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Next-generation Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines for allergic rhinitis based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and real-world evidence

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Next-generation ARIA guidelines for allergic rhinitis based on GRADE and real-world evidence

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193

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266 **Abstract**

267 The selection of pharmacotherapy for patients with allergic rhinitis aims to control the disease and
268 depends on many factors. GRADE (Grading of Recommendations Assessment, Development and
269 Evaluation) guidelines have considerably improved the treatment of allergic rhinitis. However, there is
270 an increasing trend to use real-world evidence to inform clinical practice, especially as randomized
271 controlled trials are often limited with regards to the applicability of results. The MACVIA (*Contre les*
272 *MAladies Chroniques pour un Vieillissement Actif*) algorithm has proposed an allergic rhinitis treatment
273 by a consensus group. This simple algorithm can be used to step-up or step-down allergic rhinitis
274 treatment. Next-generation guidelines for the pharmacologic treatment of allergic rhinitis were
275 developed using existing GRADE-based guidelines for the disease, real-world evidence provided by
276 mobile technology and additive studies (allergen chamber studies) to refine the MACVIA algorithm.

277 **Key words**

278 Allergic rhinitis, ARIA, GRADE, guidelines, real-world evidence

279 **Abbreviations**

280 AIRWAYS ICPs: Integrated care pathways for airway diseases
281 ARIA: Allergic Rhinitis and Its Impact on Asthma
282 Aze: Azelastine hydrochloride
283 DG Santé: European Commission's Directorate-General for Health and Food Safety
284 FF: Fluticasone furoate
285 FP: Fluticasone propionate
286 GRADE: Grading of Recommendations Assessment, Development and Evaluation
287 MACVIA: Contre les MAladies Chroniques pour un Vieillissement Actif
288 MASK: Mobile Airways Sentinel NetworK
289 MF: Mometasone furorate
290 **mHealth: Mobile health**
291 MPaZeFlu: Azelastine-Fluticasone propionate combination
292 MPR: Medication Possession Ratio
293 OTC: Over-the-counter
294 PDC: Proportion of days covered
295 RWE: Real-world evidence
296 VAS: Visual analogue scale
297 WHO: World Health Organization

298

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300 Introduction

301 The selection of pharmacotherapy for patients with allergic rhinitis aims to control the disease and
302 depends on (i) patient empowerment, preferences and age, (ii) prominent symptoms, symptom severity
303 and multimorbidity, (iii) efficacy and safety of treatment (1), (iv) speed of onset of action of treatment,
304 (v) current treatment, (vi) historic response to treatment, (vii) impact on sleep and work productivity
305 (2, 3), (viii) self-management strategies and (ix) resource use (4, 5).

306 An algorithm was devised (5) and digitalized (6) to step-up or step-down allergic rhinitis treatment based
307 on control. However, its use varies depending on the availability of medications and resources.
308 Algorithms require testing with real-world evidence (RWE) that includes randomized controlled trials
309 and observational research with real-world data (7-9).

310 To evaluate estimates of effects, the GRADE (Grading of Recommendations Assessment, Development
311 and Evaluation) methodology explicitly considers all types of study designs from Randomized Control
312 Trials to case reports, although guideline developers often restrict guidelines to Randomized Control
313 Trials (10-12). GRADE also considers evidence on prognosis, diagnosis, values and preferences,
314 acceptability and feasibility or directness of findings. There is an increasing trend to use real-world data
315 to inform clinical practice, especially as Randomized Control Trials are often limited to the
316 applicability of results (13). The trade-off that is made is one between risk of bias, primarily selection
317 and confounding bias, and applicability. Ideally, both types of evidence are merged.

318 Guidelines are not sufficiently followed because they are not close enough to patients' needs and
319 probably do not reflect real life. In cluster-randomized trials, guideline-driven treatment is more
320 effective than free-treatment choice (14, 15). Moreover, guidelines (in rhinitis but also in asthma) have
321 led to a better understanding of the treatment of the disease and have had an important teaching role
322 which has led to change management (16).

323 In addition, there is a need to support the transformation of the health care system for integrated care
324 with organizational health literacy (17, 18). During a recent meeting held in Paris (December 3, 2018)
325 for chronic disease care, MASK (Mobile Airways Sentinel NetworK) (19) and POLLAR (Impact of Air
326 POLLution on Asthma and Rhinitis, EIT Health: European Institute for Innovation and Technology-
327 Health) (20), in collaboration with professional and patient organizations in the field of allergy and
328 airway diseases (Figure 1), recommended the evaluation of real-life care pathways (ICPs) centred
329 around the patient with rhinitis and asthma.

