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Bousquet, Jean; Schünemann, Holger J.; Hellings, Peter W.; Arnavielhe, Sylvie; Bachert, Claus; Bedbrook, Anna

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MACVIA clinical decision algorithm in adolescents and adults with allergic rhinitis



Jean Bousquet, MD,^{a,b,c} Holger J. Schünemann, MD,^d Peter W. Hellings, MD,^e Sylvie Arnavielhe, PhD,^f Claus Bachert, MD,^g Anna Bedbrook, BSc,^b Karl-Christian Bergmann, MD,^h Sinthia Bosnic-Anticevich, PhD,ⁱ Jan Brozek, MD,^d Moises Calderon, MD,^j G. Walter Canonica, MD,^k Thomas B. Casale, MD,^l Niels H. Chavannes, MD,^m Linda Cox, MD,ⁿ Henry Chrystyn, PhD,^o Alvaro A. Cruz, MD,^p Ronald Dahl, MD,^q Giuseppe De Carlo, MD,^r Pascal Demoly, MD,^{s,t} Phillipe Devillier, MD,^u Gérard Dray, PhD,^v Monica Fletcher, MSc,^w Wytske J. Fokkens, MD,^x Joao Fonseca, MD,^y Sandra N. Gonzalez-Diaz, MD,^z Lawrence Grouse, MD,^{aa} Thomas Keil, MD,^{bb} Piotr Kuna, MD,^{cc} Désirée Larenas-Linnemann, MD,^{dd} Karin C. Lodrup Carlsen, MD,^{ee} Eli O. Meltzer, MD,^{ff} Joaquim Mullol, MD,^{gg} Antonella Muraro, MD,^{hh} Robert N. Naclerio, MD,ⁱⁱ Susanna Palkonen, MD,^r Nikolaos G. Papadopoulos, MD,^{jj} Giovanni Passalacqua, MD,^k David Price, MD,^{kk} Dermot Ryan, MD,^{ll} Boleslaw Samolinski, MD,^{mmm} Glenis K. Scadding, MD,ⁿⁿ Aziz Sheikh, MD,^{oo} François Spertini, MD,^{pp} Arunas Valiulis, MD,^{qq} Erka Valovirta, MD,^{rr} Samantha Walker, PhD,^{ss} Magnus Wickman, MD,^{tt} Arzu Yorgancioglu, MD,^{uu} Tari Haahtela, MD,^{vv} and Torsten Zuberbier, MD,^h on behalf of the MASK study group* *Montpellier, Paris, St-Quentin-en-Yvelines, and Alès, France; Hamilton, Ontario, Canada; Leuven, Ghent, and Brussels, Belgium; Berlin and Wuerzburg, Germany; Glebe, Australia; London, Cambridge, Warwick, Manchester, Aberdeen, and Edinburgh, United Kingdom; Genoa and Padua, Italy; Tampa and Davie, Fla; Bahia, Brazil; Leiden and Amsterdam, The Netherlands; Odense, Denmark; Porto, Portugal; Nuevo León and Mexico City, Mexico; Seattle, Wash; Lodz and Warsaw, Poland; Oslo, Norway; San Diego, Calif; Barcelona, Spain; Chicago, Ill; Athens, Greece; Vilnius, Lithuania; Turku, Finland; Stockholm, Sweden; Manisa, Turkey; and Lausanne, Switzerland*

The selection of pharmacotherapy for patients with allergic rhinitis (AR) depends on several factors, including age, prominent symptoms, symptom severity, control of AR, patient preferences, and cost. Allergen exposure and the resulting symptoms vary, and treatment adjustment is required. Clinical

decision support systems (CDSSs) might be beneficial for the assessment of disease control. CDSSs should be based on the best evidence and algorithms to aid patients and health care professionals to jointly determine treatment and its step-up or step-down strategy depending on AR control. Contre les

