



**HAL**  
open science

## 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

Jean Bousquet, Holger Schünemann, Akdis Togias, Claus Bachert, Martina Erhola, Peter Hellings, Ludger Klimek, Oliver Pfaar, Dana Wallace, Ignacio Ansotegui, et al.

### ► To cite this version:

Jean Bousquet, Holger Schünemann, Akdis Togias, Claus Bachert, Martina Erhola, et al.. 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. *Journal of Allergy and Clinical Immunology*, 2020, 145 (1), pp.70-80.e3. 10.1016/j.jaci.2019.06.049 . hal-03371318

**HAL Id: hal-03371318**

<https://hal.umontpellier.fr/hal-03371318v1>

Submitted on 7 Mar 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

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

J Bousquet MD (1, 2), HJ Schünemann MD (3), A Togias MD (4)\*, C Bachert MD (5), M Erhola MD (6), PW Hellings MD (7), L Klimek MD (8), O Pfaar MD (9), D Wallace MD (10), I Ansotegui MD (11), I Agache MD (12), A Bedbrook BSc (1), KC Bergmann MD (13), M Bewick MD (14), P Bonniaud MD (15), S Bosnic-Anticevich PhD (16), I Bossé MD (17), J Bouchard MD (18), LP Boulet MD (19), J Brozek MD (3), G Brusselle MD (20), MA Calderon MD (21), GW Canonica MD (22), L Caraballo MD (23), V Cardona MD (24), T Casale MD (25), L Cecchi MD (26), DK Chu MD (3), E Costa PhD (27), AA Cruz MD (28), W Czarlewski MD (29), G D'Amato MD (30), P Devillier MD (32), M Dykewicz MD (33), M Ebisawa MD (34), JL Fauquet MD (35), WJ Fokkens MD (36), JA Fonseca MD (37), JM Fontaine MD (38), B Gemiciglu MD (39), R Gerth van Wijk MD (40), T Haahtela MD (41), S Halken MD (42), D Ierodiakonou MD (43), T Inuma MD (44), JC Ivancevich MD (45), M Jutel MD (46), I Kaidashev MD (47), M Khaitov MD (48), O Kalayci MD (49), J Kleine Tebbe MD (97), ML Kowalski MD (50), P Kuna MD (51), V Kvedariene MD (52), S La Grutta MD (53), D Larenas-Linemann MD (54), S Lau MD (55), D Laune PhD (56), L Le MD (57), P Lieberman MD (58), KC Lodrup Carlsen MD (59), O Lourenço PhD (60), G Marien MD (61), P Carreiro-Martins MD (62), E Melén MD (63), E Menditto PhD (64), H Neffen MD (65), G Mercier MD (66), R Mosques MD (67), J Mullol MD (68), A Muraro MD (69), L Namazova MD (70), E Novellino PhD (71), R O'Hehir MD (72), Y Okamoto MD (44), K Ohta MD (98), HS Park MD (73), P Panzner MD (74), G Passalacqua MD (75), N Pham-Thi MD (76), D Price FRCGP (77), G Roberts MD (78), N Roche MD (79), C Rolland BSc (80), N Rosario MD (81), D Ryan MD (82), B Samolinski MD (83), M Sanchez-Borges MD (84), GK Scadding MD (85), MH Shamji MD (86), A Sheikh MD (87), A Todo Bom MD (88), S Toppila-Salmi MD (89), I Tsiligianni MD (43), M Valentin-Rostan MD (90), A Valiulis MD (91), E Valovirta MD (92), MT Ventura MD (93), S Walker MD (94), S Wasserman MD (95), A Yorgancioglu MD (96), T Zuberbier MD (13) and the ARIA Working Group

\*: Dr. Togias' co-authorship of this publication does not constitute endorsement by the US National Institute of Allergy and Infectious Diseases or by any other United States government agency

1. MACVIA-France, Fondation partenariale FMC VIA-LR, Montpellier, France.
2. VIMA. INSERM U 1168, VIMA : Ageing and chronic diseases Epidemiological and public health approaches, Villejuif, Université Versailles St-Quentin-en-Yvelines, UMR-S 1168, Montigny le Bretonneux, France, Euforea, Brussels, Belgium, and Charité, Universitätsmedizin Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Comprehensive Allergy Center, Department of Dermatology and Allergy, Berlin, Germany.
3. Department of Health Research Methods, Evidence, and Impact, Division of Immunology and Allergy, McMaster University, Hamilton, ON, Canada.
4. Division of Allergy, Immunology, and Transplantation (DAIT), National Institute of Allergy and Infectious Diseases, NIH, Bethesda, US.
5. Upper Airways Research Laboratory, ENT Dept, Ghent University Hospital, Ghent, Belgium.
6. National Institute for Health and Welfare, Helsinki, Finland.
7. Dept of Otorhinolaryngology, Univ Hospitals Leuven, Belgium, and Academic Medical Center, Univ of Amsterdam, The Netherlands and Euforea, Brussels, Belgium.