330 During the ICPs meeting in Paris, **next-generation guidelines** for the pharmacologic treatment of
331 allergic rhinitis were developed using existing GRADE-based guidelines for allergic rhinitis (5, 21-23),

332 RWE provided by Randomized Control Trials, real-world data using mobile technology (24, 25) and
333 chamber studies (Figure 2). These recommendations were used to refine the algorithm for allergic
334 rhinitis treatment proposed by a consensus group (5).

335 The present report describes the process of next-generation ARIA-GRADE guidelines for the
336 pharmacologic treatment of allergic rhinitis.

337

338 **1- Documents considered for the development of ARIA care** 339 **pathways**

340 **1-1- MACVIA algorithm proposing a stepwise approach for allergic** 341 **rhinitis pharmacologic treatment**

342 An algorithm based on the visual analogue scale (VAS) (26) has been devised by the ARIA (Allergic
343 Rhinitis and its Impact on Asthma) expert group (i) for the selection of pharmacotherapy for allergic
344 rhinitis patients and (ii) to step-up or step-down treatment depending on control (5) (Figures 3a and 3b).

345 The ARIA algorithm for allergic rhinitis was revised by an expert group and a proposal was made to
346 classify allergic rhinitis treatments (Table 1) (6).

347 **1-2- ARIA 2010, 2016 revision and US Practice Parameters 2017**

348 Although few head-to-head comparisons of medications during Randomized Control Trials are
349 available (27-30), the comparison of allergic rhinitis medications has been proposed by several reviews
350 (1) and guidelines (5, 21-23). A Health Technology Assessment evaluation concluded that most allergic
351 rhinitis medications had a similar effect (31). However, this study used a method that did not enable
352 differentiation between medications.

353 The ARIA revision 2016 (22) and the US Practice Parameters 2017 (23) were developed independently
354 and used the same methodological approach: GRADE (10-12). Interestingly, the same questions were
355 considered. Two major outcomes were considered in the treatment of moderate-severe rhinitis: efficacy
356 and speed of action (Table 2).

357 Although the GRADE approach suggests the use of all relevant evidence, developers of
358 recommendations have focused on Randomized Control Trials .

359 **ARIA 2016 revision (22) and US Practice Parameters 2017 (23) mainly based on Randomized Control Trials**
360 **support the MACVIA algorithm (5)**

361 **1-3- Speed of onset of action of medications**

362 The US Food and Drug Administration has proposed three study types to assess the onset of action of
363 allergic rhinitis medications (32, 33): the standard Phase III double-blind Randomized Control Trial,
364 park setting studies and allergen exposure chamber (AEC) studies (34). Randomized Control Trials are
365 informative but cannot provide sufficient precision to assess the onset of efficacy as they cannot allow
366 repeated timing over short periods of time (minutes). Allergen exposure chambers offer some
367 advantages over Randomized Control Trials in assessing the onset of action of medications which can
368 be demonstrated in minutes (34). The allergen exposure chamber allows consistent allergen exposure.
369 However, it is a manipulated *in vivo* procedure, while the park study mirrors real-life exposure. Park
370 studies have not captured the early time as well as the allergen exposure chamber. It appears that a cross-
371 over trial would be difficult with a park study due to variations of allergen exposure between days. On
372 the other hand, the allergen exposure chamber cannot replace real-world allergen exposure but only
373 complement it. Allergen exposure chamber studies appear more robust than park studies. To date, the
374 allergen exposure chamber studies that have been conducted have been monocentric and have followed
375 protocols unique to each centre. Because there are technical differences in each allergen exposure
376 chamber, it is not easy to compare the results obtained in the different allergen exposure chambers (35)
377 although standardization has begun for some of them (36).

