# Complete Summary

## GUIDELINE TITLE

Allergic rhinitis and its impact on asthma.

## BIBLIOGRAPHIC SOURCE(S)

Allergic rhinitis and its impact on asthma. Geneva (Switzerland): World Health Organization (WHO); 2008. [2241 references]

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001 Nov;108(5):S147-334.

## COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

## SCOPE

### DISEASE/CONDITION(S)

Allergic rhinitis and asthma

### GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Diagnosis
Management
Prevention
Treatment

## CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Infectious Diseases
Internal Medicine
Nursing
Otolaryngology
Pediatrics
Preventive Medicine
Pulmonary Medicine

## INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Health Plans
Managed Care Organizations
Nurses
Physician Assistants
Physicians

## GUIDELINE OBJECTIVE(S)

- To update clinicians' knowledge of allergic rhinitis
- To highlight the impact of allergic rhinitis on asthma
- To provide an evidence-based documented revision on the diagnosis methods
- To provide an evidence-based revision on the treatments available
- To provide a stepwise approach to the management of the disease

## TARGET POPULATION

Patients of all ages in all geographic locations who have allergic rhinitis and asthma

## INTERVENTIONS AND PRACTICES CONSIDERED

### Diagnosis

1. History and general ear, nose, and throat (ENT) examination
2. Symptom assessment
3. Skin tests (allergen specific immunoglobulin E [IgE])
4. In vitro tests, including serum allergen-specific IgE
5. Nasal challenge tests
6. Diagnosis of inhalant allergy, food allergy, and occupational allergy
7. Other ENT diagnosis and tests, as indicated
8. Assessment of the severity and control of rhinitis
    - Control questionnaires and visual analogue tests
    - Objective measures of severity

### Management

1. Environmental control
2. Drug treatment
    - Second generation oral or intranasal $H_1$-antihistamines
    - Topical $H_1$-antihistamines
    - Intranasal glucocorticosteroids
    - Montelukast
    - Combination therapy with intranasal glucocorticosteroids
    - Cromones
    - Intranasal and oral decongestants
    - Intranasal ipratropium
    - Systemic glucocorticosteroids
3. Allergen-specific immunotherapy (subcutaneous, sublingual, intranasal)
4. Surgical treatment
5. Treatment of allergic rhinitis and co-morbidities
6. Preventive measures, including breastfeeding, avoidance of environmental tobacco smoke, and primary prevention of occupational airway disease

### MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of diagnostic tests
- Side effects of treatment
- Response of symptoms (sneezing, rhinorrhea, nasal obstruction, nasal itch, eye symptoms) to treatment
- Quality of life
- Cost-effectiveness of treatments

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

#### Identifying and Summarizing the Evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to developing guidelines postulates that before grading the quality of evidence and strength of each recommendation, guideline developers should first identify a recently well-done systematic review of the appropriate evidence answering the relevant clinical questions, or conduct one when there is none available. This should be followed by a transparent evidence summary, such as creation of GRADE evidence profiles, on which to base judgments.

For the Allergic Rhinitis and its Impact on Asthma (ARIA) guideline 2008 update, this postulate is partially fulfilled. Members of the ARIA guideline panel, including the GRADE representatives, performed extensive literature searches addressing the clinical questions covered by the guideline. In addition, they identified up-to-date valid systematic reviews by searching the MEDLINE database, Cochrane Library, and in selected cases also reference lists of the most recent narrative

views, related systematic reviews, or studies on the topic. They based their judgments on these systematic reviews and, if applicable, on additional randomized trials published afterwards. They developed GRADE evidence profiles (see Figure 1 in the methodology document [see the "Availability of Companion Documents"] field) based on the systematic reviews. These concise evidence profiles allowed panel members to base their judgments on the same and concisely summarized evidence.

When there was no recent systematic review available, the panel did not perform its own systematic reviews, but followed a pragmatic approach and searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar for relevant randomized trials.