From ^aUniversity Hospital, Montpellier; ^bMACVIA-LR, Contre les Maladies Chroniques pour un Vieillessement Actif en Languedoc-Roussillon, European Innovation Partnership on Active and Healthy Ageing Reference Site, Montpellier; ^cINSERM, VIMA: Ageing and Chronic Diseases, Epidemiological and Public Health approaches, Paris, and Université Versailles St-Quentin-en-Yvelines; ^dthe Departments of Clinical Epidemiology and Biostatistics and Medicine, McMaster University, Hamilton; ^ethe Laboratory of Clinical Immunology, Department of Microbiology and Immunology, KU Leuven; ^fKyomed, Montpellier; ^gthe Upper Airways Research Laboratory, ENT Department, Ghent University Hospital; ^hAllergy-Centre-Charité at the Department of Dermatology, Charité–Universitätsmedizin Berlin, and Secretary General of the Global Allergy and Asthma European Network (GA²LEN); ⁱthe Woolcock Institute of Medical Research, University of Sydney and Sydney Local Health District, Glebe; ^jImperial College London–National Heart and Lung Institute, Royal Brompton Hospital NHS, London; ^kthe Allergy and Respiratory Diseases Clinic, DIMI, University of Genoa, IRCCS AOU San Martino-IST, Genoa; ^lthe Division of Allergy/Immunology, University of South Florida, Tampa; ^mthe Department of Public Health and Primary Care, Leiden University Medical Center; ⁿthe Department of Medicine, Nova Southeastern University, Davie; ^oRiRL, Cambridge; ^pProAR–Núcleo de Excelencia em Asma, Federal University of Bahia, and GARD Executive Committee; ^qthe Department of Dermatology and Allergy Centre, Odense University Hospital, Odense; ^rEFA European Federation of Allergy and Airways Diseases Patients’ Associations, Brussels; ^sEPAR U707 INSERM, Paris and EPAR UMR-S UPMC, Paris VI, Paris; ^tthe Department of Respiratory Diseases, Montpellier University Hospital; ^uLaboratoire de Pharmacologie Respiratoire UPRES EA220, Hôpital Foch, Suresnes Université Versailles Saint-Quentin; ^vEcole des Mines, Alès; ^wEducation for Health, Warwick; ^xthe Department of Otorhinolaryngology, Academic Medical Centre, Amsterdam; ^ythe Center for Research in Health Technologies and Information Systems–CINTESIS, Universidade do Porto; the Allergy Unit, Instituto CUF Porto e Hospital CUF Porto; the Health Information and Decision Sciences Department–CIDES, Faculdade de Medicina, Universidade do Porto; Faculdade de Medicina da Universidade do Porto, Porto; ^zUniversidad Autónoma de Nuevo León; ^{aa}the

University of Washington School of Medicine, Faculty of the Department of Neurology, Seattle; ^{bb}the Institute of Social Medicine, Epidemiology and Health Economics, Charité–Universitätsmedizin Berlin, and the Institute for Clinical Epidemiology and Biometry, University of Wuerzburg; ^{cc}the Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz; ^{dd}Clínica de Alergia, Asma y Pediatría, Hospital Médica Sur, Mexico City; ^{ee}the Department of Paediatrics, Oslo University Hospital, Oslo, and the Faculty of Medicine, Institute of Clinical Medicine, University of Oslo; ^{ff}the Allergy and Asthma Medical Group and Research Center, San Diego; ^{gg}Unitat de Rinologia i Clínica de l’Olfacte, Servei d’ORL, Hospital Clínic, Clinical & Experimental Respiratory Immunology, IDIBAPS, Barcelona; ^{hh}Food Allergy Referral Centre Veneto Region, Department of Women and Child Health, Padua General University Hospital; ⁱⁱthe Section of Otolaryngology-Head and Neck Surgery, University of Chicago Medical Center and Pritzker School of Medicine, University of Chicago; ^{jj}the Center for Pediatrics and Child Health, Institute of Human Development, Royal Manchester Children’s Hospital, University of Manchester, and the Allergy Department, 2nd Pediatric Clinic, Athens General Children’s Hospital “P&A Kyriakou,” University of Athens; ^{kk}the Academic Centre of Primary Care, University of Aberdeen, and Research in Real-Life, Cambridge; ^{ll}Honorary Clinical Research Fellow, Allergy and Respiratory Research Group, University of Edinburgh; ^{mm}the Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw; ⁿⁿRoyal National TNE Hospital, University College London; ^{oo}the Allergy and Respiratory Research Group, Centre for Population Health Sciences, University of Edinburgh; ^{pp}Service d’Immunologie et Allergie, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne; ^{qq}Vilnius University Clinic of Children’s Diseases, Vilnius; ^{rr}the Department of Lung Diseases and Clinical Allergology, University of Turku; ^{ss}Asthma UK, London; ^{tt}“Sachs’ Children’s Hospital, Stockholm, and the Institute of Environmental Medicine, Karolinska Institutet, Stockholm; ^{uu}the Department of Pulmonology, Celal Bayar University Manisa, Turkey, and GARD Executive Committee; and ^{vv}Skin and Allergy Hospital, Helsinki University Hospital, Helsinki.

Maladies Chroniques pour un Vieillessement Actif en Languedoc-Roussillon (MACVIA-LR [fighting chronic diseases for active and healthy ageing]), one of the reference sites of the European Innovation Partnership on Active and Healthy Ageing, has initiated an allergy sentinel network (the MACVIA-ARIA Sentinel Network). A CDSS is currently being developed to optimize AR control. An algorithm developed by consensus is presented in this article. This algorithm should be confirmed by appropriate trials. (J Allergy Clin Immunol 2016;138:367-74.)