378 In the Ontario and Vienna allergen exposure chambers, several medications have been tested (Tables
379 3A and B).

380 **The Ontario Chamber studies show the rapid onset of efficacy for Azelastine and its combinations. There does**
381 **not seem to be a difference between Azelastine alone or in combination. Other intranasal H₁-antihistamines**
382 **have a slower onset of action. INCS (alone or with oral H₁-antihistamines) are not effective before 2 hrs.**

383 **The Vienna chamber studies show that Azelastine and Levocabastine/FF are the fastest-acting medications**
384 **by comparison with oral H₁-antihistamines.**

385 **1-4- Real-world evidence using mobile technology**

386 According to the World Health Organization (WHO), mHealth (Mobile Health) has the potential to
387 transform health service delivery globally (37). Next-generation ARIA guidelines should consider
388 testing the recommendations based on the GRADE approach with direct RWE using data obtained by
389 mHealth tools in order to confirm or refine current GRADE-based recommendations.

390 Although many mHealth tools are available for the assessment of allergic rhinitis (38), only MASK
391 (Mobile Airways Sentinel network) has reported data on medications that can be used in RWE. MASK,
392 a new development of ARIA, is an information and communication technology (ICT) system centred

393 around the patient (adolescents and adults) (20, 39). MASK, freely available in Google Play and Apple
394 Stores, can inform patient decisions on the basis of a self-care plan proposed by the health care
395 professional (19, 20). It uses a treatment scroll list including all medications customized for each
396 country as well as visual analogue scales (VASs) to assess rhinitis control and work productivity.
397 MASK is a ~~Good Practice following CHRODIS recommendations~~ deployed in 23 countries and 17
398 languages (40) with over 30,000 users. It was selected by the European Commission's Directorate-
399 General for Health and Food Safety (DG SANTE) and by the newly established Commission Expert
400 Group "Steering Group on Health Promotion, Disease Prevention and Management of Non-
401 Communicable Diseases" as a Good Practice (GP) that can be scaled up in the field of digitally-enabled,
402 integrated, person-centred care (41).

403 **1-4-1- Messages from MASK**

404 Two studies in over 9,000 users and 22 countries (25, 42) confirmed a pilot study (24) and allowed
405 differentiation between ALLERGIC RHINITIS treatments. They also showed that the assessment of
406 days was useful in understanding treatment patterns. Their results combine to indicate that, in real life:

- 407 (i) Patients are poorly adherent to treatment (24, 42).
- 408 (ii) No treatment trajectory could be identified (25) and most patients self-medicate.
- 409 (iii) Most rhinitis patients use on-demand treatment when they are sub-optimally controlled. When
410 uncontrolled, they change their medications daily in order to be controlled (24).
- 411 (iv) The vast majority of patients do not follow guidelines or physicians' prescriptions (24, 25, 42).
- 412 (v) When physicians are allergic, they behave like patients (43), suggesting the need for behavioural
413 science to improve control.
- 414 (vi) Patients who do not take medications are usually well-controlled (24, 25).
- 415 (vii) Patients reporting monotherapy with intranasal corticosteroids (INCS)-containing medications
416 have a similar control level (24, 25). However, MPAzeFlu (intra-nasal Azelastine-Fluticasone
417 Propionate combination) is significantly more often administered as a single therapy than
418 fluticasone Furoate (FF) or Mometasone Furoate (MF).
- 419 (viii) Patients reporting oral H₁-antihistamines monotherapy have a poorer level of control than those
420 reporting INCS-containing medications (24, 25).
- 421 (ix) Most patients have a worse control level with increasing medications (24, 25) contradicting
422 guidelines that propose to increase the treatment level to achieve control.

- 423 (x) These results indicate that when patients are controlled, either they do not take a medication or
424 remain with a single treatment. When they are uncontrolled, they co-medicate.
- 425 (xi) Considering control level and co-medication, MPAzeFlu is more effective than INCS (24, 25).
- 426 (xii) Resistant hypertension is defined by the number of medications used to control the disease (44),
427 and a similar classification may be proposed in allergic rhinitis confirming the SCUAD (severe
428 chronic upper airway disease) concept (45).

429 **1-4-2- Limitations of MASK**

430 As for all studies using participatory data, potential biases include (i) the likelihood of sampling bias,
431 which makes it difficult to assess generalizability of the study, (ii) outcome misclassification that cannot be
432 assessed and (iii) due to ethical considerations, availability of very little information on patient (or day)
433 characteristics. App users are not representative of all patients with rhinitis.

434 MASK studies have used days in cross-sectional analyses (19, 20) because there is no clear pattern for
435 a defined treatment, and a longitudinal study was not feasible since users mostly use the App
436 intermittently.