For many questions randomized trials were not available, and the panel relied on available observational studies that were identified for a prior ARIA guideline edition, its subsequent updates, or additional non-structured searches for observational studies. Panel members evaluated the original observational studies to inform judgments about the quality of the underlying evidence. In such situations, they based the judgments about the quality of evidence on a crude examination of the most important studies.

**NUMBER OF SOURCE DOCUMENTS**

Not stated

**METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

**RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

See "Rating Scheme for the Strength of the Recommendations."

**METHODS USED TO ANALYZE THE EVIDENCE**

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

**DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

**METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

**DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

### Formulation of Recommendations

Guidelines make a set of recommendations advising the clinicians, patients, and other healthcare professionals which of the alternative management strategies is likely to be most beneficial for patients. Consequently, wording of the recommendations in the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines update clearly states what is the proposed course of action. In this document, the guideline panel followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group's advice to use the phrase "we recommend" for strong recommendations and a less definitive "we suggest" for weak recommendations. Wording of strong and weak recommendations was particularly important since the ARIA guidelines are intended for patients and clinicians in different regions, cultures, traditions, and usage of language. When appropriate, recommendations are supplemented with an explanatory statement of values and preferences that the members of the guideline panel considered in formulating the recommendation and determining its strength. Further remarks occasionally follow, when the panel thought that additional statements are justified (such as dosing), but are not recommended actions per se.

### Panel Meeting

Based on the available evidence, the estimates of effect and their gradients, assumed values and preferences, and resource utilization issues, members of the ARIA guideline panel made decisions regarding the strength of each recommendation. To achieve this, guideline panel held a 1-day meeting on June 20$^{th}$, 2007, under the auspices of Agenzia Italiana del Farmaco (AIFA) in Rome, Italy, which included 6 members of ARIA and 2 members of AIFA, to discuss the procedures and to draft recommendations. After having agreed on the procedures and additional work that needed to be done, a second meeting was arranged to discuss the final recommendations based on a second draft of the updated guidelines. During this subsequent meeting on 15 September 2007 in Stockholm, Sweden, members of the ARIA guideline panel reviewed these judgments and made decisions on the quality of evidence, the balance of benefits and downsides (harms, burden, and occasionally cost) of a considered management strategy, and on the final strength of each recommendation. Recommendations are based on a consensus of the panel. For the formulation and discussion about the final recommendations, all panel members were asked to consider their own and other conflicts during the discussion and decision making as well as to abstain from discussion and voting if necessary. Subsequent interaction and discussion took place through email, but recommendations were not changed after the final meeting except for minor wording changes or correction of factual errors.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

| Notation | Strength of Recommendation and Quality of Evidence | Clarity of Balance Between Desirable and Undesirable Effects | Quality of Supporting Evidence | Implications |
|---|---|---|---|---|
| 1A | Strong recommendation<br><br>High quality evidence | Desirable effects clearly outweigh undesirable effects or vice versa | Consistent evidence from randomized controlled trials (RCTs) or exceptionally strong evidence from unbiased observational studies | Recommendation can apply to most patients in most circumstances.<br><br>Further research is unlikely to change the confidence of the estimate of effect |
| 1B | Strong recommendation<br><br>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.<br><br>Further research (if performed) is likely to have an important impact on the confidence in the estimate of effect and may change the estimate. |
| 1C | Strong recommendation<br><br>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.<br><br>Further research (if performed) is likely to have an important impact on the confidence in the estimate of effect and is |

| Notation | Strength of Recommendation and Quality of Evidence | Clarity of Balance Between Desirable and Undesirable Effects | Quality of Supporting Evidence | Implications |
|---|---|---|---|---|
| | | | | likely to change the estimate. |
| 1D | Strong recommendation<br><br>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.<br><br>Any estimate of the effect for at least one critical outcome is very uncertain. |
| 2A | Weak recommendation<br><br>High quality evidence | Desirable effects closely balance 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.<br><br>Further research is very unlikely to change the confidence in the estimate of effect. |
| 2B | Weak recommendation<br><br>Moderate quality evidence | Desirable effects closely balance 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 is likely to be better for some patients under some circumstances.<br><br>Further research (if performed) is likely to have an important impact on the confidence of the estimate of effect and may |

