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Rhinitis, Sinusitis, and Upper Airway Disease

Allergic Rhinitis and Its Impact on Asthma (ARIA)-EAACI Guidelines—2024–2025 Revision: Part I—Guidelines on Intranasal Treatments

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Abbreviations: ARIA, allergic rhinitis and its impact on asthma; GRADE, grading of recommendations, assessment, development, and evaluation; INAH, intranasal antihistamines; INCS, intranasal corticosteroids.

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ABSTRACT

Background: Allergic rhinitis (AR) impacts quality of life, work and school productivity. Over the last years, an important body of evidence resulting from mHealth data has led to a better understanding of AR. Such advances have motivated an EAACI-endorsed update of the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines (ARIA 2024–2025). This manuscript presents the ARIA 2024–2025 recommendations for intranasal treatments, one of the mainstays for AR management.

Methods: The ARIA 2024–2025 guideline panel issued recommendations following the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) evidence-to-decision framework. Several sources of evidence were used to inform panel judgments and recommendations, including systematic reviews, evaluation of mHealth and pharmacovigilance data, as well as a survey of experts on costs.

Results: Eleven guideline questions concerning intranasal treatments for AR were prioritized, leading to recommendations. Overall, these questions concern the choice between different classes of intranasal medications—most notably, intranasal corticosteroids (INCS), antihistamines (INAH), fixed combinations of INAH+INCS and decongestants—or between different individual medications within each class. Four questions had not been evaluated in previous ARIA guidelines, while for the other three there was a change in the strength or directionality of recommendations. Overall, recommendations point to the suggested use of INAH+INCS over INAH or INCS and INCS over INAH.

Conclusion: This ARIA 2024–2025 article supports patients, their caregivers, and healthcare professionals in choosing an intranasal treatment. However, decisions on AR treatment should consider the clinical variability of the disease, patients' values, and the affordability of medications.

1 | Introduction

Allergic rhinitis (AR) is a common chronic disease [1, 2] that substantially impacts quality of life, work and school productivity, and social activities [3–5]. Several guidelines have been produced for AR management. In particular, the Allergic Rhinitis and its Impact on Asthma (ARIA) group first proposed its guidelines for AR and asthma multimorbidity in 2001 [6]. Subsequent revisions were published in 2008 [7], 2010 [8], 2016 [9], and 2020 [10], reflecting the development of new therapeutic options and/or improvements in its methodology. The ARIA 2010 and 2016 updates were developed following the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach [9].

Further advances in the evidence landscape have motivated the development of a 2024–2025 revision of the ARIA guidelines (ARIA 2024–2025). In particular, over the last years, evidence from mHealth data has shed light on medication use patterns and adherence [11, 12], patients' satisfaction with treatments [13], and the impact of AR on work productivity [3].

Considering the above, ARIA 2024–2025 guidelines have been conceived as person-centered, digitally enabled, and assisted by artificial intelligence (AI), using the GRADE approach [14]. This emphasis on a person-centered guideline is relevant due to inter-individual variability in (i) exposure and responses to triggers/allergens, (ii) impact of AR on daily life, (iii) values and preferences in relation to rhinitis health states,

and (iv) disease management (ranging from self-management to treatment by specialists).

This paper presents the first set of recommendations of ARIA 2024–2025, namely those on intranasal treatments for AR. Most guideline questions addressed in this paper concern intranasal corticosteroids (INCS), intranasal H_1-antihistamines (INAH) and fixed combinations of INAH+INCS. The target audience of these guidelines includes health professionals managing adults or children with AR, patients with AR, and health policymakers. ARIA 2024–2025 is supported by the European Academy of Allergy and Clinical Immunology (EAACI).

2 | Questions Addressed by This Guideline

In ARIA 2024–2025, 42 questions on AR management were voted by guideline panel members as "prioritized questions" [15]. Among these, 11 concerned exclusively intranasal AR treatments and are addressed by this paper. The full set of questions is listed in Table 1, alongside their corresponding recommendations and capsule justifications.

3 | Methodology

A full description of the methods used to develop recommendations in these guidelines is available elsewhere (Bousquet et al., under review). Here, we provide a brief methodological description to facilitate the interpretation of the guidelines.

3.1 | Questions and Outcomes of Interest

In ARIA 2024–2025, four approaches were used for the development of guideline clinical questions, including (i) identification of questions answered by previous ARIA guidelines and US Practice Parameters, (ii) surveying of ARIA panel members (healthcare professional-centered questions), (iii) identification of questions resulting from MASK-air studies, and (iv) use of AI to support the generation of guideline questions [15] (patient-centered questions). Questions were then subject to the GRADE formal process of prioritization [16] using GRADEpro [17].

Each question was assessed by considering the following set of outcomes (prioritized using GRADE formal processes [16]): nasal symptoms, ocular symptoms, quality of life, total symptoms, serious adverse events, and occurrence of any adverse event. Therefore, efficacy outcomes were nasal, ocular and total symptoms, as well as quality of life. Safety outcomes include any/total adverse events and serious adverse events.

3.2 | Evidence Review and Development of Recommendations

For each question, we gathered evidence on the different criteria of the evidence-to-decision (EtD) framework, a systematic and transparent approach that aims to support the formulation of recommendations [18, 19]. The EtD comprises 12 criteria: priority, desirable and undesirable effects, certainty of evidence, values and preferences, balance of effects, resources required (and corresponding certainty of evidence), cost-effectiveness, equity, acceptability, and feasibility. In addition, the ARIA 2024–2025 guidelines included a 13th criterion—planetary health [20, 21]—to account for the effects of interventions on both human health and the health of the planet.

Evidence on desirable and undesirable effects was obtained by conducting four systematic reviews (SRs) of randomized controlled trials (RCTs): (i) comparison of intranasal medications versus placebo in adults [22–24], (ii) comparisons among intranasal medications in adults [25, 26], (iii) comparisons among intranasal medications in children [27], and (iv) comparison of nonfixed treatment combinations in adults and children (in preparation). In addition, evidence on undesirable effects was complemented by an analysis of pharmacovigilance data. In particular, we queried VigiBase, the World Health Organization (WHO) global database of adverse event reports for medicines and vaccines [28].

For values and preferences, we conducted a SR of the literature [29]. For the remaining criteria, we performed nonsystematic evidence reviews, which were complemented by evidence from other sources. In particular, we have conducted a survey of ARIA experts assessing the availability and costs of different AR medications (in preparation). Furthermore, we analyzed MASK-air direct patient data to obtain information on treatment acceptability (in particular, adherence, satisfaction, and use of co-medication) and indirect costs associated with productivity losses. The WHO List of Essential Medicines was consulted to inform judgments on equity [30].

