Allergic Rhinitis (AR) ACE Clinical Guideline (ACG)

Evidence-to-Recommendation (EtR) Framework

This document captures the draft ACG recommendations and their associated evidence to recommendation (EtR).

In ACGs, the strength of a recommendation reflects the confidence that the desirable effects of the recommended practice outweigh undesirable effects across the range of patients for whom the recommendation applies, based on the best available evidence:

- A strong recommendation is usually made when benefits clearly outweigh the risks, based on at least moderate-certainty evidence.
- A weak or conditional recommendation may be needed when there is a closer balance between benefits and harms, evidence is of low certainty, there is significant variability in patients' values and preferences, or important concerns with resourcing and feasibility of the recommended practice.

Recommendation 1:
Diagnose allergic rhinitis based on the patient's history, particularly their symptoms, combined with a physical examination.

Strength of recommendation:

Strong | Conditional

Summary: A strong recommendation for clinical approach to diagnosing allergic rhinitis (AR) is proposed, centred on detailed history-taking and physical examination, without requiring the use of any specific diagnostic test. This approach is consistent with guideline consensus and current practice, as well as no concerns for resources or feasibility considerations.

Balance of benefits and harms

A **combined approach of patient history and physical examination** improves diagnostic accuracy and, according to reference guidelines, is the recommended first-line evaluation strategy for AR. Using either history or examination on their own is not recommended, as physical findings are non-specific and can overlap with non-allergic rhinitis or viral rhinitis, lowering predictive value.[1]

Patient history

A thorough patient history capturing symptoms, context, and triggers of symptoms, helps to differentiate AR from other rhinitis subtypes (e.g., non-allergic, infectious).[2-6]

Asking about relevant comorbidities and family history identify at-risk patients and guide integrated disease management.[2-4, 7] For example, **AR often coexists with other atopic and airway conditions** such as asthma, allergic conjunctivitis, and atopic dermatitis. Identifying these comorbidities help clinicians anticipate complications (e.g., poor asthma control linked to untreated AR), optimise treatment strategies, and coordinate care across specialties. Also, a **family history of atopic disorders** (e.g., asthma, eczema) is a recognised risk factor for developing AR.[2-4]

Physical examination

Complementing patient history with a physical examination (e.g., inspection of the nasal cavity, anterior rhinoscopy, eye exam) increases diagnostic confidence through observable findings (e.g., allergic shiners, turbinate hypertrophy, conjunctival erythema).

Telemedicine is increasingly utilised in primary care, with its safety and utility widely acknowledged. Nonetheless, virtua**l consultations restrict the ability to conduct physical examinations**, thereby limiting the evaluation or exclusion of potential causes of symptoms. Consequently, reference guidelines strongly recommend performing a physical examination as part of the diagnostic process for AR.

Supporting tests (allergy testing, nasal endoscopy) may be considered when needed to guide management.

Certainty of evidence	**Values and preferences**
Not applicable; the balance of benefits and harms have been summarised using positions from high-quality guidelines.	No relevant literature was found, though it is plausible that **patients would value diagnosis accuracy,** which is in line with the benefits associated with the **proposed Recommendation 1.**
Resources and feasibility	**Acceptability and other considerations**
No significant concern identified with resources or feasibility. The proposed practice aligns with standard clinical approach locally.	No specific evidence was available on patient preferences for diagnostic approaches. However, an accurate diagnosis based on non-invasive methods (patient history and clinical examination) would generally be preferred before moving to more invasive methods (e.g. allergy testing, nasal endoscopy).

Recommendation 2:
Conduct allergy testing only when clinically warranted, for example when diagnosis is unclear, or when optimised pharmacotherapy provides inadequate symptom control.

Strength of recommendation:

Strong Conditional

Summary: Allergy testing is **not routinely required** for AR diagnosis and management, but can be useful in cases of diagnostic uncertainty, persistent AR despite optimised pharmacotherapy and when immunotherapy is being considered. Based on reference guidelines, both **SPT and sIgE tests** are widely accepted for confirming IgE-mediated sensitisation in suspected AR cases, with **SPT considered the preferred first-line option** due to its lower cost, immediate results, and high sensitivity/specificity. However, in cases where SPT is not feasible, e.g. due to resource requirements or when not recommended (e.g. patients with severe dermatoses or are unable to stop antihistamines), sIgE testing is acknowledged as a safe and reliable alternative. sIgE testing offers broader allergen panels and less variability in results, though at higher cost and slower turnaround compared to SPT.

