. Calderon M, Cardona V, Demoly P, on behalf of the EAACI 100 Years of Immunotherapy Experts Panel. One hundred years of allergen immunotherapy European Academy of Allergy and Clinical Immunology celebration: review of unanswered questions. *Allergy.* 2012;67:462–76.