437 The diagnosis of allergic rhinitis was not supported by a physician but was a response to the question:
438 “Do you have allergic rhinitis? Yes/No”. Some users with no rhinitis may therefore have responded
439 “Yes” to the question but >95% of responders declared symptoms of rhinitis by questionnaire. There
440 are potential measurement biases when using apps including collection of information, education of the
441 patient, age, availability and ability to use a smartphone (24). Precise patient characterization is
442 impossible using an App, but every observational study using MASK has been able to identify days
443 with poor control or criteria of severity (46-50).

444 Adherence to treatment is impossible to obtain directly as patients do not report data every day and may
445 not report all medications used. Electronic counters on delivery devices could be used to obtain more
446 complete data on adherence.

447 Nonetheless, mobile technology is becoming an important tool for better understanding and managing
448 allergic rhinitis. It adds novel information that was not available with other methods (46-52). In
449 addition, the mere number of observations that mobile technology can provide offers an unprecedented
450 body of evidence that can complement conventional Randomized Control Trials for RWE.

451 **1-4-5- Other real-world evidence studies using mobile technology**

452 To our knowledge, no other mHealth study has assessed the efficacy of different medications at large
453 scale.

454 **1-5- Physician's perspectives**

455 There is a complete disconnection between the physician's prescriptions and the patient's behaviour
456 for the treatment of pollen-induced allergic rhinitis. The vast majority of allergists prescribe
457 medications for the entire season, recommending the patient to use them regularly, even during days
458 with few symptoms. Some allergists prescribe a pre-season treatment without clear evidence of
459 efficacy. On the other hand, the vast majority of patients use their medications on-demand when their
460 allergic rhinitis is not well controlled and they do not follow guidelines (19, 20).

461 When physicians are patients themselves, they behave like patients when they treat their own allergic
462 rhinitis and do not follow the prescriptions, as recently reported (43). Health literacy is an important
463 component of adherence to medications (53, 54), but, given the behaviour of allergists as patients, it
464 appears that other factors are more important. Possibly, it is human nature that drives adherence to
465 treatment whether or not the patient is a physician, and behavioural science is an important need to be
466 considered in medical care.

467 **Lack of adherence is very common in allergists who suffer from allergic rhinitis and prescribe long-term**
468 **treatment**

469 **2- Next-generation ARIA-GRADE guidelines**

470 Recommendations have been refined with RWE and chamber studies (Table 4). The algorithm proposed
471 in Figure 3 is also supported by the present data.

472 The approach proposed in this paper confirms most GRADE recommendations for allergic rhinitis and
473 the classification of allergic rhinitis treatments proposed by ARIA (Table 1 (6)). Some conditional
474 evidence was supported by RWE. In particular:

- 475 • The combination of oral H₁-antihistamines with INCS was not found more effective than INCS
476 alone
- 477 • The combination of intra-nasal H₁-antihistamines with INCS was found more effective than INCS
478 alone and
- 479 • Intra-nasal H₁-antihistamine-containing medications are effective within minutes.

480 **3- Next-generation ARIA algorithm**

481 The overall ARIA algorithm (5) was found appropriate and no change is needed. The step-up and step-
482 down approach proposed by ARIA experts (6) based on the ARIA algorithm has been confirmed (Table
483 5). However, the different steps need further validation with RWE.

484 **Conclusions**

485 In this report, we present the first GRADE-based guideline integrating RWE and supportive studies
486 (chamber studies) in the management of allergic rhinitis. This approach could be considered as a model
487 for chronic diseases.

488 These guidelines will inform ICPs and will be included in the DG Santé **digitally-enabled, integrated,**
489 **person-centred care** (55). They will represent the Change Management strategy of ARIA Phase 4 (17).

490

491

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719 **Figure 1: Organizations supporting the meeting (Paris, December 3, 2018)**

720 POLLAR: Impact of Air POLLution in Asthma and Rhinitis, EIT Health: European Institute for Innovation and
721 Technology, ARIA: Allergic Rhinitis and its Impact on Asthma, Euforea: European Forum for Research and
722 Education in Allergy and Airways Diseases GA²LEN: Global Allergy and Asthma European Network, CEmPac:
723 Centre for Empowering Patients and Communities, EAACI: European Academy of Allergy and Clinical
724 Immunology, EFA: European Federation of Allergy and Airways Diseases Patients' Associations, ERS: European
725 Respiratory Society, ERS: European Rhinology Society, GARD: Global Alliance against Chronic Respiratory
726 Diseases (WHO Alliance), GINA: Global Initiative for Asthma, MACVIA: Fondation MACVIA-LR, SPLF:
727 Société de Pneumologie de Langue Française, SFA: Société française d'Allergologie, WAO: World Allergy
728 Organization