The voting members of the ARIA 2024–2025 panel (i.e., members without conflicts of interest) convened at recurrent online meetings (average of two meetings per PICO question, with 3–4 PICO questions being discussed per meeting), where they issued a judgment for each criterion of each question through GRADEpro PanelVoice [17]. Based on all the provided judgments, the panel issued a recommendation for the respective guideline question. Recommendations were worded following the GRADE working group guidance (see "How to use these guidelines" section) [31]. In addition, for each recommendation, we present (i) considerations for preschool and school-aged children and adolescents (and, if evidence is available, other special populations, such as patients with asthma), and (ii) implementation considerations. The latter include, among others, aspects related to the application of recommendations in low- and middle-income countries, or to concerns with specific adverse events.

For both judgments and recommendations, we sought consensus among voting members of the guideline panel. If consensus was not reached, a formal voting process was set. The final form of guideline recommendations and their wording, as well as the final guideline document, has been reviewed and approved by all panel members.

4 | How to Use These Guidelines

The ARIA 2024–2025 guidelines are not intended to impose a standard of care for individual countries. They provide the basis

TABLE 1 | Recommendations of the ARIA 2024–2025 guidelines for the prioritized questions on intranasal treatments.

Recommendation	Capsule justification	Subgroup considerations	Implementation considerations
(A) New questions in ARIA 2024–2025			
Should a combination of an INAH+INCS vs. no treatment be used for the treatment of AR?			
In patients with AR in whom monotherapy is unlikely to lead to significant improvement in symptoms, we recommend using INAH+INCS over no treatment (strong recommendation|moderate CoE for seasonal AR and very low CoE for perennial AR)	INAH+INCS are effective in improving nasal symptoms, ocular symptoms and quality-of-life. INAH+INCS are overall safe, tendentiously cost-effective and well accepted by patients	Recommendation applicable to children and adolescents	None specific
Should any specific INCS vs. other INCS be used for the treatment of AR?			
In patients with AR, we suggest using specific INCS (in particular, fluticasone furoate or fluticasone propionate) over others namely beclomethasone, budesonide, ciclesonide, mometasone and triamcinolone (conditional recommendation|low-very low CoE)	Fluticasone furoate and fluticasone propionate are the most effective INCS in improving nasal symptoms and quality of life in patients with seasonal AR. Individual INCS display a similar safety and satisfaction profile. Costs vary across countries	In children and adolescents, evidence was not sufficient to support a specific recommendation	In low- and middle-income countries, other INCS may be preferred based on local availability and affordability (budesonide is on the WHO List of Essential Medicines). From a planetary health perspective, locally produced generics may be preferrable.
Should any specific combination of an INAH+INCS vs. other combination of an INAH+INCS be used for the treatment of AR?			
In patients with AR, we suggest using azelastine-fluticasone over olopatadine-mometasone (conditional recommendation|moderate CoE)	Azelastine-fluticasone is the most effective INAH+INCS in improving ocular symptoms and quality of life in patients with seasonal AR. Both INAH+INCS display a similar safety profile	In children and adolescents, we suggest either using azelastine-fluticasone or olopatadine-mometasone	In patients experiencing bitter taste with azelastine-fluticasone, olopatadine-mometasone may be preferred
Should a combination of an INCS and an intranasal decongestant vs. an INCS alone be used for the treatment of AR?			
In patients with AR, we suggest against using a combination of an INCS and an intranasal decongestant over an INCS alone (conditional recommendation|very low CoE)	Adding an intranasal decongestant to an INCS does not result in an increase in efficacy but is associated with a higher risk of adverse events, costs and impact on planetary health	Recommendation applicable to children and adolescents	In some specific situations, using intranasal decongestants for a short period of time when INCS are being introduced can be considered
(B) Questions with changed recommendation in terms of strength or directionality (compared to ARIA 2010/2016)			
Should an INAH vs. no treatment be used for the treatment of AR?			
In patients with AR, we recommend using INAH over no treatment (strong recommendation|moderate CoE)	INAH are effective in improving nasal symptoms, ocular symptoms and quality-of-life. INAH are overall safe, cost-effective and moderately accepted by patients	Recommendation applicable to children and adolescents	None specific

(Continues)

TABLE 1 | (Continued)

Recommendation	Capsule justification	Subgroup considerations	Implementation considerations
Should an intranasal decongestant vs. no treatment be used for the treatment of AR?			
In adolescents and adults with AR, we suggest against using intranasal decongestants in the long term (longer than 5 days) over no treatment (conditional recommendation|very low CoE)	Decongestants display a trivial effect on nasal and ocular symptoms and are associated with an increased risk of adverse events	In pregnant women, children and the elderly, we suggest against using intranasal decongestants.	Recommendation concerning oxymetazoline, xylometazoline and tramazoline. The ARIA panel recommends against the use of ephedrine-based decongestants
Should a combination of an INAH+INCS vs. an INCS alone be used for the treatment of AR?			
In patients with AR, we suggest using a combination of an INAH+INCS over an INCS alone (conditional recommendation|moderate CoE for seasonal AR and very low CoE for perennial AR)	INAH+INCS and INCS display a similar efficacy and safety profile. INAH+INCS are frequently cost-effective and typically associated with a faster onset of action and higher satisfaction	Recommendation applicable to children and adolescents	INAH+INCS may be particularly favored in patients with more severe symptoms. In low-income countries or low-resource settings, INCS may be preferred
(C) Other questions in ARIA 2024–2025			
Should an INCS vs. no treatment be used for the treatment of AR?			
In patients with AR, we recommend using INCS over no treatment (strong recommendation|moderate CoE)	INCS are effective in improving nasal symptoms, ocular symptoms and quality-of-life. INCS are overall safe, cost-effective and well-accepted by patients	Recommendation applicable to children and adolescents	None specific
Should an INCS vs. an INAH be used for the treatment of AR?			
In patients with AR, we suggest using INCS over INAH (conditional recommendation|moderate CoE)	INCS and INAH display a similar efficacy and safety profile. INCS are typically less expensive (and/or cost-effective) and associated with higher adherence and satisfaction	Recommendation applicable to children and adolescents	INCS may be particularly recommended for patients having taste alterations when using INAH. For patients with corticosteroid-phobia, epistaxis or glaucoma, or having poor medication adherence, INAH may be considered
Should a combination of an INAH+INCS vs. an INAH alone be used for the treatment of AR?			
In patients with AR, we suggest using a combination of an INAH+INCS over an INAH alone (conditional recommendation|moderate CoE for seasonal AR and very low CoE for perennial AR)	INAH+INCS are more effective in improving nasal symptoms and quality of life. INAH+INCS display a similar safety profile. INAH+INCS tend to be cost-effective and are associated with higher adherence and satisfaction	Recommendation applicable to children and adolescents, even though evidence is scarcer	None specific