Balance of benefits and harms

While **clinical history and a physical examination** is generally sufficient to diagnose AR, reference guidelines agree that **allergy testing is useful** in providing **diagnostic confirmation**, in **persistent AR cases despite optimal pharmacotherapy**, and when the specific allergen needs to be identified. Allergy testing is also essential when **allergen immunotherapy (AIT)** is being explored[8]

Based on several studies and one systematic review, **SPT has been demonstrated to be a safe method of allergy testing** with sensitivity and specificity of greater than 80%.[9-12] However, there are associated adverse effects from testing such as discomfort, pruritus and erythema. Additionally, **SPT is not recommended in certain patient groups** such as in patients with uncontrolled or severe asthma or cardiovascular disease, skin conditions including atopic dermatitis (AD) (since there is a possibility of false positives) and pregnancy.[13]

sIgE testing is seen as a safe and effective alternative to SPT and can also test for a wider panel of allergens.[8, 14, 15] While referenced studies do not provide direct comparisons between the two tests, sIgE testing demonstrated comparable sensitivities of 67–96% and specificities of 80–100%.[13] However, **sIgE testing also faces similar harms with SPT**, such as discomfort from blood tests, and risk of inaccurate test results from false positives,[13] and are also costlier.

For diagnosis, negative allergy tests may not rule out AR completely, as patients may have **local allergic rhinitis (LAR)** (i.e. patients with AR-like symptoms but test negative for both SPT and sIgE).[16] These patients may require **nasal provocation testing** for confirmation as they may still have local IgE production confined to the nasal mucosa.

Considering the potential false positives and negatives of allergy testing, reference guidelines have emphasised that the AR diagnostic process should still include patient history and physical examination as described in **Recommendation 1.**

Certainty of evidence	**Values and preferences**
The certainty is **high** for both SPT and sIgE tests, supported by prospective studies, systematic reviews, and multiple guidelines.[2, 4, 9-11, 17-22] Both tests **demonstrated high diagnostic accuracy** (SPT: sensitivity and specificity >80%; sIgE: sensitivity 67–96%, specificity 80–100%). favourable safety profile, with a **minimal risk of bias.**	Patients generally value the **accuracy of the results from allergy testing** as it gives them **clarity on the root cause of their symptoms**. This allows them to **receive tailored management or targeted immunotherapy** when appropriate. Minor harms associated with allergy testing such as temporary discomfort are generally acceptable given the perceived value of obtaining a definitive diagnosis.
Resources and feasibility	**Acceptability and other considerations**
Allergy testing mainly requires referral to allergy specialists. Additionally, allergy testing requires trained personnel and lab infrastructure, hence this testing should only be **recommended when diagnosis is still unclear in primary care settings,** or where AIT is being explored as a treatment option.	Allergy testing is generally **acceptable to patients** when clearly explained and recommended as part of a structured diagnostic or management process. Acceptability may vary depending on **patient expectations, cost, and access** to allergy testing services. Patients with limited financial means, mild or seasonal symptoms, or ready response to empirical therapy may be less motivated to undergo testing. In contrast, those with **persistent, severe, or unclear symptoms** tend to express stronger preference for confirmatory testing and specialist referral.

Recommendation 3:
Prescribe intranasal corticosteroid, oral antihistamine (2nd generation or later), or combination intranasal corticosteroid and intranasal antihistamine to manage allergic rhinitis.

Strength of recommendation:

Strong Conditional

Summary: A strong recommendation for pharmacotherapy is proposed, based on favourable benefit/risk ratio across all three treatment options, moderate-to-high quality of evidence, alignment with patients' values and preferences for outcomes and no significant resources concerns. While efficacy data are robust, treatment response and tolerability vary across patients depending on symptom profile and preference. Prescribing should therefore be individualised, balancing efficacy, onset of action, convenience, and cost.

Balance of benefits and harms

Overall, reference guidelines recognise **second-generation oral antihistamines (OAH), intranasal corticosteroids (INCS),** and **fixed-dose INCS+INAH combinations** as effective pharmacotherapy options for allergic rhinitis (AR). Among these, INCS+INAH combinations demonstrate the greatest efficacy and more rapid onset of action compared to INCS and OAH monotherapy. However, their uptake may be limited by its bitter aftertaste and higher cost. Importantly, guidelines emphasise that patient preferences, tolerability, and access should guide the choice of initial pharmacotherapy. For paediatric patients, INCS and OAH monotherapy options are indicated for AR, for patients as young as 2 years old. For INCS+INAH combinations available locally, the youngest age indicated is from 6. Benefits and harms for each treatment class are summarised below.