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730

731 **Figure 2: Development of next-generation ARIA guidelines**

732

733 **Figure 3a: Step-up algorithm in untreated patients using visual analogue scale (adolescents
734 and adults) (from (5))**

735 *The proposed algorithm considers the treatment steps and the patient's preference*

736 *VAS levels in ratio*

737 *If ocular symptoms remain once treatment has been initiated: add intra-ocular treatment*

738

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740

741 **Figure 3b: Step-up algorithm in treated patients using visual analogue scale (adolescents
742 and adults) (from (5))**

743 *The proposed algorithm considers the treatment steps and the patient's preference*

744 *VAS levels in ratio*

745 *If remaining ocular symptoms: add intra-ocular treatment*

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749 **Table 1: Classification of treatments used in allergic rhinitis (from 6)**

T1	Non-sedating H1-antihistamine (oral, intra-nasal, ocular), leukotriene receptor antagonist (LTRA) or cromones (intranasal, ocular)
T2	Intranasal corticosteroids (INCS)
T3	INCS + intranasal Azelastine
T4	Oral corticosteroid as a short course and an add-on treatment
T5	Consider referral to a specialist and allergen immunotherapy

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752 **Table 2: Overall recommendations using GRADE**

753 **A- ARIA 2016 (22)**

- | | |
|-----|---|
| 754 | 1. In patients with SAR, we suggest either a combination of INCS + OAH or INCS alone, but potential net |
| 755 | benefit may not justify spending additional resources. |
| 756 | 2. In patients with PAR, INCS alone are recommended rather than a combination of INCS + OAH |
| 757 | 3. In patients with SAR, we suggest either a combination of INCS + INAH or INCS alone, but the choice of |
| 758 | treatment depends on patient preferences. At initiation of treatment (first 2 weeks), a combination of INCS |
| 759 | + INAH might act faster than INCS alone and might therefore be preferred by some patients. In settings in |
| 760 | which additional cost of combination therapy is not large, a combination therapy might be a reasonable |
| 761 | choice. |
| 762 | 4. In patients with PAR, we suggest either a combination of INCS + INAH or INCS alone. |
| 763 | <i>For all of these recommendations, the level of evidence was low (2, 3) or very low (1,4).</i> |

764 **B- US Practice Parameters 2017 (23)**

- | | |
|-----|---|
| 765 | For initial treatment of nasal symptoms of SAR in patients ≥ 12 years of age, clinicians: |
| 766 | • Should routinely prescribe monotherapy with an INCS rather than a combination of INCS and oral H ₁ - |
| 767 | antihistamine. |
| 768 | • Should recommend an INCS over LTRA (for ≥ 15 years of age). |
| 769 | • For moderate to severe symptoms, may recommend the combination of an INCS and INAH. |
| 770 | |

771 **Table 3: Comparison of the time of onset of action using environmental exposure**
 772 **chambers**

773 **A: Ontario environmental exposure chamber (from (56))**

Drug (dose)	Formulation	Onset of Action	Parameter	Reference
Azelastine	Nasal spray	15 min	TNSS	(57)
MPAzeFlu	Nasal spray	5 min	TNSS	(56)
FP + oral Loratadine (10 mg)	Nasal spray + tablet	160 min		
Olopatadine	Nasal spray	90 min	TNSS	(58)
Ciclesonide	Nasal spray	60 min	TNSS	(59)
Budesonide	Nasal spray	8 h	TNSS	(60)
Budesonide & Azelastine	Nasal spray	20 min		
CDX-313 (solubilized Budesonide + Azelastine)	Nasal spray	20 min		
Levocetirizine	Tablet	160 min	MSS	(61)