Key words: Allergic rhinitis, conjunctivitis, Allergic Rhinitis and its Impact on Asthma, MACVIA-LR, information and communication technology, clinical decision support system

The selection of pharmacotherapy for patients with allergic rhinitis (AR) depends on several factors, such as age, prominent symptoms, symptom severity, control of AR, patient preferences, availability of treatment, and cost.¹ With allergen exposure and the resulting symptoms varying daily, patients with AR would

Working group members:* Werner Aberer, MD; Mitsuru Adachi, MD; Ioana Agache, MD; Cezmi Akdis, MD; Mubeccel Akdis, MD; Isabella Annesi-Maesano, MD; Ignacio J. Ansotegui, MD; Josep M. Anto, MD; S. Hasan Arshad, MD; Ilaria Baiardini, MD; Abay K. Baigenzhin, MD; Cristina Barbara, MD; Eric D. Bateman, MD; Bianca Beghé, MD; Elisabeth H. Bel, MD; Ali Ben Kheder, MD; Kazi S. Bennoor, MD; Michael Benson, MD; David Bernstein, MD; Bewick Michael, MD; Bieber Thomas, MD; Carsten Bindslev-Jensen, MD; Leif Bjermer, MD; Hubert Blain, MD; Attilio Boner, MD; Matteo Bonini, MD; Sergio Bonini, MD; Isabelle Bosse, MD; Jacques Bouchard, MD; Louis-Philippe Boulet, MD; Rodolphe A. Bourret, PhD; Philippe J. Bousquet, MD; Fulvio Braido, MD; Andrew H. Briggs, PhD; Christopher E. Brightling, MD; Roland Buhl, MD; Peter Burney, MD; Andrew Bush, MD; Fernando Caballero-Fonseca, MD; Davide P. Caimmi, MD; Paulo Camargos, MD; Thierry Camuzat; Kai-Hakon Carlsen, MD; Warner Carr, MD; Thomas B. Casale, MD; Alfonso Cepeda Sarabia, MD; Leda Chatzi, PhD; Yuzhi Chen, MD; Raphaël Chiron, MD; Ekaterine Chkhartishvili, MD; Alexander Yuchalin, MD; Georgio Ciprandi, MD; Ieva Cirule; Jaime Correia de Sousa, MD; David Costa, MD; George Crooks, MD; Adnan Custovic, MD; Sven-Erik Dahlén, MD; Ulf Darsow, MD; Frédéric De Blay, MD; Esteban De Manuel Keenoy, MD; Tony Dedeu, MD; Diana Deleanu, MD; Judah Denburg, MD; Alain Didier, MD; Anh-Tuan Dinh-Xuan, MD; Dejan Dokic, MD; Habib B. Douagui, MD; Ruta Dubakiene, MD; Stephen Durham, MD; Mark Dykewicz, MD; Yehia El-Gamal, MD; Regina Emuzyte, MD; Antje Fink-Wagner, PhD; Alessandro Fiocchi, MD; Francesco Forastiere, MD; Amiran Gamkrelidze, MD; Bilun Gencioğlu, MD; Jose E. Gereda, MD; Roy Gerth van Wijk, MD; Maia Gotua, MD; Ineta Grisle, MD; M. Antonieta Guzmán, MD; Tari Hahtela, MD; Joachim Heinrich, PhD; Birthe Hellquist-Dahl, PhD; Friedrich Horak, MD; Peter H. Howarth, MD; Marc Humbert, MD; Michael Hyland, PhD; Juan-Carlos Ivancevich, MD; Edgardo J. Jares, MD; Sebastian L. Johnston, MD; Olivier Jonquet, MD; Guy Joos, MD; Ki-Suck Jung, MD; Jocelyne Just, MD; Marek Jutel, MD; Igor P. Kaidashev, MD; Musa Khaibov, MD; Omer Kalayci, MD; Fuat Kalyoncu, MD; Paul Keith, MD; Nikolai Khaltaev, MD; Jorg Kleine-Tebbe, MD; Ludger Klimek, MD; Bernard Koffi N'Goran, MD; Vitezlav Kolek, MD; Gerard H. Koppelman, MD; Marek Kowalski, MD; Inger Kull, PhD; Violeta Kvedariene, MD; Bart Lambrecht, MD; Susanne Lau, MD; Daniel Laune, PhD; Lan Le Thi Tuyet, MD; Jing Li, MD; Phillipe Lieberman, MD; Brian J. Lipworth, MD; Louis Renaud, MD; Yves Magard, MD; Antoine Magnan, MD; Bassam Mahboub, MD; Ivan Majer, MD; Mika Makela, MD; Peter J. Manning, MD; Mohamad R. Masjedi, MD; Marcus Maurer, MD; Sandra Mavale-Manuel, MD; Erik Melén, MD; Elisabete Melo-Gomes, MD; Jacques Mercier, MD; Hans Merk, MD; Neven Micolinic, MD; Florin Mihaltan, MD; Branslava Milenkovic, MD; Yousser Mohammad, MD; Mathieu Molimard, MD; Isabelle Momas, PhD; Anna Montilla-Santana, MD; Mario Morais-Almeida, MD; Ralph Mösges, MD; Rachel Naddif, PhD; Leyla Namazova-Baranova, MD; Hugo Neffen, MD; Kristof Nekam, MD; Angelos Neou, MD; Bodo Niggemann, MD; Dieudonné Nyembue, MD; Robyn O'Hehir, MD; Ken Ohta, MD; Yoshitaka Okamoto, MD; Kim Okubo, MD; Solange Ouedraogo, MD; Pier-Luigi Paggiaro, MD; Isabella Pali-Schöll, MD; Stephen Palmer, MSc; Petr Panzner, MD; Alberto Papi, MD; Hae-Sim Park, MD; Ian Pavord, MD; Ruby Pawankar, MD; Oliver Pfaar, MD; Robert Picard, PhD; Bernard Pigearias, MD; Isabelle Pin, MD; Davor Plavec, MD; Wolfgang Pohl, MD; Todor Popov, MD; Dirkje S. Postma, MD; Paul Potter, MD; Lars K. Poulsen, PhD; Klaus F. Rabe, MD; Filip Raciborski, PhD; Françoise Radier Pontal, MD; Sakari Reitamo, MD; Maria-Susana Repka-Ramirez, MD; Carlos Robalo-Cordeiro, MD; Graham Roberts, MD; Francisco Rodenas,