OAH:
Based on systematic reviews, 2nd-generation OAH are superior to placebo for **AR symptoms and QoL improvements.**[23-31] Outcomes were assessed using symptom scores such as the **TNSS** (*Total Nasal Symptom Score),* **PNIF** (*Peak Nasal Inspiratory Flow) and* **RQLQ** (*Rhinoconjunctivitis Quality of Life Questionnaire).* The effect size is **modest overall**: for example, the systematic review conducted by Zhang et. al reported statistically significant but not clinically meaningful improvements in RQLQ, and PNIF changes were not significant.[26] There is **low sedation risk (for 2nd generation-and later OAH)**, with no major adverse effects and good tolerability across both paediatric and adult populations.[23, 32] Second-generation OAH is safer than 1st-generation OAH, with the latter causing sedation and cognitive impairment.[33, 34]

INCS:
Systematic reviews conducted from the ARIA 2024 guideline consistently demonstrated the value of INCS in improving nasal symptoms, as measured by the TNSS, and improving ocular symptoms, measured by the TOSS **(***Total Ocular Symptom Score***)**.[35-37] Additionally, INCS are **superior to OAH** for overall nasal symptom control, especially for **nasal congestion and obstruction.**[38-40] INCS significantly improves **symptom control**, with added benefits in **QoL**. However, the onset of action of INCS is slightly slower than OAH,

with initial effects experienced within **3–60 hours** and maximal effect after 2 weeks.[41-43] Harms are local (irritation, epistaxis, aftertaste) and generally mild.

INCS+INAH:
Systematic reviews from the ARIA 2024 guideline have also demonstrated the effectiveness of INCS+INAH in improving nasal symptoms as measured by the TNSS and improving quality of life as measured by the RQLQ.[35-37] However, when compared to INCS monotherapy, INCS+INAH were not associated with a significantly higher improvement in both symptom control and QoL improvement.[35, 36]

This was also observed in a recently conducted SR and MA of **13 studies** by KAAACI, which showed that combination INCS+INAH provides **a modest but consistent added benefit** compared to INCS monotherapy for multiple outcomes.[44] Outcomes include,

- **TNSS[45-49]:** significant reduction (MD −0.44; 95% CI −0.61 to −0.27; $P < 0.00001$; $I^2 = 8\%$)
- **TOSS[46, 47, 49]:** significant improvement (MD −0.62; 95% CI −1.05 to −0.19; $P = 0.005$; $I^2 = 36\%$)
- **RQLQ[45-47, 49, 50]:** greater gains in QoL (MD −0.24; 95% CI −0.42 to −0.06; $P = 0.009$; $I^2 = 79\%$)
- **TSS[49, 50] (***Total Symptom Score***):** trend towards benefit, although not statistically significant (MD −0.66; 95% CI −2.02 to 0.71; $P = 0.34$; $I^2 = 98\%$)

In terms of safety, compared to INCS monotherapy, treatment **adverse effects** increased with INCS+INAH combination (RR 1.52; 95% CI 1.28–1.81), though absolute incidence was low (131/1,000 vs 93/1,000).[45-47, 49, 51, 52] Dysgeusia (i.e. altered taste) is higher with INCS+INAH combination (RR 7.40; 95% CI 3.60–15.23), but still infrequent (19/1,000 vs 3/1,000).

Certainty of evidence	Values and preferences
OAH: Certainty is **moderate to high**. Multiple SRs/MAs[23-31] confirmed that OAH are superior to placebo for sneezing, itching, and rhinorrhoea, but effect sizes are modest overall. **INCS:** Certainty is **high**. Multiple SRs/MAs[36-40] consistently demonstrate effectiveness of INCS in AR symptom control, and their superiority over OAH for certain AR symptoms such as nasal congestion, with robust QoL improvements. **INCS+INAH:** Certainty is **moderate**. Evidence summarised in the SRs show consistent improvements in TNSS, TOSS, and RQLQ compared with placebo and INCS alone.[36, 44] However, from the KAACI study, there was heterogeneity in QoL	A systematic review of 36 studies assessing patient values and preferences in AR reported that patients consistently **prioritise nasal symptoms**, particularly **nasal congestion**, over functional status or care-related experience.[53] **Nasal symptoms (mainly nasal congestion)** followed by breathing disorders, general and ocular symptoms were also rated as the symptoms with the highest impact. For pharmacotherapy, attributes related to **reduction and relief of symptoms** were rated as more important for adult patients than the risk of side effects. Patients also **showed a preference for more efficacious treatments than for treatments acting faster.**