(Continues)

TABLE 1 | (Continued)

Recommendation	Capsule justification	Subgroup considerations	Implementation considerations
Should an INAH vs. an intranasal chromone be used for the treatment of AR?			
In patients with AR, we suggest using INAH over intranasal chromones (conditional recommendation|very low CoE)	INAH appear to be more effective in improving nasal and ocular symptoms, and are associated with higher satisfaction. INAH and intranasal chromones display a similar safety profile	Recommendation applicable to children and adolescents	None specific

Abbreviations: AR, allergic rhinitis; CoE, certainty of evidence; INAH, intranasal antihistamines; INCS, intranasal corticosteroids.

for rational, informed decisions, so that their recommendations do not correspond to dictates. Recommendations provide guidance for typical patients but cannot account for all unique individual circumstances. Thus, clinicians are encouraged to tailor their practice considering the clinical presentation of each patient and the specificities of the respective local context, and to reach decisions via shared decision-making.

For each question, in accordance with GRADE, we issued either a "strong" or "conditional" recommendation. The fact that a recommendation is "strong" or "conditional" reflects the panel's confidence that following it would result in a more beneficial outcome for patients and other interest-holder categories (terminological clarification in Box 1). The wording of the recommendations reflects their strength, with "we recommend" implying a strong recommendation and "we suggest" implying a conditional recommendation. In each recommendation, we present information on the certainty of evidence across the different outcomes of interest (quality of the whole body of evidence, considering altogether desirable and undesirable effects; Box 1).

This manuscript provides a brief summary of the evidence underlying each recommendation ("brief justification"). Full EtDs for each question can be found online through links provided alongside each question.

Importantly, when summarizing our results on desirable and undesirable effects ("efficacy and safety"), we frequently report on the probability of differences between interventions being nontrivial (i.e., with corresponding effect sizes being sufficiently large that they are considered clinically important; Box 1 for terminological clarification).

5 | Recommendations and Summary of Findings

Table 1 lists the recommendations for each prioritized question. Below, we discuss, for each question, the rationale underlying each recommendation; we first present questions that are new in relation to ARIA 2010/2016, followed by those for which the strength or directionality of recommendations has changed, and finally by the remainder. Of note, we do not specifically refer to patients' values and preferences in individual questions, as the same findings for values and preferences are applicable to all questions. In particular, we observed that patients generally (i) value the efficacy of interventions more over their safety, and (ii) consider nasal symptoms as those with the highest impact [29]. Table 2 presents, for each question, the judgment of the effect size and the certainty of the evidence for each outcome.

5.1 | New Questions in ARIA 2024–2025

5.1.1 | Should a Combination of an Intranasal H_1-Antihistamine and an Intranasal Corticosteroid vs. no Treatment Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/01/.

BOX 1 | Clarification of the terminology used in these guidelines.

Strength of recommendations

- Strong recommendation
  - *For patients*: Most patients in this situation would want the recommended course of action, and only a small proportion would not.
  - *For clinicians*: Most patients should receive the intervention. Adherence to a strong recommendation could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help patients make decisions consistent with their values and preferences.
  - *For health care policy makers*: The recommendation can be adopted as a policy or performance measure in most situations.
- Conditional recommendation
  - *For patients*: Most patients in this situation would want the suggested course of action, but many would not.
  - *For clinicians*: Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids might be useful in helping patients to make decisions consistent with their values and preferences.
  - *For health care policy makers*: Policy making will require substantial debate and involvement of various stakeholders. Documentation of appropriate (e.g., shared) decision-making processes can serve as a performance measure.

Certainty of evidence: The certainty of evidence concerns how certain we are that the observed magnitude of desirable and undesirable anticipated effects lies on one side of a specified threshold or within a chosen range (reflecting the "quality" of available evidence). The certainty of evidence can be classified as "very low", "low", "moderate" or "high". The certainty of evidence is independent of the directionality of the recommendation and of the effect sizes of the associations.

Categorization of the effect sizes: The magnitude of the anticipated desirable and undesirable effects ("benefits and harms") is classified by the GRADE working group as "trivial or none", "small", "moderate" or "large". A trivial effect is observed when the magnitude of the effects is so small that it is not sufficiently important in terms of anticipated health consequences. Nontrivial effects can be considered "small", "moderate" or "large" depending on the magnitude of effect sizes.

Context: Fixed combinations of INAH+INCS are one of the mainstays for the treatment of AR, combining some of the advantages of INCS with those of INAH. However, INAH+INCS may not be affordable in all countries.

Recommendation: In patients with AR in whom monotherapy is unlikely to lead to significant improvement in symptoms, we recommend using INAH+INCS over no treatment. (Strong recommendation based on moderate certainty of evidence for seasonal AR and very low certainty of evidence for perennial AR).

- Considerations in children and adolescents: The recommendation is applicable to children and adolescents, with available studies having assessed children aged as low as 4 years old.
- Implementation considerations: None specific.

Brief justification: See online supplement.

5.1.2 | Should Any Specific Intranasal Corticosteroid vs. Another Intranasal Corticosteroid Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/02/.

Context: There are several INCS available, rendering it important not only to provide recommendations at a class level but also on what may be the most indicated individual INCS.

Recommendation: In adult patients with AR, we suggest using specific INCS (in particular, fluticasone furoate or fluticasone propionate) over others (namely, beclomethasone, budesonide, ciclesonide, mometasone and triamcinolone). (Conditional recommendation based on very low or low certainty of evidence for most comparisons).

- **Considerations in children and adolescents**: In children and adolescents, evidence was not sufficient to support recommending a specific INCS (insufficient number of primary studies). Daily doses in children aged < 12 years old may be lower (e.g., half) of those used in adults.
- **Implementation considerations**: In low- and middle-income countries, other specific INCS may be preferred based on local availability and affordability (e.g., budesonide is on the WHO List of Essential Medicines). From a planetary health perspective, locally produced generics may be preferrable.

5.1.2.1 | Brief Justification.

- Efficacy and safety:
  - A network meta-analysis suggested that, in seasonal AR, fluticasone furoate and fluticasone propionate were the INCS displaying the highest probability of being more effective in improving nasal symptoms. In perennial AR, budesonide was the INCS displaying the highest probability of being the most effective in improving nasal symptoms, but it was only assessed by one trial.
  - In seasonal AR, beclomethasone and fluticasone furoate were the INCS having the highest probability of being the most effective in improving ocular symptoms. In perennial AR, fluticasone furoate was the most effective INCS for ocular symptoms.

TABLE 2 | Judgments on the effect sizes and certainty of evidence (CoE) assessments for each outcome in each prioritized question comparing each intervention to a comparator.