| Notation | Strength of Recommendation and Quality of Evidence | Clarity of Balance Between Desirable and Undesirable Effects | Quality of Supporting Evidence | Implications |
|---|---|---|---|---|
| | | | | change the estimate. |
| 2C | Weak recommendation<br><br>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.<br><br>Further research is very likely to have important impact on the confidence in the estimate of effect and is likely to change the estimate. |
| 2D | Weak recommendation<br><br>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.<br><br>Any estimate of the effect for at least one critical outcome is very uncertain. |

**COST ANALYSIS**

The panel could have considered cost or resource expenditure as one of the outcomes when weighing up desirable (less resource expenditure) and undesirable (more resource expenditure) consequences of competing interventions for each recommendation. Resource expenditure, however, is much more variable over jurisdictions, time, and availability of the over-the-counter medications. In addition, the resource implications also vary widely. Thus, while higher costs will reduce the likelihood of a strong recommendation in favour of a particular intervention, the context of the recommendation can be critical. In considering resource allocation issues, guideline panels must thus be very specific about the setting to which a recommendation applies and the perspective that they had chosen, i.e., which costs were considered and whether resource expenditure was

considered from the perspective of the patient (depending on insurance status, these costs differ) or society within a given health care system (this includes indirect or opportunity cost saved or incurred by following a recommendation). Furthermore, recommendations that are heavily influenced by costs are likely to change over time as resource implications evolve. The Allergic Rhinitis and its Impact on Asthma (ARIA) guideline panel considered cost implicitly and not in detail, mostly because ARIA guidelines are intended for users around the world and drug costs are highly variable between different regions. However, when resource utilization was likely to play a role and influenced a recommendation, this was labeled in the values and preferences section in the original guideline document.

### METHOD OF GUIDELINE VALIDATION

Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

#### Summary of Major Recommendations

1. Allergic rhinitis is a major chronic respiratory disease due to its:
    - Prevalence
    - Impact on quality of life
    - Impact on work/school performance and productivity
    - Economic burden
    - Links with asthma
2. In addition, allergic rhinitis is associated with sinusitis and other co-morbidities such as conjunctivitis.
3. Allergic rhinitis should be considered as a risk factor for asthma along with other known risk factors.
4. A new subdivision of allergic rhinitis has been proposed:
    - Intermittent (IAR)
    - Persistent (PER)
5. The severity of allergic rhinitis has been classified as "mild' and "moderate/severe" depending on the severity of symptoms and quality-of-life outcomes.
6. Depending on the subdivision and severity of allergic rhinitis, a stepwise therapeutic approach has been proposed.
7. The treatment of allergic rhinitis combines:
    - Allergen avoidance (when possible)
    - Pharmacotherapy
    - Immunotherapy
    - Education
8. Patients with persistent allergic rhinitis should be evaluated for asthma by means of a medical history, chest examination and, if possible and when

necessary, the assessment of airflow obstruction before and after bronchodilator.

9. Patients with asthma should be appropriately evaluated (history and physical examination) for rhinitis.
10. Ideally, a combined strategy should be used to treat the upper and lower airway diseases in terms of efficacy and safety.

