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REVIEW

Guidelines for allergic rhinitis need to be used in primary care

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Abstract

Clinical Practice Guidelines for allergic rhinitis have been developed over the past 15 years and have been found to improve the care for patients with allergic rhinitis. The ARIA (allergic rhinitis and its impact on asthma) guideline was the first of these evidenced-based guidelines, developed with primary care physicians. Subsequent guidelines include those by the IPCRG, BSACI, the AAAAI/ACAAI Practice Parameters for the diagnosis and management of rhinitis, and the ARIA 2008 Update. These guidelines were based on various evidence-based models, but the first to use GRADE methodology (Grading of Recommendations Assessment, Development and Evaluation) is the ARIA 2009 Revision. Since primary care physicians treat the majority of patients with allergic rhinitis it is essential that they are involved in the development and implementation of guidelines for allergic rhinitis. Prior to their implementation, guidelines should be evaluated for their accuracy and user friendliness – specifically for primary care physicians – but such validation is rarely performed. This is of great importance, in particular as regards evaluating the applicability of evidence from high quality randomised controlled trials (RCTs) which are often based on highly selected patients not representing the population of patients seen in day-to-day practice.

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Keywords allergic rhinitis, primary care, guideline, guideline evolution, methodology, ARIA, implementation

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Introduction

Allergic rhinitis represents a global health problem. It is a common disease worldwide affecting up to 40% of the population in young adults and its prevalence is increasing.[1] Although allergic rhinitis is not usually a severe disease, it alters the social life of patients, and affects school performance and work productivity.[2,3] Moreover, the costs incurred by rhinitis are substantial. Asthma and rhinitis are common co-morbidities suggesting the concept of "one airway, one disease".

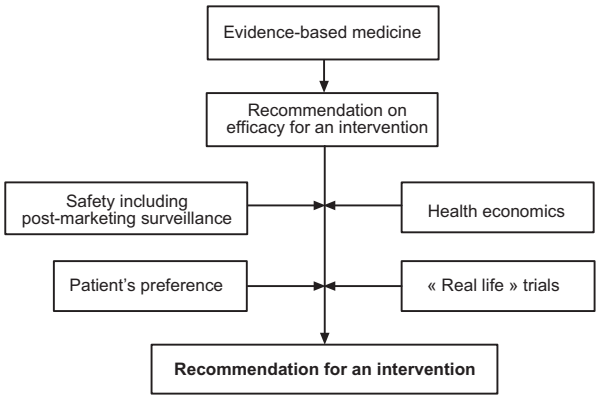
Clinical Practice Guidelines for allergic rhinitis have been developed over the past 15 years[4-6] and have been found to improve care for patients with allergic rhinitis.[7] ARIA (allergic rhinitis and its impact on asthma) was the first evidenced-based guideline.[8] It was developed with primary care physicians. Newer guidelines have been developed[2,9-11] based on various evidence-based models, but the first using GRADE methodology[12] is the ARIA 2009 Revision.[12a]

Primary care physicians treat the majority of patients with allergic rhinitis[13,14] and it is essential that they are involved in the development and implementation of guidelines for allergic rhinitis.

Evolution of concepts in guideline development

The development of clinical guidelines follows strict processes.[15] Early guidelines were predominantly derived from unsystematically-compiled opinions of experts based on clinical trials and mechanistic approaches (Opinion-based medicine).[16] "Evidence-based medicine" (EBM) has become an essential component in the preparation of guidelines. It is the ability to track down, appraise critically (for its validity and usefulness) and incorporate the information obtained from the best available evidence (ideally randomised controlled trials, RCTs, but the emphasis is on "best") in order to establish the clinical basis for diagnosis, prognosis and therapeutics.[17,18] A systematic evaluation of the available evidence has now become an essential component in the preparation of guidelines, which are an integral component of EBM defined as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients".[19] It requires a bottom-up approach that integrates the best external evidence with individual clinical expertise and patient choice. Evidence-based medicine attempts to provide a logical and convenient framework from which the quality and relevance of clinical studies may be assessed in an unbiased manner.[20] Systematic reviews contribute to resolving uncertainty when original research, reviews and editorials disagree.[21] The Cochrane Collaboration has led the way in setting new standards for the preparation of systematic reviews[22] despite existing criticism.[23,24]

Figure 1. Development of a guideline.