Question		Seasonal allergic rhinitis					Perennial allergic rhinitis				
		Nasal symptoms	Ocular symptoms	Quality of life	AE	Serious AE	Nasal symptoms	Ocular symptoms	Quality of life	AE	Serious AE
Should a combination of an INAH+INCS vs. no treatment be used for the treatment of AR?	Effect size	Moderate	Small	Moderate	Trivial	Trivial	Small	—[b]	Small	Trivial	Trivial
	CoE	Moderate	Moderate	Moderate	Moderate	Moderate	Very low	—[b]	Very low	Very low	Very low
Should any specific INCS vs. other INCS be used for the treatment of AR?	Effect size	Small	Trivial	Small	Trivial	Trivial	Trivial	Trivial	Small	Trivial	Trivial
	CoE	Very low/Low[a]	Very low/ Low[a]	Very low/ Low[a]	Very low/ Low[a]	Very low/ Low[a]	Very low/Low[a]	Very low	Very low/ Low[a]	Very low/ Low[a]	Very low/ Low[a]
Should any specific combination of an INAH+INCS vs. other specific combination of an INAH+INCS be used for the treatment of AR?	Effect size	Trivial	Small	Small	Trivial	Trivial	—[b]	—[b]	—[b]	—[b]	—[b]
	CoE	Moderate	Moderate	Moderate	Moderate	Moderate	—[b]	—[b]	—[b]	—[b]	—[b]
Should a combination of an INCS and an intranasal decongestant vs. an INCS alone be used for the treatment of AR?	Effect size	Trivial	—[b]	Trivial	Small	Trivial	Trivial	—[b]	Trivial	Trivial	Trivial
	CoE	Very low	—[b]	Low	Very low	Very low	Very low	—[b]	Very low	very low	Very low
Should an INAH vs. no treatment be used for the treatment of AR?	Effect size	Small	Small	Small	Trivial	Trivial	Small	—[b]	Small	Trivial	Trivial
	CoE	Moderate	High	High	Low	Low	High	—[b]	High	Moderate	Moderate
Should an intranasal decongestant vs. no treatment be used for the treatment of AR?	Effect size	Trivial	—[b]	Trivial	Trivial	—[b]	Trivial	—[b]	Trivial	Small	—[b]
	CoE	Very low	—[b]	Low	Moderate	—[b]	Low	—[b]	Very low	Low	—[b]

(Continues)

TABLE 2 | (Continued)

Question		Seasonal allergic rhinitis					Perennial allergic rhinitis				
		Nasal symptoms	Ocular symptoms	Quality of life	AE	Serious AE	Nasal symptoms	Ocular symptoms	Quality of life	AE	Serious AE
Should a combination of an INAH+INCS vs. an INCS alone be used for the treatment of AR?	Effect size	Trivial	Trivial	Trivial	Trivial	Trivial	Trivial	—[b]	Trivial	Trivial	Trivial
	CoE	Moderate	High	High	Moderate	Moderate	Very low	—[b]	Very low	Very low	Very low
Should an INCS vs. no treatment be used for the treatment of AR?	Effect size	Small	Small	Small	Trivial	Trivial	Small	Small	Small	Trivial	Trivial
	CoE	Moderate	High	Moderate	Moderate	Moderate	High	Moderate	Moderate	Moderate	Moderate
Should an INCS vs. an INAH be used for the treatment of AR?	Effect size	Trivial	Trivial	Trivial	Trivial	Trivial	Trivial	—[b]	Trivial	Trivial	Trivial
	CoE	Low	Moderate	High	Moderate	Moderate	High	—[b]	Low	Moderate	Moderate
Should a combination of an INAH+INCS vs. an INAH alone be used for the treatment of AR?	Effect size	Trivial	Trivial	Small	Trivial	Trivial	Small	—[b]	Trivial	Trivial	Trivial
	CoE	High	Moderate	High	Moderate	Moderate	Very low	—[b]	Very low	Moderate	Moderate
Should an INAH vs. an intranasal chromone be used for the treatment of AR?	Effect size	Small	Small	—[b]	Trivial	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]
	CoE	Very low	Very low	—[b]	Very low	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]

Abbreviations: AE, adverse events; AR, allergic rhinitis; INAH, intranasal antihistamines; INCS, intranasal corticosteroids. Colour code: Effect size: The darker the blue the larger the effect size. CoE: Green=High, Yellow=Moderate, Orange=Low, Red=Very low.

[a]Most common CoE assessments for the considered comparisons.

[b]No available evidence.

- In terms of rhinoconjunctivitis-related quality of life (RQLQ), fluticasone furoate and fluticasone propionate were the INCS displaying the highest probability of being the most effective in seasonal AR. In perennial AR, the most effective INCS were fluticasone furoate and beclomethasone.
- Similar frequencies and patterns of adverse events and serious adverse events were observed with the different INCS based on data from RCTs and pharmacovigilance.

- **Resources required, cost-effectiveness and equity**: A survey of ARIA experts suggested that the least and most expensive INCS vary widely across countries. We did not identify any cost-effectiveness study comparing INCS, but MASK-air data suggests that mometasone and budesonide tend to be more frequently cost-effective interventions compared to other INCS. Budesonide is the only INCS on the WHO List of Essential Medicines.
- **Acceptability and feasibility**: MASK-air data suggest that fluticasone furoate and mometasone are the INCS associated with higher adherence. The different INCS are associated with similar levels of treatment satisfaction. However, fluticasone furoate and fluticasone propionate seem to be used more often in co-medication than other individual INCS.
- **Planetary health**: No specific evidence was found in terms of comparative impact on planetary health.

5.1.3 | Should Any Specific Combination of an Intranasal H_1-Antihistamine and an Intranasal Corticosteroid vs. Another Combination of an Intranasal H_1-Antihistamine and an Intranasal Corticosteroid Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/03/.

Context: There are two widely used INAH+INCS—azelastine-fluticasone and olopatadine-mometasone, rendering it important not only to provide recommendations at a class level but also on what may be the most indicated individual INAH+INCS.

Recommendation: In adult patients with AR, we suggest using azelastine-fluticasone over olopatadine-mometasone. (Conditional recommendation based on moderate certainty of evidence for seasonal AR).

- **Considerations in children and adolescents**: In children and adolescents, we suggest either using azelastine-fluticasone or olopatadine-mometasone based on the available scarce evidence.
- **Implementation considerations**: In patients experiencing bitter taste with azelastine-fluticasone, olopatadine-mometasone may be preferred.

5.1.3.1 | Brief Justification.