## Specific Recommendations

### Diagnosis

*Diagnosis of Allergic Rhinitis*

- The diagnosis of allergic rhinitis is based upon the coordination between a typical history of allergic symptoms and diagnostic tests.
- Typical symptoms of allergic rhinitis include rhinorrhea, sneezing, nasal obstruction, and nasal pruritus.
- Ocular symptoms are common, in particular in patients allergic to outdoor allergens.
- Diagnostic tests are based on the demonstration of allergen-specific immunoglobulin E (IgE) in the skin (skin tests) or the blood (specific IgE).
- The measurement of total IgE is not useful in the diagnosis of allergic rhinitis.
- Many asymptomatic subjects can have positive skin tests and/or detectable serum-specific IgE.
- Many patients have positive tests which are irrelevant.
- In some countries, the suspicion of allergic rhinitis may be raised in the pharmacy.
- Patients with persistent and/or moderate/severe symptoms of rhinitis should be referred to a physician.
- Most patients with rhinitis are seen in primary care and, in developed countries, allergy tests are available to screen for allergy.
- Patients with persistent and/or moderate/severe symptoms of rhinitis need a detailed allergy diagnosis.

### Management

*Environmental Control*

<u>Tertiary Environmental Control</u>

- The vast majority of single preventive measures of indoor allergen control have failed to achieve any clinically relevant improvement of asthma and rhinitis. Tertiary prevention of indoor allergens is not a public health measure.
- In patients allergic to furred pets who have symptoms on contact with the allergen, pet avoidance is recommended.
- In low-income settings with a high load of pollutants (and allergens), a multifaceted intervention may be useful.
- Total avoidance of occupational agents is recommended in sensitized subjects.
- Occupational agent control may be useful when total avoidance is not possible.

*Drug Treatment*

Pharmacotherapy of Allergic Rhinitis and Conjunctivitis

- Second-generation oral or intranasal $H_1$-antihistamines are recommended for the treatment of allergic rhinitis and conjunctivitis in adults and children.
- First-generation oral $H_1$-antihistamines are not recommended when second-generation ones are available due to safety concerns.
- Topical $H_1$-antihistamines are recommended for the treatment of allergic rhinitis and conjunctivitis.
- Intranasal glucocorticosteroids are recommended for the treatment of allergic rhinitis in adults and children. They are the most effective drugs for the treatment of allergic rhinitis.
- Intra-muscular glucocorticosteroids and long-term use of oral glucocorticosteroids are not recommended due to safety concern.
- Topical cromones are recommended in the treatment of allergic rhinitis and conjunctivitis, but they are only modestly effective.
- Montelukast is recommended in the treatment of seasonal allergic rhinitis in patients over 6 years of age.
- Intranasal ipratropium is recommended in the treatment of rhinorrhea associated with allergic rhinitis.
- Intranasal decongestants may be used for a short period of time in patients with severe nasal obstruction.
- Oral decongestants (and their associations) may be used in the treatment of allergic rhinitis in adults, but side effects are common.
- The treatment of allergic rhinitis should consider the severity and duration of the disease, the patient's preference, as well as the efficacy, availability, and costs of drugs.
- A stepwise approach depending on the severity and duration of rhinitis is proposed.
- A tailored approach is needed for each individual patient.
- Not all patients with moderate/severe allergic rhinitis are controlled despite optimal pharmacotherapy.

*Allergen-Specific Immunotherapy: Therapeutic Vaccines for Allergic Disease*

Specific Immunotherapy

- Allergen-specific immunotherapy is classically administered by subcutaneous route but local routes are now available.
- Specific immunotherapy needs a precise diagnosis of IgE-mediated allergy.
- Subcutaneous immunotherapy is effective in adults and children for pollen and mite allergy, but it is burdened by the risks of side effects. These reactions may be exceptionally life-threatening.
- Sublingual immunotherapy is recommended for the treatment of pollen allergy in adults.
- Sublingual immunotherapy may be used for the treatment of patients with mite allergy.
- Intranasal immunotherapy may be used for the treatment of patients with pollen allergy.
- Allergen-specific immunotherapy may alter the natural course of allergic diseases.

- Subcutaneous immunotherapy appears to be effective several years after its cessation.
- Immunotherapy appears to reduce the development of new sensitizations.
- Administered to patients with rhinitis, subcutaneous immunotherapy appears to reduce the development of asthma.