outcomes (I^2 up to 79%) and increased incidence of minor adverse events (e.g., dysgeusia), which reduces the overall certainty to moderate.	
Resources and feasibility	**Acceptability and other considerations**
INCS are widely available, relatively inexpensive through subsidies on the SDL, and effective with brief technique training. **OAH** are also subsidised and readily available in primary care. **INCS+INAH** is currently not subsidised and may not be available in some primary care settings (e.g. polyclinics). Additionally, no generic formulations are not yet available, and costs can be **upwards of ten times higher than generic INCS monotherapy**. No local cost-effectiveness analyses for INCS+INAH have been performed to date.	Some patients may opt to start with **oral formulations** due to convenience in administration, which contributes to the continued uptake of OAH despite their **modest efficacy** in AR symptom management.[26, 54] Optimising **technique with intranasal preparations (e.g. INCS, INCS+INAH)** (spray direction, head position) reduces local effects and improves effectiveness, enhancing acceptability and adherence.

Recommendation 4:
Offer allergen avoidance advice to all AR patients as an adjunct to pharmacological therapy, focusing on accessible and practical strategies.

Strength of recommendation:

Strong Conditional

Summary: Overall, a strong recommendation is proposed for allergen avoidance strategies. While evidence has limitations and is of low/very-low quality, allergen avoidance remains a practical, low-risk strategy that complements pharmacotherapy in AR management.

We recognise the importance of this strategy for all patients with AR. Therefore, we opted for a strong recommendation, with a specific emphasis on prioritising the most accessible and practical allergen avoidance strategies. Resource considerations vary depending on the specific allergen avoidance intervention.

For this EtR, we evaluated strategies focused on HDM avoidance to acknowledge its high prevalence, and its established evidence base over other allergens. A local cohort study showed that HDM is the predominant allergen in Singapore, with over 80% of allergic individuals sensitised to it, and environmental exposure in the local climate strongly drives this sensitisation.[55]

As for other allergens, we plan to include a general statement in the ACG to acknowledge that allergen avoidance should also be explored.

Balance of benefits and harms

House dust mites (HDMs) are a common trigger for AR, and also highly prevalent in Singapore.[55-57] Therefore, reducing exposure to HDM through **physical** and **chemical interventions** are potentially beneficial options in AR management.[13]

Physical interventions

Physical interventions (e.g., impermeable bedding, HEPA filters, air purifiers, vacuuming) can reduce HDM levels, but this effect **did not reliably translate into symptom improvement** for AR.[58-65] Additionally, referenced trials are small, often methodologically weak, and heterogeneous. There are associated costs with these interventions, e.g. equipment (bedding, filters, purifiers) and with cost-effectiveness not evaluated, uptake of to these interventions may be poor.[66]

Chemical interventions

Acaricides in household cleaners have been utilised as a chemical technique to reduce HDM concentration. Studies evaluated the usage of an acaricide spray showing **improved mean symptom scores** versus controls.[59, 67] Additionally, a **crossover study** to investigate an **acaricide-containing bag placed beneath bed mattresses** in children with AR and asthma, reporting **improved AR symptom scores** and **better disease-specific QoL** (measured through the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) compared to control.[68]

<table>
<tr><td colspan="2">Overall, based on the evidence base for HDM, allergen avoidance is best considered an adjunctive strategy to pharmacotherapy due to their limited benefits in alleviating AR symptoms.</td></tr>
<tr><td>Certainty of evidence</td><td>Values and preferences</td></tr>
<tr><td>Very low to low quality: most studies are small RCTs with methodological limitations, heterogeneous interventions, and risk of bias.[58-65, 67-69]</td><td>While no specific literature was identified on which outcomes are most valued by patients with AR when it comes to allergen avoidance strategies, it is plausible to assume that symptom reduction and improved quality of life would the prioritised ones. Based on clinical effectiveness, there may therefore be a disconnect as such interventions may not lead to desirable reductions in AR symptoms.</td></tr>
<tr><td>Resources and feasibility</td><td>Acceptability and other considerations</td></tr>
<tr><td>Physical measures (bedding encasements, HEPA filters, air purifiers) involve moderate to high upfront costs and regular ongoing usage. Chemical acaricides require regular application.

Cost-effectiveness of these allergen avoidance measures have not been evaluated. Regardless, some interventions are compatible with broader lifestyle modifications (improved ventilation, cleaning).</td><td>Acceptability of allergen avoidance strategies generally depends on the perceived benefit, cost and effort required to carry out the strategy.

For HDM reduction, interventions such as regular washing of bedding in hot water, use of impermeable mattress and pillow covers, and routine cleaning are generally well accepted because they are low-risk and familiar household practices. However, compliance with more intensive or costly measures (e.g. HEPA air filters, acaricide sprays, specialised bedding) tends to be low, reflecting uncertainty about financial burden and associated clinical benefit.</td></tr>
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