- **Efficacy and safety**:
  - A network meta-analysis suggested that, compared to olopatadine-mometasone, azelastine-fluticasone is associated with a 23% probability of resulting in a non-trivial improvement in nasal symptoms in seasonal AR. For ocular symptoms and RQLQ, this probability was 56%.
  - For perennial AR, no evidence was available for the comparison between azelastine-fluticasone versus olopatadine-mometasone.
  - Similar frequencies of adverse events were observed with azelastine-fluticasone and olopatadine-mometasone (trivial difference). Serious adverse events associated with these interventions are rare and most of those reported in RCTs have been judged unlikely to be related to the treatment.
- **Resources required, cost-effectiveness and equity**: A survey of ARIA experts suggested olopatadine-mometasone to be more expensive than azelastine-fluticasone in 8 out of 14 countries for which data were available. We did not identify any cost-effectiveness study comparing these two medications. Neither azelastine-fluticasone nor olopatadine-mometasone are on the WHO List of Essential Medicines, but azelastine-fluticasone seems to be available in a wider number of countries.
- **Acceptability and feasibility**: MASK-air data suggest that azelastine-fluticasone is associated with higher adherence and treatment satisfaction. However, azelastine-fluticasone is associated with higher odds of being used in co-medication (a proxy of poor rhinitis control) than olopatadine-mometasone. In addition, there are studies on sensory attributes that favor olopatadine-mometasone. Both azelastine-fluticasone and olopatadine-mometasone display a fast onset of action.

Planetary health: No specific evidence was found in terms of comparative impact on planetary health. Both branded products are manufactured in Asia, with olopatadine-mometasone being distributed in a plastic vial and azelastine-fluticasone being distributed in a glass vial.

5.1.4 | Should a Combination of an Intranasal Corticosteroid and an Intranasal Decongestant vs. an Intranasal Corticosteroid Alone Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/04/.

Context: Patients with AR using INCS often do co-medication with intranasal decongestants (oxymetazoline, xylometazoline or tramazoline), particularly as the latter have a rapid onset and may help relieve nasal congestion.

Recommendation: In patients with AR, we suggest against using a combination of an INCS + intranasal decongestant over an INCS alone. (Conditional recommendation based on very low certainty of evidence).

- Considerations in children and adolescents: The recommendation is applicable to children and adolescents.

- Implementation considerations: This recommendation is particularly applicable to long-term treatment (longer than 5 days). In some specific situations using intranasal decongestants for a short period of time—less than 5 days—when INCS are being introduced (to "compensate" for the slow onset of action of INCS) can be considered. However, if available and affordable, this can also be achieved with INAH+INCS (e.g., patients who cannot be treated for a long period of time with INAH+INCS due to costs or intolerance to bitter taste can have INAH+INCS for few days—to achieve fast symptom relief—followed by INCS). The ARIA panel recommends against the use of ephedrine-based decongestants due to safety and legal concerns.

5.1.4.1 | Brief Justification.

- Efficacy and safety
  - Primary studies assessing nasal symptoms were too different to allow for estimating meta-analytical measures. However, these studies point to trivial differences when comparing the improvement of nasal symptoms between INCS + intranasal decongestants versus INCS alone.
  - For ocular symptoms, a single study indicated that "nonsignificant differences were identified for patients with seasonal AR" (no further information was provided).
  - Results from a network meta-analysis suggested that INCS + intranasal decongestants and INCS are associated with a similar improvement in RQLQ, both in seasonal AR and perennial AR (trivial differences).
  - INCS + decongestants were associated with increased risk of adverse events compared to INCS (small but important difference). Of note, the long-term use of decongestants has been linked to rhinitis medicamentosa. Serious adverse events associated with these interventions are rare and most of those reported in RCTs have been judged unlikely to be related to the treatment.
- **Resources required, cost-effectiveness and equity**: A survey of ARIA experts suggested INCS + intranasal decongestants to represent up to more $200 per year than INCS alone for countries for which data were available. No cost-effectiveness studies have been identified comparing INCS + intranasal decongestants versus INCS alone. There is both an INCS (budesonide) and a decongestant (xylometazoline) on the WHO List of Essential Medicines.
- **Acceptability and feasibility**: MASK-air data suggest that INCS + decongestants are associated with lower adherence and treatment satisfaction. Intranasal decongestants display a faster onset of action than INCS.
- **Planetary health**: Considering that INCS + intranasal decongestants are not produced as fixed combinations, the additional use of intranasal decongestants implies the use of additional resources with environmental impact.

5.2 | Questions With a Change in Recommendation Directionality and/or Strength in ARIA 2024–2025

5.2.1 | Should an Intranasal H_1-Antihistamine vs. no Treatment Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/05/.

Context: INAH are one possible therapeutic option in patients with AR, being often considered for patients with corticosteroid phobia and displaying a fast onset of action.

Recommendation: In patients with AR, we recommend using INAH over no treatment. (Strong recommendation based on moderate certainty of evidence).

- **Considerations in children and adolescents**: The recommendation is applicable to children and adolescents.
- **Implementation considerations**: None specific.

Brief justification: See online supplement.

5.2.2 | Should an Intranasal Decongestant vs. no Treatment Be Used For the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/06/.

Context: Intranasal decongestants (oxymetazoline, xylometazoline and tramazoline) are frequently used by patients with AR, particularly considering that they are commonly sold over-the-counter and display a fast onset of action in nasal congestion.

Recommendation: In patients with AR, we suggest against using intranasal decongestants in the long term (longer than 5 days) over no treatment. (Conditional recommendation based on very low certainty of evidence).

- Considerations in specific age groups and conditions: For preschool and young school-aged children (< 12 years), there should be avoidance of intranasal decongestants. There should also be avoidance of intranasal decongestants in pregnant women, especially in the first trimester, considering the potential teratogenic effects of nasal decongestants. Considering the risk of serious adverse events, the use of intranasal decongestants in the elderly is also discouraged.
- Implementation considerations: This recommendation concerns oxymetazoline, xylometazoline and tramazoline. The panel suggests that the use of intranasal decongestants should be restricted to short-term relief (not longer than 5 days and preferably shorter) of nasal congestion. The ARIA panel also recommends against the use of ephedrine-based decongestants due to safety and legal concerns.

Brief justification: See online supplement.

5.2.3 | Should a Combination of an Intranasal H_1-Antihistamine and an Intranasal Corticosteroid vs. an Intranasal Corticosteroid Alone Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/07/.

Context: INCS+INAH offer some advantages in relation to INCS in terms of onset of action and, potentially, effectiveness. However, INCS are more widely available and are more affordable.

Recommendation: In patients with AR, we suggest using a fixed combination of an INAH and INCS over an INCS alone. (Conditional recommendation based on moderate certainty of evidence for seasonal AR and on very low certainty of evidence for perennial AR).