Abbreviations used

AR: Allergic rhinitis
CDSS: Clinical decision support system
MACVIA-LR: Contre les MALadies Chroniques pour un Vieillessement Actif en Languedoc-Roussillon
MASK: MACVIA-ARIA Sentinel Network
MCID: Minimal clinically important difference
QOL: Quality of life
RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire
VAS: Visual analog scale

benefit from regular monitoring of their symptoms to facilitate treatment adjustment. Clinical decision support systems (CDSSs) might be beneficial for the accomplishment of this task by assessing disease control, such as in response to treatment.² A CDSS is a health information technology system designed to assist health care professionals and patients with clinical decision-making

PhD; Christine Rolland, MD; Miguel Roman Rodriguez, MD; Antonino Romano, MD; José Rosado-Pinto, MD; Nelson A. Rosario, MD; Larry Rosenwasser, MD; Menachem Rottem, MD; Mario Sanchez-Borges, MD; Joaquim Sastre-Dominguez, MD; Peter Schmid-Grendelmeier, MD; Eli Serrano, MD; F. Estelle R. Simons, MD; Juan-Carlos Sisul, MD; Ingebjorg Skirind, MD; Henriette A. Smit, PhD; Dirceu Solé, MD; Talant Sooronbaev, MD; Otto Spranger; Rafael Stelmach, MD; Timo Strandberg, MD; Jordi Sunyer, MD; Carel Thijs, MD; Ana-Maria Todo-Bom, MD; Massimo Triggiani, MD; Rudolf Valenta, MD; Antonio L. Valero, MD; Marianne van Hage, MD; Olivier Vandenplas, MD; Giorgio Vezzani, MD; Pakit Vichyanond, MD; Giovanni Viegi, MD; Martin Wagenmann, MD; Ulrich Wahn, MD; Wang De Yun, MD; Denis Williams, PhD; John Wright, MD; Barbara P. Yawn, MD; Panayiotis Yiallourous, MD; Osman M. Yusuf, MD; Heather J. Zar, MD; Mario Zernotti, MD; Luo Zhang, MD; Nanshan Zhong, MD; Mihaela Zidarn, MD.

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tasks. Knowledge-based CDSSs consist of 3 parts: the knowledge base, an inference engine, and a mechanism to communicate.^{3,4} The knowledge base contains the rules and associations of compiled data. The inference engine combines the rules from the knowledge base with the patient's data. The communication mechanism allows the system to show the results to the user, as well as have input into the system. CDSSs should be based on the best evidence and algorithms to aid patients and health care professionals to jointly determine the treatment and its step-up or step-down strategy depending on AR control.¹ Thus CDSSs should help optimize treatment.

Contre les MALadies Chroniques pour un Vieillessement Actif en Languedoc-Roussillon (MACVIA-LR [fighting chronic diseases for active and healthy ageing], <http://macvia.cr-langue-docroussillon.fr>) is one of the reference sites of the European Innovation Partnership on Active and Healthy Ageing.⁵ It initiated the project Integrated Care Pathways for Airway diseases

(AIRWAYS ICPs)⁶ and the allergy sentinel network MACVIA-ARIA Sentinel Network (MASK).² A knowledge-based CDSS is currently being developed to optimize AR control. The communication mechanism of MASK uses interconnected tablets and cell phones.^{7,8} The proposed algorithm of the MACVIA-CDSS is presented in this article.