Classifications of Systemic Reactions Induced by Immunotherapy

I. **No symptoms or non-immunotherapy related symptoms**

II. **Mild systemic reactions**

*Symptoms*: Localized urticaria, rhinitis or mild asthma (Peak flow [PF] <20% decrease from baseline)

III. **Moderate systemic reactions**

*Symptoms*: Slow onset (>15 min) of generalized urticaria and/or moderate asthma (PF <40% decrease from baseline)

IV. **Severe (non-life-threatening) systemic reactions**

*Symptoms*: Rapid onset (<15 min) of generalized urticaria, angioedema, or severe asthma (PF >40% decrease from baseline)

V. **Anaphylactic shock**

*Symptoms*: Immediate evoked reaction of itching, flushing, erythema, generalized urticaria, stridor (angioedema), immediate asthma, hypotension, etc.

Considerations for Initiating Immunotherapy

1. Presence of a demonstrated IgE-mediated disease:
    - Positive skin tests and/or serum-specific IgE
2. Documentation that specific sensitivity is involved in symptoms:
    - Exposure to the allergen(s) determined by allergy testing related to appearance of symptoms
    - If required allergen challenge with the relevant allergen(s)
3. Characterization of other triggers that may be involved in symptoms
4. Severity and duration of symptoms:
    - Subjective symptoms
    - Objective parameters, e.g., work loss, school absenteeism
    - Pulmonary function (essential in asthmatics): exclude patients with severe asthma
    - Monitoring of the pulmonary function by peak flow
5. Response of symptoms to pharmacotherapy
6. Availability of standardized or high-quality vaccines
7. Contraindications:
    - Treatment with beta-blockers
    - Other immunologic disease
    - Inability of patients to comply

    - Starting immunotherapy with inhalant allergens during known pregnancy
8. Sociologic factors:
    - Cost
    - Occupation of candidate
9. Objective evidence of efficacy of immunotherapy for the selected patient (availability of randomized controlled studies)

Indications for Subcutaneous Immunotherapy

- Patients with symptoms induced predominantly by allergen exposure
- Patients with clinical symptoms due to a single or few allergens
- Patients with a prolonged season or with symptoms induced by succeeding pollen seasons
- Patients with rhinitis and symptoms from the lower airways during peak allergen exposure
- Patients in whom antihistamines and moderate dose topical glucocorticoids insufficiently control symptoms
- Patients who do not want to be on constant or long-term pharmacotherapy
- Patients in whom pharmacotherapy induces undesirable side effects

Indications for Sublingual Immunotherapy

High-dose sublingual-swallow specific immunotherapy may be indicated in the following cases:

- Carefully selected patients with rhinitis, conjunctivitis, and/or asthma caused by pollen and mite allergy
- Patients insufficiently controlled by conventional pharmacotherapy
- Patients who have presented with systemic reactions during injection-specific immunotherapy
- Patients showing poor compliance with or refusing injections

*Complementary and Alternative Medicine*

- Many patients who use complementary and alternative medicine appear to be satisfied.
- Evidence-based recommendations are difficult to propose for most complementary and alternative medicine interventions due to methodological problems.
- Butterbur was found to be effective in the treatment of allergic rhinitis, but more data are needed.
- Safety of phytotherapy raises concerns.

**Health Promotion and Prevention**

*Primary and Secondary prevention*

- Breastfeeding is recommended irrespective of the atopic background of the infant.

- Current dietary manipulations of maternal and infant feeding do not have a preventive role for atopic diseases and are not recommended.
- Environmental tobacco smoke should be avoided in pregnant women and children although more data are needed.
- Conflicting data exist concerning early-life exposure to pets and the development atopy. No general recommendation can be made.
- House dust mite avoidance in infancy has inconsistent effect on the development allergy or asthma and cannot be recommended.
- Primary prevention of occupational airway disease is recommended.
- Secondary prevention of asthma is still a matter of debate and more data are needed.

**Links between Rhinitis and Asthma**

See the original guideline document for epidemiologic links between rhinitis and asthma, commonalities and differences in their mechanisms, and the effect of rhinitis and asthma on quality of life (QOL).