774 TNSS: total nasal symptom score, MSC: mixed symptom score

775 **B: Vienna environmental exposure chamber**

Drug (dose)	Formulation	Onset of Action	Parameter	Ref
Astemisole-D, Loratadine-D	Tablet	65-70 min	No placebo MSS	(62)
Astemisole, Loratadine, terfenadine-forte	Tablet	107-153 min	No placebo MSS	(63)
Azelastine (IN), desloratadine	Nasal/ Tablet	Aze: 15 min DL: 150 min	TNSS	(64)
Bilastine, cetirizine, fexofenadine	Tablet	No assessment before 60 min	TNSS	(65)
Cetirizine-D, budesonide	Nasal/ Tablet		No placebo	(66)
Cetirizine-D, xylometazoline nasal spray	Nasal/ Tablet		No placebo	(67)
Desloratadine	Tablet	30 min	obstruction	(68)
Fluticasone furorate and levocabastine	Nasal spray	Combi: 15 min No data for FF or Levocabastine	TNSS	(69)
Levocetirizine, loratadine	Tablet	Levo: 45 min Lora: 60 min	MSS	(70)
Rupatadine	Tablet	15 min	TNSS	(71)

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Table 4: Information used to support the next-generation ARIA-GRADE guidelines

	GRADE recommendation	mHealth RWE	Chamber studies
Oral H₁-antihistamines are less potent than INCS BUT many patients prefer oral drugs	(21) No information on patient's preference	(24)(25) No information on patient's preference	
Intra-nasal H₁-antihistamines are less effective than INCS	(21)		
Intra-nasal H₁-antihistamines are effective within minutes	(21)		(57, 64)
INCS should continue being prescribed as first line therapy in moderate-severe rhinitis	(21, 23)	(24, 25)	
The onset of action of INCS takes a few hours to a few days (ciclesonide has a faster onset)	(21)		(59, 60)
The combination of INCS and oral H₁-antihistamines offers no advantage over INCS	(22, 23)	(24, 25)	
The combination of INCS and intra-nasal H₁-antihistamines is more effective than INCS	YES in moderate-severe patients: (23) With restriction: (22)	(24, 25)	
The combination of INCS and intra-nasal H₁-antihistamines is effective within minutes			(56, 60, 69)
Leukotriene antagonists are less potent than INCS	(23)		(56, 60, 69)

781 **Table 5: Consensus opinion for the different scenaria (from 6)**

Part 1: Approach to treatment				
	Patient VAS	Phenotype	Tx	Consensus
1	≥5	IAR or PER	Yes	Step-up
2	≥2 to <5	IAR	Yes	Continue
3	<2	IAR	Yes	Step-down
4	≥2 to <5	PER	Yes	Continue or Step-up
5	<2	PER	Yes	Step-down
6	≥5	IAR	No	Initiate
7	≥5	PER	No	Initiate
8	<5	IAR or PER	No	Initiate
Part 2: Specific treatment step-ups				
	Current Tx	Step-ups		Notes
9	T1	T2 or T3		
10	T2	T3		
11	T3	T3 + T4 ^a		Consider T5 ^b
12	T1 + T2	T3		Consider T5 ^b
13	T1 + T3	T3 + T4 ^a		Consider T5 ^b
14	T2 + T3	T3 + T4		Consider T5 ^b
15	T5 + VAS ≥5	T5 + T>2 or T3		
16	T5 + VAS ≥2 to <5	T5 + T1, T2 or T3		T5 + T2 or T3 if congestion
17	T5 + T1	T5 + T2 or T3		
18	T5 + T2	T5 + T3		
19	T5 + T3	Continue		Consider referral
Part 3: Specific treatment step-downs				
	Current Tx	Step-down		Notes
20	T3	T2 or T1		T2 if congestion
21	T2	T1		Continue T2 if congestion
22	T1	Stop		NOT exposed to allergen
23	T1	Continue		EXPOSED to allergen
24	T1 + T2	T1 or T2		T2 if congestion
25	T1 + T3	T1 or T3		T3 if congestion
26	T2 + T3	T2 or T3		
27	T5 + T3	T5 + T1 or T2		T5 + T2 if congestion
28	T5 + T2	T5 + T1		Continue T5 + T2 if congestion
29	T5 + T1	T5		NOT exposed to allergen
30	T5 + T1	T5 + T1		EXPOSED to allergen
31	T5	T5		Until end of course
Part 4: treatment initiation				

	Patients	Tx	Consensus	Note
32	IAR; VAS \geq 5	No	T1,T2 or T3	T2 or T3 if congestion
33	PER; VAS \geq 5	No	T2 or T3	
34	IAR or PER VAS <5	No	T1, T2 or T3	T2 or T3 if congestion