While there is increasing agreement on the components of proper clinical practice guidelines and what constitutes high quality evidence, it is also clear that the highest quality evidence from RCTs is often based on selected patients. Therefore, RCTs may fall short of representing the entire population.[25] Nonetheless, RCTs offer the most methodologically rigorous approach to establishing cause and effect, thereby providing the highest quality evidence. A number of approaches have been used to grade the quality of evidence and the resulting strength of recommendations.[26,27] The large number of systems for measuring the quality of evidence and recommendations is confusing[28] and all approaches used previously for grading levels of evidence and the strength of recommendations have important shortcomings.[15,26]

Great progress has been made in obtaining reliable evidence on the beneficial effects of interventions, but developments in the identification, interpretation, and reporting of harmful effects is more challenging.[29,30] The European Medicines Agency (EMEA) and the USA Food and Drug Administration (FDA) have clearly stated that RCTs are insufficient to assess the side effects of treatments largely because of their small size, and that post-marketing surveillance is needed to pick up rare events occurring in the at-risk population. There is a need to include evidence about harms (risks) in recommendations (Figure 1).

Shortcomings of RCTs are well known and include selection bias and concerns regarding external and internal validity. Thus, "real life" studies – conducted in the whole patient population without excluding many patients – are needed to support the recommendations based on RCTs.

More recently, the "Guidelines for WHO [World Health Organisation] guidelines" recommended using a specific, uniform grading system.[31] The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach is one of the recommended systems[27] and is being used increasingly by a number of organisations.[32-37] It grades

Table 1. Grading the strength of recommendations and quality of evidence in the ARIA guidelines according to the GRADE system.

Notation*	Strength of recommendation and quality of evidence	Clarity of balance between desirable and undesirable effects	Quality of supporting evidence	Implications
1A	Strong recommendation High-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies.	Recommendation can apply to most patients in most circumstances. Further research is unlikely to change our confidence in the estimate of effect.
1B	Strong recommendation Moderate-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise) or unusually strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
1C	Strong recommendation Low-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least one critical outcome from RCTs with serious flaws, observational studies, or indirect evidence	Recommendation may change when higher quality evidence becomes available. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
1D	Strong recommendation Very low-quality evidence (very rarely applicable)	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least one of the critical outcomes from unsystematic clinical observation or very indirect evidence	Recommendation may change when higher quality evidence becomes available. Any estimate of the effect for at least one critical outcome is very uncertain.
2A	Weak recommendation High-quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patients' or societal views. Further research is very unlikely to change our confidence in the estimate of the effect.
2B	Weak recommendation Moderate-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise) or unusually strong evidence from unbiased observational studies	Alternative approach likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on our confidence of the estimate of effect and may change the estimate.
2C	Weak recommendation Low-quality evidence	Uncertainty in the estimates of desirable and undesirable effects; desirable effects may be closely balanced with undesirable effects	Evidence for at least one critical outcome from RCTs with serious flaws, observational studies, or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have important impact on our confidence in the estimate of effect and is likely to change the estimate.
2D	Weak recommendation Very low-quality evidence	Major uncertainty in the estimates of desirable and undesirable effects; desirable effects may be closely balanced with undesirable effects	Evidence for at least one critical outcome from unsystematic clinical observation or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of the effect for at least one critical outcome is very uncertain.

* Notation is not a part of GRADE system; it was adopted for the ARIA guideline to simplify the presentation.

RCT – randomised controlled trial

Adapted from Schünemann *et al.* (27) and Brozek *et al* (12)

recommendations into two levels – strong and weak – and quality evidence into four categories – high, moderate, low and very low.[27,28] While the quality of evidence is one of the factors influencing the strength of a recommendation, this strength is also influenced by the balance between the benefits and harms, resource utilisation and patients' views[3] (Tables 1 and 2). The GRADE approach is therefore closer to patients' needs than former grading systems based on RCT results.

Table 2. Implications of strong and weak recommendations.

Implications	Strong recommendation	Weak recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognise that different choices will be appropriate for different patients, and that you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may well be useful helping individuals making decisions consistent with their values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations	Policy making will require substantial debates and involvement of many stakeholders

From Schünemann *et al.* (27) and Brozek *et al* (12)

Table 3. Guidelines for allergic rhinitis.