CONTROL OF AR AND RHINOCONJUNCTIVITIS

In asthmatic patients, the treatment strategy is based on disease control and current treatment.⁹⁻¹¹ The variability in symptom control is challenging and necessitates careful monitoring, as well as the step up/step down of individualized therapeutic regimens over time. Both long- and short-term maintenance and reliever approaches have been proposed,¹² including the combination of an inhaled corticosteroid and fast-onset long-acting β -agonist inhaler as maintenance and reliever therapy.¹³

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Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Meda, Merck, Mundipharma, Novartis, Pfizer, SkyePharma, Takeda, and Teva; has received payment for manuscript preparation from Mundipharma and Teva; has a patent with AKL Ltd; has received payment for developing educational presentations from GlaxoSmithKline and Novartis; has stock in AKL Ltd; has received travel support from Aerocrine, Boehringer Ingelheim, Mundipharma, Napp, Novartis, and Teva; has received funding for patient enrolment or completion of research from Almirall, Chiesi, Teva, and Zentiva; has served as a peer reviewer for grant committees for the Medical Research Council, Efficacy and Mechanism Evaluation Programme, and HTA; and is 80% owner of Research in Real Life, which receives unrestricted funding for investigator-initiated studies from Aerocrine, AKL Ltd, Almirall, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, Orion, Takeda, Teva, and Zentiva. D. Ryan is on the Boards for Stallergenes and Uriach; has received consultancy fees from Meda; is employed by Optimum Patient Care and University of Edinburgh; has received lecture fees from Meda, Chiesi, Teva, AstraZeneca, and Boehringer Ingelheim; has received payment for developing educational presentation from Meda; and is Chairman of the European Academy of Allergy and Clinical Immunology (EAACI) Primary Care Interest Group. A. Valiulis is a board member without financial interest of the nonprofit organizations the European Academy of Paediatrics, European Paediatric Association, European Confederation of Primary Care Paediatricians, Lithuanian Paediatric Society, and Lithuanian Paediatric Respiratory Society; has received research support from European Union Social Fund and Lithuanian Ministry of Health; has received travel support from the European Academy of Pediatrics; is Chairman of Executive Board of IPOKRaTES Lithuania Fund. E. Valovirta has received travel support from Stallergenes. M. Wickman has received research support and lecture fees from Thermo Fisher, has received consultancy fees from Thermo Fisher and Microtest DX, and has received payment for developing educational presentations from Stallergenes. T. Zuberbier has received consultancy fees from Ansell, Bayer Schering, DST, FAES, Fujisawa, HAL, Henkel, Kryolan, Leti, Menarini, Merck, MSD, Novartis, Procter & Gamble, Ranbaxy, Sanofi-Aventis, Schering Plough, Stallergenes, Takeda, and UCB; is on the German Society for Allergy and Clinical Immunology Scientific Advisory Board; is head of the European Centre for Allergy Research Foundation; is a World Health Organization Initiative Allergic Rhinitis and its Impact on Asthma committee member; is a member of the World Allergy Organization Communications Council; and is Secretary General of the Global Allergy and Asthma European Network. The rest of the authors declare that they have no relevant conflicts of interest.

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Corresponding author: Jean Bousquet, MD, CHRU Arnaud de Villeneuve, Département de Pneumologie, 371 Avenue du Doyen Gaston, Giraud, 34295 Montpellier Cedex 5, France. E-mail: jean.bousquet@orange.fr.

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Box 1. Summary of recommendations for the treatment of AR and conjunctivitis used in the algorithm

- Oral or intranasal H₁-antihistamines are less effective than intranasal corticosteroids for the control of all rhinitis symptoms.²⁸⁻³³
- Leukotriene receptor antagonists are usually considered less effective than oral H₁-antihistamines.^{30,34,35}
- Comparisons between oral and intranasal H₁-antihistamines differ between recommendations, and thus no definite conclusions have yet been reached.
- Combined intranasal fluticasone propionate and azelastine hydrochloride in a single device is more effective than monotherapy and is indicated for patients when monotherapy with either an intranasal H₁-antihistamine or glucocorticoid is considered inadequate.^{1,34-37}
- Intranasal antihistamines and intranasal corticosteroids are effective for ocular symptoms, with no significant difference between them.^{38,39} However, the combination of azelastine and fluticasone propionate was more effective than fluticasone propionate alone.^{36,37}
- In most studies, combinations of oral antihistamines or leukotriene receptor antagonists and intranasal corticosteroids are in general not more effective than monotherapy with intranasal corticosteroids.^{40,41}
- Intraocular H₁-antihistamines or cromones are effective for ocular symptoms.⁴² The importance of decongestants is debatable.³⁰ However, the efficacy of treatment varies with individual patient response.
- In clinical practice, intranasal corticosteroids need a few days to be fully effective, whereas intranasal H₁-antihistamines or combined intranasal fluticasone and azelastine are rapidly effective.⁴³
- All recommended medications are considered safe at the usual dosage. First-generation oral H₁-antihistamines are sedating and should be avoided.⁴⁴
- Oral or nebulized corticosteroids can be helpful in patients with severe disease whose symptoms are uncontrolled by other treatment, although studies are lacking in patients with AR.⁴⁵
- Further studies are needed in preschool children to make more firm recommendations possible, although recent studies show the efficacy of oral H₁-antihistamines.⁴⁶

The symptoms of AR can cause considerable morbidity in physical and emotional comfort, as well as in functional capacity and quality of life (QOL). The control and severity of AR have been defined in a similar manner to asthma.^{2,14,15} Measures of AR control include symptom scores, patients' self-administered visual analog scales (VASs), objective measures of nasal obstruction, a recent modification of the Allergic Rhinitis and its Impact on Asthma severity classification, and patients' reported outcomes, such as QOL or scores with several items.^{16,17} However, the challenges of managing AR are increased by the fact that patients do not often recognize their AR symptoms or confuse them with those of asthma.¹⁸ Therefore it is important for patients to be able to use an AR symptom scoring system that is simple to use and rapidly responsive to change.