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VAS: visual analogue scale, Tx: treatment, IAR: Intermittent allergic rhinitis, PER: persistent allergic rhinitis, T1: anti-histamine (oral, intranasal, eye drop), leukotriene receptor antagonist or cromones (intranasal or eye drops), T2 : intranasal corticosteroids (INCS), T4 : INCS + intranasal antihistamine, T5 : consider referral and allergen immunotherapy



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European Innovation Partnership on Active and Healthy Ageing



American College of Allergy, Asthma & Immunology



EAACI EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY



EFA European Federation of Allergy and Airways Diseases Patients' Associations



ERS EUROPEAN RESPIRATORY SOCIETY



ERS European Rhinologic Society Founded 1963



GALEN Global Allergy and Asthma European Network Network of Excellence



A world where all people breathe freely



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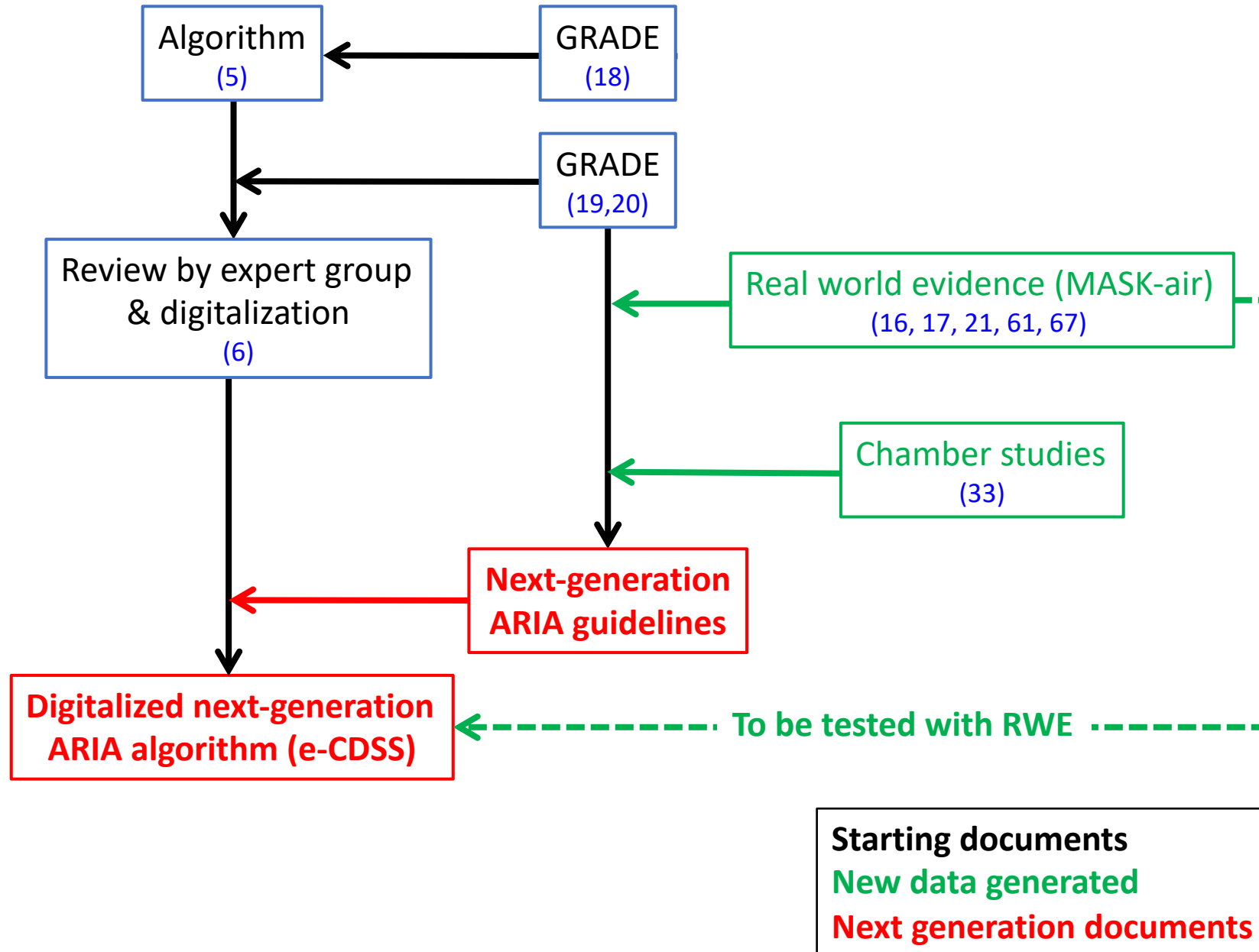