	Year of development	Ref no.		Evidence model	Pocket guideRhinitis classification		
					GPs	Pharmacists	
International consensus	1993-1994	(4)	International	None			Seasonal-perennial
Practice parameters	1996-1997	(5)	USA	None			Seasonal-perennial
EAACI consensus	1999	(6)	Europe	None			Seasonal-perennial
ARIA	1999-2001	(8)	International	Shekelle (38)	yes	(42)	Intermittent-persistent
IPCRG	2003-2006	(9)	International	Royal College of General Practionners (43)			Intermittent-persistent
ARIA 2008 Update	2006-2008	(2)	International	Shekelle (38)	(44)		Intermittent-persistent
BSACI	2006-2008	(10)	UK	Shekelle (38)			Seasonal-perennial
2008 Practice parameters	2006-2007	(11)	USA	Shekelle (38)			Seasonal-perennial
ARIA 2009 Revision	2009	(12a)	International	GRADE (12)			Intermittent-persistent

Evolution of concepts in allergic rhinitis guidelines

The first three guidelines for allergic rhinitis set the scene for evidence-based guidelines, although they were opinion-based.[4-6] Two of them proposed a stepwise approach (Table 3).

The ARIA initiative[8] was developed in collaboration with the WHO as a state-of-the-art guideline for the specialist as well as for the general practitioner (GP):

- To update their knowledge of allergic rhinitis.
- To highlight the impact of allergic rhinitis on asthma.
- To provide an evidence-based documented revision of diagnostic methods.
- To provide an evidence-based revision to treatments available in rhinitis.
- To set goals for treatment.
- To propose a stepwise approach to disease management for rhinitis and for rhinitis and asthma co-morbidities.

In the ARIA document, a new subdivision of allergic rhinitis was proposed, with patients categorised as having intermittent or persistent rhinitis (superseding the previous categories of seasonal and perennial). This classification is closer to patient needs and is easier for GPs to use. Most patients are polysensitised and different allergen exposures are superseded so that it is often difficult to differentiate seasonal and perennial symptoms. Moreover, many if not most patients allergic to indoor allergens have intermittent symptoms.[38] The severity of allergic rhinitis has been classified as "mild' and "moderate/severe" depending on the severity of symptoms and effect on quality of life defined by physical and social activities as well as school and work performance.

ARIA considered the treatment of patients with rhinitis based on previously published documents but offered for the first time an evidence-based documentation of recommendations.[38] The management of allergic rhinitis included allergen avoidance (rarely effective), medications (pharmacological treatment), immunotherapy, and education. Depending on the category and severity of allergic rhinitis, a stepwise therapeutic approach was proposed.

The International Primary Care Respiratory Group (IPCRG) Guideline on the management of rhinitis in primary care[9] is fully consistent with the ARIA guidelines. It was developed as part of a set of several guidelines written by GPs specifically to aid the management of respiratory diseases in the primary care setting.[39,40] It highlights the treatment goals and the classification of the condition according to symptom frequency (intermittent or persistent) and severity (mild or moderate-severe). It covers the need for allergen avoidance, pharmacologic therapy including immunotherapy, alternative therapies, management of ocular symptoms, the management of co-existing allergic rhinitis and asthma, and the need for follow-up and ongoing care for patients with rhinitis.[9]

The British Society of Allergy and Clinical Immunology (BSACI) guidelines for the management of patients with rhinitis are intended for use by any physician treating allergic conditions.[10] Evidence for the recommendations was obtained by using electronic literature searches. Each article was reviewed for suitability for inclusion in the guideline. The recommendations were evidence-graded at the time of preparation of these guidelines and the grades of recommendation and levels of evidence are defined according to Shekelle.[38] During the development of these guidelines, a web-based system was used to allow consultation with all BSACI members. The draft guidelines were amended by the Standards of Care Committee after careful consideration of all comments and suggestions. Where evidence was lacking, a consensus was reached among the experts on the committee.

The Practice Parameters for the diagnosis and management of allergic rhinitis from the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) have recently been published.[11] This is an update of the previous document published in 1998[41] using the model of evidence of Shekelle.[38] They reviewed new medications available, combination therapy, the need to consider benefits versus safety and proposed a rhinitis action plan.