- **Considerations in children and adolescents**: The recommendation is applicable to children and adolescents.
- **Implementation considerations**: Aspects such as adherence, baseline severity and history of medication use may be relevant to be considered. Fixed combinations of INAH+INCS may be particularly favored in patients with severe symptoms. In low-income countries or low-resource settings, INCS may be preferred.

5.2.3.1 | Brief Justification.

- Efficacy and safety
  - A network meta-analysis suggested that INAH+INCS and INCS are associated with a similar improvement in nasal and ocular symptoms, as well as in RQLQ, both in seasonal AR and perennial AR (trivial differences).
  - Similar frequencies of adverse events were observed with INAH+INCS and INCS (trivial difference). Serious adverse events associated with these interventions are rare and most of those reported in RCTs have been judged unlikely to be related to the treatment.
- **Resources required, cost-effectiveness and equity**: A survey of ARIA experts suggested INAH+INCS to be more expensive than INCS in 34 out of 36 countries for which data were available. However, INAH+INCS are likely cost-effective in most countries both when considering a willingness-to-pay of $50,000/QALY gained or of one time the GDP per capita/QALY gained (the only exception may be some low- and middle-income countries). One INCS—budesonide—is on the WHO List of Essential Medicines, but the same does not occur with INAH+INCS.
- **Acceptability and feasibility**: MASK-air data suggest that INAH+INCS are associated with higher treatment satisfaction and with lower odds of being used in co-medication (a proxy of poor rhinitis control). In addition, INAH+INCS display a faster onset of action.

Planetary health: No specific evidence was found in terms of comparative impact on planetary health, even though it is possible that the production of two active compounds may have a higher environmental impact than the production of one.

5.3 | Other Questions Evaluated in ARIA 2024–2025

5.3.1 | Should an Intranasal Corticosteroid vs. no Treatment Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/08/.

Context: INCS are one of the mainstays of the treatment of AR, being widely available. Budesonide is listed in the WHO List of Essential Medicines.

Recommendation: In patients with AR, we recommend using INCS over no treatment. (Strong recommendation based on moderate certainty of evidence).

- **Considerations in children and adolescents**: The recommendation is applicable to children and adolescents.
- **Implementation considerations**: None specific.

Brief justification: See online supplement.

5.3.2 | Should an Intranasal Corticosteroid vs. an Intranasal H_1-Antihistamine Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/09/.

Context: INCS and INAH are two of the most commonly used classes for the treatment of AR. These two treatment classes have distinct profiles in terms of acceptability and affordability, among others.

Recommendation: In patients with AR, we suggest using INCS over INAH. (Conditional recommendation based on moderate certainty of evidence).

- Considerations in children and adolescents: The recommendation is applicable to children and adolescents.
- Implementation considerations: INCS may be particularly recommended for patients having taste alterations when using INAH. For patients with corticosteroid-phobia, epistaxis secondary to INCS or glaucoma, or having poor medication adherence, INAH may be the preferred intervention.

5.3.2.1 | Brief Justification.

- Efficacy and safety
  - A network meta-analysis suggested that, compared to INAH, INCS are associated with a trivial improvement in nasal symptoms and in RQLQ in seasonal and perennial AR.
  - For ocular symptoms, either differences between treatments were trivial (seasonal AR) or evidence was not found (perennial AR).
  - Similar frequencies of adverse events were observed with INCS and INAH (trivial difference). Serious adverse events associated with these interventions are rare and most of those reported in RCTs have been judged unlikely to be related to the treatment. Although rare,

pharmacovigilance data suggested glaucoma to be more frequent with INCS than INAH.

- **Resources required, cost-effectiveness and equity**: A survey of ARIA experts suggested INAH to be more expensive than INCS in 21 out of 29 countries for which data were available. In addition, in most countries where INCS are more expensive than INAH, INCS were found to be cost-effective when considering a willingness-to-pay of $50,000/Quality Adjusted Life Years (QALY) gained or of one time the Gross Domestic Product (GDP) per capita/QALY gained. One INCS—budesonide—is on the WHO List of Essential Medicines, but the same does not occur with INAH. In addition, INCS are available in more countries than INAH.
- **Acceptability and feasibility**: MASK-air data suggest that INCS are associated with higher adherence and treatment satisfaction, as well as with lower odds of being used in co-medication (a proxy of poor rhinitis control). However, INAH display a faster onset of action.
- **Planetary health**: No specific evidence was found in terms of comparative impact on planetary health.

5.3.3 | Should a Combination of an Intranasal H_1-Antihistamine and an Intranasal Corticosteroid vs. an Intranasal H_1-Antihistamine Alone Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/10/.

Context: INCS+INAH have been proposed as the first-line treatment of AR by previous guidelines. However, some patients are corticosteroid-phobic or have glaucoma. Thus, INAH alone may be of interest.

Recommendation: In patients with AR, we suggest using a fixed combination of an INAH+INCS over an INAH alone. (Conditional recommendation based on moderate certainty of evidence for seasonal AR and on very low certainty of evidence for perennial AR).

- **Considerations in children and adolescents**: The recommendation is applicable to children and adolescents, even though evidence is scarcer (no studies on perennial AR and the only desirable outcome for which INAH+INCS are favored over INAH is rhinoconjunctivitis-related quality-of-life).
- **Implementation considerations**: None specific.

5.3.3.1 | Brief Justification.

- **Efficacy and safety**
  - A network meta-analysis suggested that, compared to INAH, INAH+INCS are associated with an improvement in nasal symptoms in seasonal and perennial AR (25% and 45% probability of nontrivial improvement in nasal symptoms, respectively).
  - For ocular symptoms, either differences between treatments were trivial (seasonal AR) or evidence was not found (perennial AR).
  - INAH+INCS displayed a higher probability of resulting in a nontrivial improvement of RQLQ in patients with seasonal AR (83%) than in patients with perennial AR (16%).
  - Similar frequencies of adverse events were observed with INAH+INCS and INAH (trivial difference). Serious adverse events associated with these interventions are rare and most of those reported in RCTs have been judged unlikely to be related to the treatment.
- **Resources required, cost-effectiveness and equity**: A survey of ARIA experts suggested INAH+INCS to be more expensive than INAH in 23 out of 27 countries for which data were available. However, INAH+INCS are likely cost-effective in most countries both when considering a willingness-to-pay of $50,000/QALY gained or of one time the GDP per capita/QALY gained (the only exception may be some low-income countries). No INAH+INCS or INAH are on the WHO List of Essential Medicines.
- **Acceptability and feasibility**: MASK-air data suggest that INAH+INCS are associated with higher adherence and treatment satisfaction, as well as with lower odds of being used in co-medication (a proxy of poor rhinitis control). In addition, INAH+INCS seem to display a faster onset of action.
- **Planetary health**: No specific evidence was found in terms of comparative impact on planetary health, even though it is possible that the production of two active compounds may have a higher environmental impact than the production of one.