WAO WORLD ALLERGY ORGANIZATION

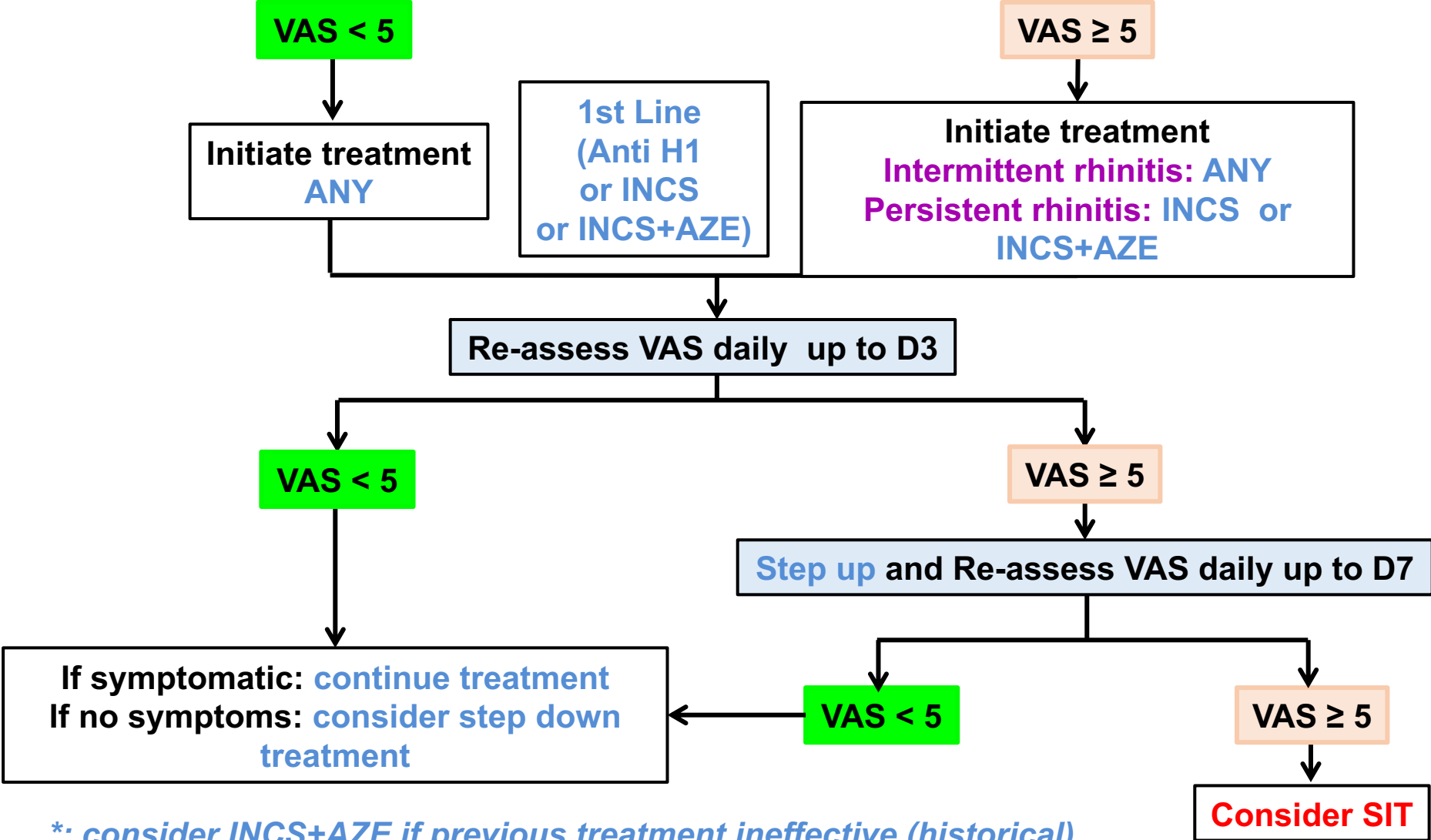


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Assessment of control in untreated symptomatic patient



**: consider INCS+AZE if previous treatment ineffective (historical)*

Assessment of control in treated symptomatic patient