The ARIA 2009 Revision[12a] is based on GRADE. Clinical questions covered by this document were developed in consultation with the ARIA guideline panel. The key questions can be summarised briefly as:

- Should allergen avoidance methods be used by parents to avoid development of allergy in children?
- Should occupational allergen avoidance methods be used?
- Should patients with allergic rhinitis and/or conjunctivitis use H1-antihistamines, glucocorticosteroids, antileukotrienes, chromones, decongestants, or ipratropium bromide? What is the relative effect of these medications?
- Should allergen specific immunotherapy be used in patients with allergic rhinitis? What is the effect of subcutaneous, intranasal, and sublingual specific immunotherapy?
- Should complementary and alternative treatments be used for allergic rhinitis?
- Should medications for the treatment of allergic rhinitis be used in patients with concomitant asthma for the treatment of asthma?

Some of the allergic rhinitis guidelines are reviewed in Table 3.

Importance of guidelines for the management of allergic rhinitis

Prior to their implementation, guidelines should be tested for their accuracy and user-friendliness. Unfortunately such a validation has not been performed for most guidelines. In allergic rhinitis, two studies have attempted to elicit whether a guideline-based treatment is more effective than free treatment choice. The International Consensus of Rhinitis[4] was tested in patients with seasonal allergic rhinitis using a cluster-randomised trial.[7] It was found that patients treated by primary care physicians using the recommended treatment had significantly improved quality-of-life and reduced symptoms compared to those treated by physicians who used free treatment choice. In another cluster-randomised trial, the ARIA guideline[8] was tested in patients with persistent allergic rhinitis treated by specialists. It was found that the ARIA-based approach was more effective than free treatment choice.[45] The results of these two studies support the recommendation to use guidelines for the treatment of allergic rhinitis, particularly in primary care.

Use of rhinitis guidelines at the primary care level

Primary care physicians treat the majority of patients with respiratory diseases.[13,14] However, in primary care, guidelines for chronic respiratory diseases are not widely accepted, limitations reduce the use of some guidelines, and guidelines are insufficiently implemented for asthma[46] or rhinitis.[47] With the advent of rhinitis guidelines and the high prevalence of rhinitis seen in primary care settings, it is important to investigate the knowledge, attitudes, and practices of primary care physicians with regard to these guidelines. In allergic rhinitis, about half of the physicians in France claimed to know the ARIA guidelines and said they followed them,[48] but current marketing studies show that a majority of GPs do not fully follow ARIA. In order to gain better acceptance of chronic respiratory diseases guidelines in primary care, there is a need for the development of guidelines with intense involvement of GPs.

Some of the reasons why GPs do not always implement guidelines are: inadequate organisation in practice;[49] scepticism about the effectiveness of guidelines;[50] and/or the difficulty of GPs to cope with evidence-based medicine in day-to-day practice.[50] Since clinical management following evidence-based guidelines yields better results for patients,[7,45] it is important to have access to primary care guidelines which are specifically relevant to, and provided by, primary care. The IPCRG asked primary care experts from several countries to develop primary care guidelines for the diagnosis and treatment of asthma, COPD and rhinitis.[39] However, these guidelines were based on an evidence-based model mostly based on RCT evidence. The ARIA guidelines have always been developed with primary care physicians,[2,8] and the recent ARIA 2008 pocket guide[44] was developed with the World Organisation of primary care physicians (Wonca), the IPCRG, and the European Federation of Allergy and Airway Diseases Patients Association (EFA). The ARIA 2009 revision[12a] has also been developed with primary care physicians and members of patient organisations who actively participated in the recommendations.