As is the case for asthma, the best control of AR should be achieved as early as possible to (1) improve patient satisfaction and concordance to treatment and (2) reduce the consequences of AR, including symptoms, reduced QOL, and school and work absenteeism. Untreated AR can impair driving ability and put patients at risk.¹⁹ The ultimate goal of AR control is to reduce the costs incurred by AR.²⁰⁻²³

A step-up/step-down approach to AR pharmacotherapy based on patient response might hold potential for optimal AR control and cost of treatment.¹ MASK has proposed that electronic daily monitoring with VASs might help patients achieve optimal control of AR symptoms.² Well-controlled AR is defined as a VAS score of 2 or less of 10. VAS cutoff values to step up or down treatment were proposed by comparison with pain VAS scores and step-up schemes or from the literature in the field of allergy (see the [additional material](#) in this article's Online Repository at www.jacionline.org).²⁴⁻²⁶

RECOMMENDATIONS FOR THE TREATMENT OF AR AND RHINOCONJUNCTIVITIS

The treatment of AR also requires the consideration of (1) the type (rhinitis, conjunctivitis, and/or asthma) and severity of

symptoms, (2) the relative efficacy of the treatment, (3) the speed of onset of action of treatment, (4) current treatment, (5) historic response to treatment, (6) patient's preference, (7) interest to self-manage, and (8) resource use. Guidelines²⁷ and various statements by experts for AR pharmacotherapy usually propose the approach summarized in [Box 1](#).²⁸⁻⁴⁶

Allergen immunotherapy appears to be as effective as pharmacotherapy^{47,48} but is also regarded as a disease modifier intervention with the potential of altering the natural history of allergic diseases.^{49,50} Nonpharmacologic interventions, such as nasal filters⁵¹ or saline, have been found to be effective.

PATIENTS' VIEWS

Many patients with AR are not satisfied with their current treatment,⁵²⁻⁵⁴ and this results in frequent nonadherence to therapy.^{55,56} In some studies, most patients were satisfied with their treatment, but full control was rarely achieved.^{54,57-59} Despite the vast availability of treatment options, most patients are "very interested" in finding a new medication,^{56,60} and around 25% are "constantly" trying different medications to find one that "works."⁵⁶ Patients want more effective treatments that can control all their symptoms, including ocular ones,^{61,62} and a more rapid onset of action.⁶³

Some patients believe that their health care provider does not understand their allergy treatment needs or does not take their allergy symptoms seriously.⁵² Many patients self-medicate with over-the-counter drugs for a long period of time and usually only consult a physician when their treatment is ineffective.⁵⁸ In one study, patients chose a step-down therapy to speed up the control of symptoms.⁶⁴

A patient's individual preference for an oral or intranasal route treatment needs to be considered.^{52,64,65} In addition, health care professionals need to inform the patient of the relative benefits and harms of each prescribed treatment to support their decision making.