*Therapeutic Consequences*

Treatment of Rhinitis and Asthma Using a Single Approach

- Oral $H_1$-antihistamines are not recommended in the treatment of asthma.
- Intranasal glucocorticosteroids are inconstantly and at best moderately effective in asthma.
- Intranasal glucocorticosteroids may be effective in reducing asthma exacerbations and hospitalizations.
- The role of intra-bronchial glucocorticosteroids in rhinitis is unknown.
- Montelukast is effective in the treatment of allergic rhinitis and asthma in patients over 6 years of age.
- Subcutaneous immunotherapy is recommended in both rhinitis and asthma in adults, but it is burdened by side effects, in particular asthmatics.
- Anti-IgE monoclonal antibody is effective and safe in both rhinitis and asthma.

See the original guideline document for a discussion of other co-morbidities and complications and rhinitis in children.

**Definitions**:

| Notation | Strength of Recommendation and Quality of Evidence | Clarity of Balance Between Desirable and Undesirable Effects | Quality of Supporting Evidence | Implications |
|---|---|---|---|---|
| 1A | Strong recommendation<br><br>High quality | Desirable effects clearly outweigh undesirable | Consistent evidence from randomized controlled | Recommendation can apply to most patients in most |

| Notation | Strength of Recommendation and Quality of Evidence | Clarity of Balance Between Desirable and Undesirable Effects | Quality of Supporting Evidence | Implications |
|---|---|---|---|---|
| | evidence | effects or vice versa | trials (RCTs) or exceptionally strong evidence from unbiased observational studies | circumstances.<br><br>Further research is unlikely to change the confidence of the estimate of effect |
| 1B | Strong recommendation<br><br>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.<br><br>Further research (if performed) is likely to have an important impact on the confidence in the estimate of effect and may change the estimate. |
| 1C | Strong recommendation<br><br>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.<br><br>Further research (if performed) is likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate. |
| 1D | Strong recommendation | Desirable effects clearly | Evidence for at least one of | Recommendation may change |

| Notation | Strength of Recommendation and Quality of Evidence | Clarity of Balance Between Desirable and Undesirable Effects | Quality of Supporting Evidence | Implications |
|---|---|---|---|---|
| | Very low quality evidence (very rarely applicable) | outweigh undesirable effects or vice versa | the critical outcomes from unsystematic clinical observation or very indirect evidence | when higher quality evidence becomes available.<br><br>Any estimate of the effect for at least one critical outcome is very uncertain. |
| 2A | Weak recommendation<br><br>High quality evidence | Desirable effects closely balance 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.<br><br>Further research is very unlikely to change the confidence in the estimate of effect. |
| 2B | Weak recommendation<br><br>Moderate quality evidence | Desirable effects closely balance 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 is likely to be better for some patients under some circumstances.<br><br>Further research (if performed) is likely to have an important impact on the confidence of the estimate of effect and may change the estimate. |
| 2C | Weak recommendation | Uncertainty in the estimates | Evidence for at least one | Other alternatives may |

| Notation | Strength of Recommendation and Quality of Evidence | Clarity of Balance Between Desirable and Undesirable Effects | Quality of Supporting Evidence | Implications |
|---|---|---|---|---|
| | Low quality evidence | of desirable and undesirable effects; desirable effects may be closely balanced with undesirable effects | critical outcome from RCTs with serious flaws, observational studies, or indirect evidence | be equally reasonable.<br><br>Further research is very likely to have important impact on the confidence in the estimate of effect and is likely to change the estimate. |
| 2D | Weak recommendation<br><br>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.<br><br>Any estimate of the effect for at least one critical outcome is very uncertain. |

### CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for the following:

- Diagnosis of allergic rhinitis
- Rhinitis management
- Management of allergic rhinitis in the pharmacy

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Improved diagnosis and cost-effective management of allergic rhinitis
- Improved recognition that asthma and rhinitis are common co-morbidities
- Improved respiratory function and quality of life for patient with allergic rhinitis and asthma

### POTENTIAL HARMS

The side effects associated with medications

- The safety of sublingual immunotherapy has been demonstrated in adults and children by several papers, Phase I trials and by post-marketing surveillance data Local side effects have been described in clinical trials. These include itching and swelling of the lips and under the tongue. These effects are more common in studies involving high dosage. In general, these effects are well tolerated, requiring no medication or dosage modifications, and often resolve with continued treatment.