5.3.4 | Should an Intranasal H_1-Antihistamine vs. an Intranasal Chromone Be Used for the Treatment of AR?

Link for the full EtD: https://www.mask-air.com/etd_nasal/11/.

Context: INAH and intranasal chromones are two alternatives that are often used in AR patients, including those with corticosteroid-phobia or who desire a fast onset of action.

Recommendation: In patients with AR, we suggest using INAH over intranasal chromones. (Conditional recommendation based on very low certainty of evidence).

- **Considerations in children and adolescents**: The recommendation is applicable to children and adolescents.
- **Implementation considerations**: None specific.

5.3.4.1 | Brief Justification.

- **Efficacy and safety**
  - Existing evidence is scarce and contradictory but overall suggests that intranasal antihistamines are associated with trivial or small improvements in nasal and ocular symptoms when compared to intranasal chromones.
  - For RQLQ, no evidence was found.
  - Similar frequencies of adverse events were observed with INAH and intranasal chromones (trivial difference).

Serious adverse events associated with these interventions are rare and most of those reported in RCTs have been judged unlikely to be related to the treatment.

- **Resources required, cost-effectiveness and equity**: A survey of ARIA experts suggested INAH to be more expensive than intranasal chromones in 10 out of 16 countries for which data were available (intranasal chromones are not available in many countries). However, differences in costs tended to be small. We did not identify cost-effectiveness studies comparing INAH to intranasal chromones. No INAH or intranasal chromone is on the WHO List of Essential Medicines.
- **Acceptability and feasibility**: MASK-air data suggest that INAH and intranasal chromones (i) are used in co-medication at a similar frequency, and (ii) are associated with similar adherence. However, INAH are associated with higher treatment satisfaction.
- **Planetary health**: No specific evidence was found in terms of comparative impact on planetary health.

6 | Conclusions

Intranasal medications, in particular INCS, INAH and INAH+INCS, are part of the mainstay of AR treatment. In ARIA 2024–2025, we formulated recommendations on 11 questions concerning AR intranasal treatment. Overall, we suggest using INAH+INCS over INAH or INCS and INCS over INAH. However, decisions on AR treatment should consider the clinical variability of the disease, patients' values and preferences and the affordability of treatment options.

Questions on intranasal treatments had been previously addressed in past editions of the ARIA guidelines. Box 2 and Table 3 compare recommendations on intranasal treatments of ARIA 2024–2025 *vis-à-vis* ARIA 2010/2016 guidelines. In brief, four questions were addressed in ARIA 2024–2025 for the first time, including questions comparing individual INCS and individual INAH+INCS. Among the remaining questions, a change in the strength and/or the directionality of recommendations was observed in three questions. For example, differently from the ARIA 2016 guidelines, we now suggest the use of INAH+INCS over INCS (particularly among patients with more severe symptoms). These changes reflect not only a larger amount of evidence from RCTs but also the evaluation of other evidence sources, such as mHealth data and results of a survey of ARIA experts. Considering these data sources was crucial to inform on criteria such as the acceptability and resources required for the interventions, rendering the guideline more person-centered. In addition, since these data reflect information from different countries—MASK-air is available in 30 countries, and the survey was answered by experts from more than 40 countries—their incorporation renders ARIA 2024–2025 more easily tailored to different contexts.

BOX 2 | Summary of what is new in the ARIA 2024–2025 guidelines in comparison to ARIA 2010–2016 guidelines.

New questions

- Should an INAH+INCS vs. no treatment be used for the treatment of AR?
  - Recommendation: "In patients with AR in whom monotherapy is unlikely to lead to significant improvement in symptoms, we recommend using INAH+INCS over no treatment. (Strong recommendation based on moderate certainty of evidence for seasonal AR and very low certainty of evidence for perennial AR)"
- Should any specific INCS vs. other INCS be used for the treatment of AR?
  - Recommendation: "In patients with AR, we suggest using specific INCS (in particular, fluticasone furoate or fluticasone propionate) over others (namely, beclomethasone, budesonide, ciclesonide, mometasone and triamcinolone). (Conditional recommendation based on very low or low certainty of evidence for most comparisons)"
- Should any specific INAH+INCS vs. other INAH+INCS be used for the treatment of AR?
  - Recommendation: "In patients with AR, we suggest using azelastine-fluticasone over olopatadine-mometasone. (Conditional recommendation based on moderate certainty of evidence for seasonal AR)"
- Should a combination of an INCS and an intranasal decongestant vs. an INCS alone be used for the treatment of AR?
  - Recommendation: "In patients with AR, we suggest against using a combination of an INCS + intranasal decongestant over an INCS alone. (Conditional recommendation based on very low certainty of evidence)"

Questions with changed recommendation (in terms of directionality or strength):

- Should an INAH vs. no treatment be used for the treatment of AR?
  - Recommendation changed from *conditional recommendation in favor of INAH* (2010/2016 guidelines) to a *strong recommendation in favor of INAH* (2024–2025 guidelines).
- Should an intranasal decongestant vs. no treatment be used for the treatment of AR?
  - Recommendation changed from *conditional recommendation in favor of intranasal decongestants* (2010/2016 guidelines) to a *conditional recommendation against the intervention* (2024–2025 guidelines).
- Should a combination of an INAH+INCS vs. an INCS alone be used for the treatment of AR?
  - Recommendation changed from *conditional recommendation either for either INAH + INCS or INCS* (2010/2016 guidelines) to a *conditional recommendation in favor of INAH + INCS* (2024–2025 guidelines).

AR, Allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; INAH, Intranasal H1-antihistamines; INAH+INCS, Fixed combinations of intranasal H1-antihistamines and intranasal corticosteroids; INCS, Intranasal corticosteroids.

TABLE 3 | Comparison of the recommendations on intranasal treatments of the ARIA 2024–2025 and of the ARIA 2010/2016 guidelines. Recommendations of the ARIA 2024–2025 guidelines are highlighted by a shade in a cell; recommendations of the ARIA 2010/2016 guidelines are highlighted by a border in a cell. Shade/border color code: Green = High certainty of evidence; Yellow = Moderate certainty of evidence; Orange = Low certainty of evidence; Red = Very low certainty of evidence.