Assessment of control in untreated symptomatic patient

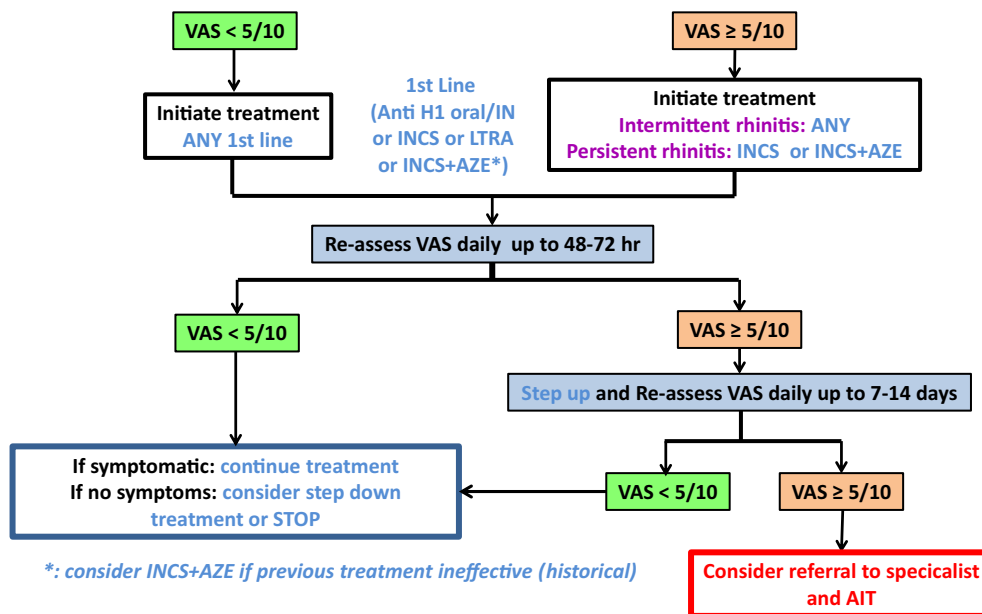


FIG 1. Step-up algorithm in untreated patients using the VAS (adolescents and adults). The proposed algorithm considers the treatment steps and patient preference and VAS levels in ratio. If ocular symptoms remain, add intraocular treatment.

ALGORITHM DECISION AID

A step-up/step-down individualized approach to AR pharmacotherapy might hold the potential for optimal control of AR symptoms while minimizing side effects and costs.¹ However, the following should be considered:

- as in asthmatic patients, treated and untreated patients should be considered differently (Figs 1 and 2);
- most patients have received a previous treatment that should guide health care professionals with regard to the current prescription; and
- patterns of medication use in previously treated patients should be evaluated when future treatment is initiated.

The step-up or step-down strategy should be discussed with the patient and should consider the following:

- efficacy of previous treatments;
- adherence to treatment;
- the patient's preference (route of administration, fear of side effects, and experience of the patient regarding the treatment);
- possible side effects or harms; and
- costs.

The step-up approach consists of the following:

- *Step 1:* For mild symptoms, use intranasal or oral nonsedating H₁-antihistamines.
- *Step 2:* For moderate-to-severe symptoms and/or persistent AR, use intranasal corticosteroids. The dose of some intranasal corticosteroids can be increased according to the package insert.
- *Step 3:* For patients with uncontrolled symptoms at step 2 (current or historical), use a combination of intranasal

corticosteroids and intranasal H₁-antihistamines. However, depending on the physicians's experience, other therapeutic strategies can be used.

- *Step 4:* It is possible that an additional short course of oral steroids might help to establish control and continue control by step 3. Intraocular cromones or H₁-antihistamines can be added to improve the control of ocular symptoms.
- Treatment should be reassessed quickly (eg, 1-7 days) to confirm control by using a step-up approach.
- Patients whose symptoms are uncontrolled at step 3 should be considered as having severe chronic upper airway disease^{66,67} and might benefit from specialist referral and assessment for allergy workup and nasal examination.⁶⁸ For example, specialist referral should be considered if there is failure to reduce the VAS score to less than 5 of 10 after 10 to 14 days, assuming the patient is adherent to therapy.
- At all times, patient adherence and intranasal device technique mastery should be regarded as potential for lack of treatment effect.

Alternatively, a step-down approach can be used, and step 3 treatment should be considered as the first option in patients with a previous treatment failure or resistance to monotherapy. After a few days of achieving complete control, consideration could be given to treatment reduction. However, the step-down approach is based on consensus, and more data are needed.

The duration of treatment is determined by the type of rhinitis (intermittent or persistent). In the patient with intermittent rhinitis, treatment should be continued daily for 2 weeks or for the duration of the pollen season or other specific allergen exposure. In the patient with persistent rhinitis, a longer course