See Table 17 in the original guideline document for information about side effects associated with medications used in allergic rhinitis.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Contraindications to immunotherapy include:

- Treatment with beta-blockers
- Other immunologic disease
- Inability of patients to comply
- Starting immunotherapy with inhalant allergens during known pregnancy

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- The Allergic Rhinitis and its Impact on Asthma (ARIA) document was not intended to be a standard-of-care document for individual countries. It was provided as a basis for physicians, health care professionals and organizations involved in the treatment of allergic rhinitis and asthma in various countries to facilitate the development of relevant local standard-of-care documents for their patients.
- Limitations of these guidelines include that the guideline developers did not consistently and explicitly define all the important outcomes that the panel should have considered for each recommendation and no formal decision on the relative importance of these outcomes. Secondly, there is a small possibility that the guideline developers missed studies, because they did not

perform full systematic reviews (in particular reviews of observational studies) for all recommendations. Thirdly, the guideline developers did not search EMBASE and some trials are published in journals not referenced in MEDLINE. As a result, methodological evaluation of the available studies was not always as rigorous as the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach warrants. The primary reason for not conducting complete systematic reviews for each relevant question was the lack of time. However, due to the extensive knowledge of the ARIA panel of the published literature, it is thought all important studies have been discussed. Fourth, when the systematic reviews were not available, the guideline developers performed only few statistical pooling exercises of primary study results. Finally, sparse data on how patients value the outcomes and what are patient preferences for recommended interventions is an additional limitation inherent to most clinical practice guidelines.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

### IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

### IOM DOMAIN

Effectiveness
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Allergic rhinitis and its impact on asthma. Geneva (Switzerland): World Health Organization (WHO); 2008. [2241 references]

## ADAPTATION

Not applicable: The guideline was not adapted from another source.

## DATE RELEASED

2001 Nov (revised 2008)

## GUIDELINE DEVELOPER(S)

Allergic Rhinitis and its Impact on Asthma Workshop Group - Independent Expert Panel

## SOURCE(S) OF FUNDING

Supported through a grant from the American Academy of Allergy, Asthma, and Immunology and Allergic Rhinitis and its Impact on Asthma (ARIA)

## GUIDELINE COMMITTEE

Allergic Rhinitis and its Impact on Asthma (ARIA) Workshop Group

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001 Nov;108(5):S147-334.

## GUIDELINE AVAILABILITY

Electronic copies of ARIA documents and resources available from the Allergic Rhinitis and its Impact on Asthma (ARIA) Web site.

## AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Allergic Rhinitis and its Impact on Asthma (ARIA) At-A-Glance Pocket Reference. 2007. 6 p. Electronic copies available from the ARIA Web site.
- ARIA Teaching Slides (Power Point Download). Electronic copies available from the ARIA Web site.
- Brozek JL, Baena-Cagnani CE, Bonini S, Canonica GW, Rasi G, van Wijk RG, Zuberbier T, Guyatt G, Bousquet J, Schünemann HJ.Methodology for development of the Allergic Rhinitis and its Impact on Asthma guideline 2008 update. Allergy. 2008 Jan; 63(1):38-46. Electronic copies available to subscribers at the *Allergy* journal Web site.

## PATIENT RESOURCES

None available

## NGC STATUS

This summary was completed by ECRI on March 19, 2003. This NGC summary was updated by ECRI Institute on April 24, 2008. The updated information was verified by the guideline developer on June 27, 2008.

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