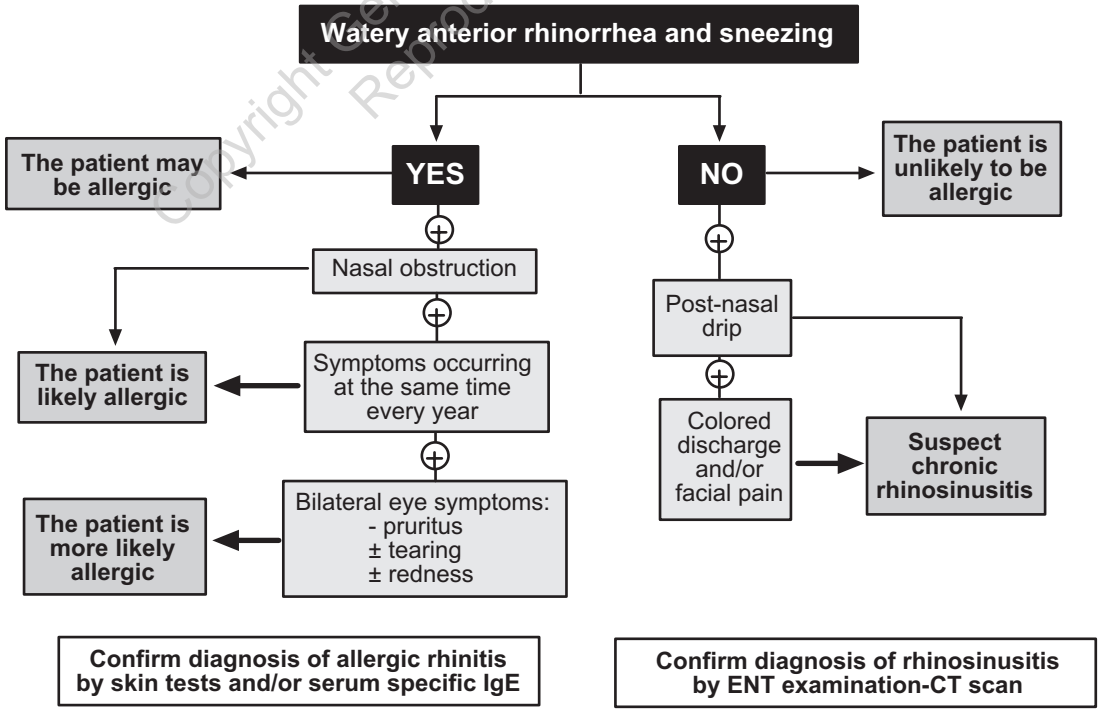
The applicability of guidelines in primary care is not always clear.[51] Whilst there is increasing agreement on the components of proper clinical practice guidelines and what constitutes high quality evidence, it is also clear that the highest quality evidence from RCTs is often based on highly selected patients not representing the population of patients seen in day-to-day practice. In a study carried out in general and specialist practices in Norway, only 5.4% of the study asthma patients met with the criteria of common RCTs carried out in asthma.[25] Therefore, clinicians need to evaluate the generalisability or directness of such RCTs to a clinical population, how close the intervention is in general practice to that of the RCT, and how important or relevant the outcomes in the trial are for general practice patients. Therefore, detailed descriptions of these factors, ideally in concise evidence profiles and summaries, are required to allow clinicians' judgment about whether the evidence used for a recommendation is applicable to their practice.

Moreover, compliance with treatment, a major problem for allergy and asthma management, is far better in RCTs than in real life. Thus, "real life" or pragmatic trials are needed but are rarely available for allergic diseases.[7,45] Furthermore, there is an urgent need to determine whether patients enrolled in allergic rhinitis RCTs are representative of the patient population seen in primary care.

The accurate diagnosis of rhinitis is essential in primary care. The IPCRG guideline on the diagnosis of respiratory diseases[40] is clearly written, evidence-based, and will be of great help for the primary care physician. It is, however, not very easy to differentiate allergic rhinitis from rhinosinusitis[52] or non-allergic rhinitis[53] (see Figure 2).

As for any document, rhinitis guidelines need to be

Figure 2. Symptoms suggestive of a diagnosis of allergic rhinitis.



From ARIA 2008 update (2)

continuously revised, mostly because the science and evidence concerning rhinitis is evolving rapidly and guidelines are based on published evidence. There is, however, a very clear need to perform high quality real life studies using, for example, cluster randomised designs to provide concrete evidence that the applicability of evidence obtained in scientifically conducted RCTs translates into daily practice.

Summary

Clinical Practice Guidelines for allergic rhinitis have been developed over the past 15 years and have been found to improve the management of patients with allergic rhinitis. They were based on various evidence-based models. ARIA (allergic rhinitis and its impact on asthma) was the first evidenced-based guideline, and the ARIA 2009 Revision is the first evidence-based guideline using GRADE methodology. ARIA was developed with primary care physicians who treat the majority of patients with allergic rhinitis.

Conflict of interest

None to declare.

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