Assessment of control in treated symptomatic patient

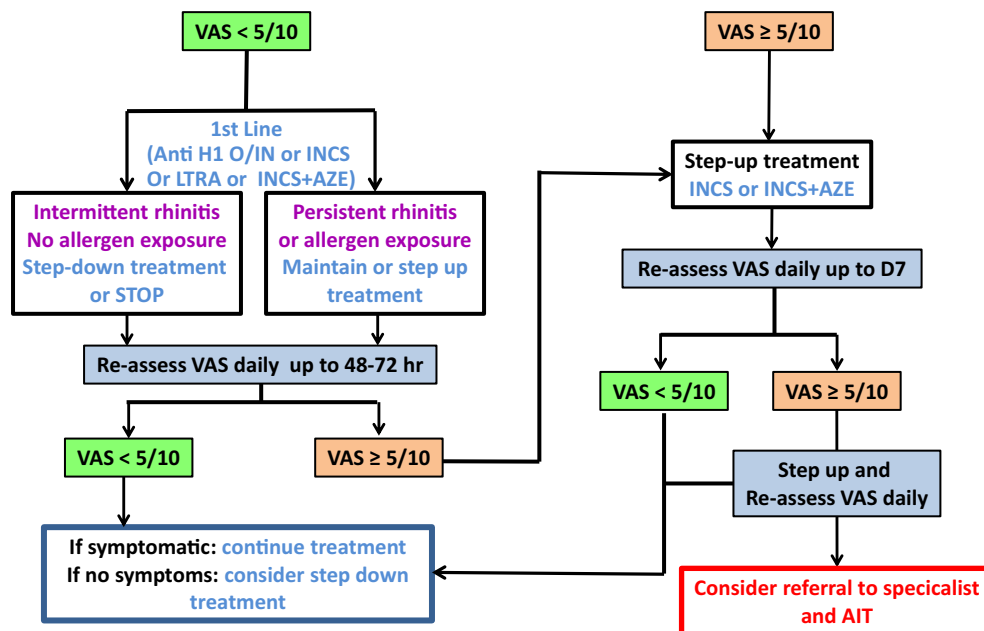


FIG 2. Step-up algorithm in treated patients using the VAS (adolescents and adults). The proposed algorithm considers the treatment steps and patient preference and VAS levels in ratio. If ocular symptoms remain, add intraocular treatment.

of treatment is often needed. Of course, it is important to assess concordance with agreed regimens because treatment failure can be a result of poor patient concordance.

CONCLUSION

We propose a simple algorithm to step up or step down AR treatment globally. However, its use varies depending on the availability of medications in different countries and depending on resources. These issues have not been approached in the present article because of their variability between countries. Inherently, algorithms are a combination of individual decision nodes that represent separate recommendations. They require testing as a complete algorithm and comparison with alternative strategies to explore whether the combination of these separate recommendations leads to more benefit than harm when applied in practice. Thus this algorithm, as with other algorithms, requires testing in large-scale trials to provide the necessary certainty in available evidence. The current algorithm is being developed by MASK² for a CDSS that will be available on Apple and Android and that will provide opportunities for evaluation.

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RATIONALE FOR USING A VAS IN THE ALGORITHM

Certain differences between groups in their VAS scores or changes in scores might have no clinical relevance, even if they achieve statistical significance. A wide range of minimal clinically important differences (MCIDs) in change scores on the pain VAS have been reported^{E1} by using different methods. MCIDs ranged from 9 to 30 mm (of 100 mm) in emergency departments.^{E2-E6} In other settings, changes of 33%^{E7} and 31 mm^{E8} have been shown to be clinically meaningful. In patients with endometriosis, the pain MCID was set at 10 mm.^{E9} The MCID for the fatigue VAS was around 10 mm in a large rheumatoid arthritis clinical practice and similar to that seen in clinical trials.^{E10} The MCID in the VAS pain score does not differ with sex, age, and cause-of-pain groups^{E3} or with the severity of pain being experienced.^{E11} However, the linearity of the pain VAS is found in some^{E12} but not all^{E1,E13,E14} studies. Pain VAS measurement error has been reported to be up to 20 mm.^{E15,E16} Consequently, change scores and the calculations of aspects, such as MCIDs, can be carefully considered by the potential lack of interval scaling of the VAS and further compromised by the magnitude of measurement error. Repeated pain VAS data meet the strict requirements of the Rasch model, including unidimensionality, and they were internally valid.^{E1} However, the pain VAS does not behave linearly, and the MCID can underestimate or overestimate true change during repeated pain VAS.

In patients with AR, to our knowledge, there is a single study that has estimated MCIDs in the VAS during treatment.^{E18} By using receiver operating characteristic curve analysis, an appropriate method for estimation of MCIDs, the established cutoff variation of 23 mm for the VAS was associated with a cutoff variation of 0.5 for the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Sensitivity analysis with RQLQ and Total Symptom Score 6 scales confirmed the aptitude of the cutoff value (23 mm) to discriminate changes in symptoms and QOL. The MCID was the same whatever the baseline VAS level.^{E18} A level of more than 23 mm appears to be a relevant cutoff. VAS changes appear to encompass both symptoms and disease-specific QOL.^{E18,E19} Another study, the Control of Allergic Rhinitis and Asthma Test,^{E20,E21} approximated the VAS MCID. In CARAT, the MCID is 4 (range, 0-30).^{E22} The real-life study of Demoly et al^{E18} in primary care used the same methods as a cluster randomized trial carried out in specialist practices.^{E23} Both studies, which were carried out in France in large populations, showed a very similar change in VAS levels during treatment depending on total symptom scores and RQLQ scores. These studies suggest that the cutoff of 23 mm^{E18} is appropriate to find a clinically significant difference.

VAS levels appear to be similar in different countries in patients with severe intermittent or persistent rhinitis. A VAS can be used in all age groups, including preschool children (guardian evaluation)^{E24} and the elderly.^{E25} Furthermore, it can be used in a wide variety of languages.^{E25-E32} VAS levels vary with the Allergic Rhinitis and its Impact on Asthma classification in many languages.^{E28,E33-E35} A VAS level of 50 (>100 mm) is suggestive of moderate-to-severe AR,^{E19,E36,E37} although in some studies the cutoff was greater than 60 mm.^{E29} AVAS was used to define severe chronic upper airway disease.^{E23} Thus the MCID found in 2 large French populations can be generalized to other countries with different languages and cultures across the lifecycle. However, future studies should refine this cutoff level.

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