Question	Disease	Recommendation				
Should a combination of an INAH+INCS vs no treatment be used for the treatment of AR?	PAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
	SAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
Should any specific INCS vs. other INCS be used for the treatment of AR?	PAR/ SAR	Strong recommendation against specific interventions	Conditional recommendation against specific interventions	Conditional recommendation for either some specific interventions or comparisons	**Conditional recommendation for specific interventions (FF or FP)**	Strong recommendation for specific intervention
Should any specific combination if an INAH+INCS vs other specific combination of an INAH+INCS be used for the treatment of AR?	SAR [a]	Strong recommendation against [azelastine-fluticasone]	Conditional recommendation against [azelastine-fluticasone]	Conditional recommendation for either [azelastine-fluticasone or olopatadine-mometasone]	**Conditional recommendation for [azelastine-fluticasone]**	Strong recommendation for [azelastine-fluticasone]
Should a combination of an INCS and an intranasal decongestant vs. an INCS alone be used for the treatment of AR?	PAR/ SAR	Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
Should an INAH vs no treatment be used for the treatment of AR?	PAR/ SAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
Should an intranasal decongestant vs. no treatment be used for the treatment of AR?	PAR/ SAR	Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
Should a combination of an INAH+INCS vs. an INCS alone be used for the treatment of AR?	PAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
	SAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
Should an INCS vs no treatment be used for the treatment of AR?	PAR/ SAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
Should an INCS vs. an INAH be used for the treatment of AR?	PAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
	SAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
Should a combination of an INAH+INCS vs. an INAH alone be used for the treatment of AR?	PAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
	SAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
Should an INAH vs. an intranasal chromone be used for the treatment of AR?	PAR/ SAR	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention

Abbreviations: AR, allergic rhinitis; FF, fluticasone furoate; FP, fluticasone propionate; INAH, intranasal antihistamines; INCS, intranasal corticosteroids; PAR, perennial allergic rhinitis; SAR, seasonal allergic rhinitis.
[a]No evidence for PAR.

Despite the new evidence incorporated in ARIA 2024–2025, there are still some knowledge gaps that would merit further research. There is a relative lack of RCTs assessing specific subgroups of participants, including those with mild disease, those with comorbid asthma or conjunctivitis, patients from ethnic minorities, older people and—for some outcomes—children. In addition, differences in the effect of interventions by sex have not been explored. Cost-utility studies comparing different treatments in AR are also lacking and, for some questions, we were not able to perform or include any study addressing the cost-effectiveness criterion. Finally, there is insufficient evidence on the planetary health impact of AR interventions (with no life cycle assessment studies having been performed for such treatments), precluding this criterion from playing a decisive role in most recommendations.

Contrary to previous ARIA guidelines, we opted not to present separate recommendations for seasonal vs. perennial AR. This decision is grounded on (i) recent studies pointing to the higher relative importance of severity over disease duration [32, 33], and (ii) the fact that our SR and meta-analyses usually found an agreement between results observed for patients with seasonal and perennial AR [23, 25]. However, since the certainty of evidence was often different between seasonal and perennial AR, there were some recommendations for which we highlighted such differences. Of note, we referred to "perennial" or "seasonal AR" considering that most RCTs did not adopt the ARIA classification (which classifies AR as "persistent" or "intermittent" [6]).

Our recommendations assume a correct use of the different intranasal medications, with inadequate use potentially resulting in lower efficacy and safety concerns [34, 35] (a video teaching patients how to use intranasal sprays can be found at https://www.youtube.com/watch?v=_ytYj1TLojM). In addition, variations in treatment duration were not explored. Future documents of the ARIA 2024–2025 guidelines will address the question of whether patients should take medications chronically or on an as-needed basis.

These guidelines have limitations. For desirable and undesirable effects, evidence was mostly obtained from RCTs. While RCTs are the paradigm for assessing the efficacy of interventions, they tend to be associated with generalisability concerns (e.g., with overrepresentation of patients with more severe disease [36]). Also, there was a relative lack of evidence on the differential impact of AR medications in patients with and without asthma. Finally, there were several comparisons on intranasal treatments of AR that we did not assess, as the corresponding questions were not prioritized [15]. The evaluated interventions were all pharmacological in nature, but it is important to note that nonpharmacological intranasal interventions (e.g., nasal washes) are often done by patients with AR. Accordingly, the off-label use of products for AR was not evaluated in these guidelines.

There are also important strengths associated with ARIA 2024–2025. We have followed the GRADE approach, using EtDs to develop recommendations. Additionally, we have used several approaches to formulate guideline questions and considered different data sources. Finally, we have conducted several SR and meta-analyses to provide updated evidence on the desirable and undesirable effects of interventions. These SR have been complemented by several other evidence sources (e.g., mHealth data, pharmacovigilance data and data from a survey of experts). These sources of data have an international scope, facilitating the tailoring of the ARIA guidelines to different regions or contexts.

In conclusion, this report compared intranasal treatments for the management of AR. The recommendations were developed following the GRADE approach and consider evidence from multiple sources, including systematic reviews of randomized controlled trials, mHealth data and a survey of experts.

Author Contributions

Bernardo Sousa-Pinto, Jean Bousquet, Holger J. Schünemann and Torsten Zuberbier were responsible for the coordination of the project (as members of the ARIA 2024–2025 guidelines steering committee) and contributed to the methodology (including evidence synthesis and analysis), discussion of the evidence and drafting of recommendations (as members of the ARIA 2024–2025 guideline panel) and writing the manuscript. Rafael José Vieira and Antonio Bognanni contributed to the methodology (including evidence synthesis and analysis), discussion of the evidence and drafting of recommendations (as members of the ARIA 2024–2025 guideline panel) and writing the manuscript. Arunas Valiulis, Sian Williams, Anna Bedbrook, Maria Jose Torres, G Walter Canonica, Leticia de las Vecillas, Mark S. Dykewicz, Cristina Jacomelli, Ludger Klimek, Lucas Leemann, Olga Lourenço, Yuliia Palamarchuk, Nikolaos G. Papadopoulos, Ana Margarida Pereira, Marine Savouré, Sanna K. Toppila-Salmi, Maria Teresa Ventura, Juan José Yepes-Nuñez, Elena Azzolini, Gilles Louis, Elena Parmelli and Jaron Zuberbier contributed to the discussion of the evidence and drafting of recommendations (as members of the ARIA 2024–2025 guideline panel) and writing the manuscript. Rita Amaral, Sara Gil-Mata, Manuel Marques-Cruz, Ewa Borowiack, Raquel Albuquerque Costa, Olga Mariana Cunha, Renato Ferreira-da-Silva, Despo Ierodiakonou, Justyna Litynska, Inês Ribeiro-Vaz, Ewelina Sadowska, Tuuli Thomander and João A. Fonseca contributed to the methodology (including evidence synthesis and analysis) and revising and editing the manuscript. All other authors were part of the international panel revising the recommendations, contributing to the guidelines by providing feedback on the recommendations and revising and editing the manuscript.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Appendix S1:** all70131-sup-0001-AppendixS1.DOC.