- 44 8. Center for Rhinology and Allergology, Wiesbaden, Germany.
- 45 9. Department of Otorhinolaryngology, Head and Neck Surgery, Section of Rhinology and Allergy, University
- 46 Hospital Marburg, Philipps-Universität Marburg, Germany.
- 47 10. Nova Southeastern University, Fort Lauderdale, Florida, USA.
- 48 11. Department of Allergy and Immunology, Hospital Quirónsalud Bizkaia, Erandio, Spain.
- 49 12. Faculty of Medicine, Transylvania University, Brasov, Romania.
- 50 13. Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu
- 51 Berlin and Berlin Institute of Health, Comprehensive Allergy-Centre, Department of Dermatology and
- 52 Allergy, member of GA<sup>2</sup>LEN, Berlin, Germany.
- 53 14. iQ4U Consultants Ltd, London, UK.
- 54 15. CHU Dijon, France.
- 55 16. Woolcock Institute of Medical Research, University of Sydney and Woolcock Emphysema Centre and
- 56 Sydney Local Health District, Glebe, NSW, Australia.
- 57 17. Allergist, La Rochelle, France.
- 58 18. Associate professor of clinical medicine, Laval's University, Quebec city, Quebec, Canada.
- 59 19. Quebec Heart and Lung Institute, Laval University, Québec City, Quebec, Canada.
- 60 20. Dept of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium.
- 61 21. Imperial College London - National Heart and Lung Institute, Royal Brompton Hospital NHS, London, UK.
- 62 22. Personalized Medicine Clinic Asthma & Allergy, Humanitas University, Humanitas Research Hospital,
- 63 Rozzano, Milan, Italy
- 64 23. Institute for Immunological Research, University of Cartagena, Campus de Zaragocilla, Edificio Biblioteca
- 65 Primer piso, Cartagena, Colombia, and Foundation for the Development of Medical and Biological Sciences
- 66 (Fundemeb), Cartagena, Colombia.
- 67 24. Allergy Section, Department of Internal Medicine, Hospital Vall 'dHebron & ARADyAL research network,
- 68 Barcelona, Spain.
- 69 25. Division of Allergy/Immunology, University of South Florida, Tampa, USA
- 70 26. SOS Allergology and Clinical Immunology, USL Toscana Centro, Prato, Italy.
- 71 27. UCIBIO, REQUIMTE, Faculty of Pharmacy, and Competence Center on Active and Healthy Ageing of
- 72 University of Porto (AgeUPNetWork), University of Porto, Portugal
- 73 28. ProAR – Nucleo de Excelencia em Asma, Federal University of Bahia, Brazil and WHO GARD Planning Group,
- 74 Brazil.
- 75 29. Medical Consulting Czarlewski, Levallois, France.
- 76 30. Division of Respiratory and Allergic Diseases, Hospital 'A Cardarelli', University of Naples Federico II, Naples,
- 77 Italy.
- 78 31. UPRES EA220, Pôle des Maladies des Voies Respiratoires, Hôpital Foch, Université Paris-Saclay, Suresnes,
- 79 France.
- 80 32. Allergy and Clinical Immunology Section, National Heart and Lung Institute, Imperial College London, United
- 81 Kingdom.
- 82 33. Section of Allergy and Immunology, Saint Louis University School of Medicine, Saint Louis, Missouri, USA.
- 83 34. Clinical Research Center for Allergy and Rheumatology, Sagami National Hospital, Sagami, Japan.
- 84 35. Unité de pneumo-allergologie de l'enfant, pôle pédiatrique Pr-Labbé, CHU de Clermont-Ferrand-Estaing,
- 85 Clermont-Ferrand, France.
- 86 36. Department of Otorhinolaryngology, Amsterdam University Medical Centres, AMC, Amsterdam, the
- 87 Netherlands.
- 88 37. CINTESIS, Center for Research in Health Technology and Information Systems, Faculdade de Medicina da
- 89 Universidade do Porto; and Medida, Lda Porto, Portugal
- 90 38. Allergist, Reims, France.
- 91 39. Department of Pulmonary Diseases, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine,
- 92 Istanbul, Turkey.
- 93 40. Department of Internal Medicine, section of Allergology, Erasmus MC, Rotterdam, the Netherlands.
- 94 41. Skin and Allergy Hospital, Helsinki University Hospital, and University of Helsinki, Helsinki, Finland.
- 95 42. Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark.
- 96 43. Department of Social Medicine, Faculty of Medicine, University of Crete and International Primary Care
- 97 Respiratory Group, Crete, Greece.
- 98 44. Dept of Otorhinolaryngology, Chiba University Hospital, Chiba, Japan.
- 99 45. Servicio de Alergia e Immunologia, Clinica Santa Isabel, Buenos Aires, Argentina.
- 100 46. Department of Clinical Immunology, Wrocław Medical University, Poland.

- 101 47. Ukrainina Medical Stomatological Academy, Poltava, Ukraine.  
102 48. National Research Center, Institute of Immunology, Federal Medicobiological Agency, Laboratory of  
103 Molecular immunology, Moscow, Russian Federation.  
104 49. Pediatric Allergy and Asthma Unit, Hacettepe University School of Medicine, Ankara, Turkey.  
105 50. Department of Immunology and Allergy, Healthy Ageing Research Center, Medical University of Lodz,  
106 Poland.  
107 51. Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz,  
108 Poland.  
109 52. Institute of Biomedical Sciences, Department of Pathology, Faculty of Medicine, Vilnius University and  
110 Institute of Clinical medicine, Clinic of Chest diseases and Allergology, faculty of Medicine, Vilnius  
111 University, Vilnius, Lithuania.  
112 53. Institute of Biomedicine and Molecular Immunology (IBIM), National Research Council (CNR), Palermo, Italy.  
113 54. Center of Excellence in Asthma and Allergy, Médica Sur Clinical Foundation and Hospital, México City,  
114 Mexico.  
115 55. Department of Paediatric Pneumology, Immunology and Intensive Care, Charité Universitätsmedizin, Berlin,  
116 Germany.  
117 56. KYomed INNOV, Montpellier, France.  
118 57. University of Medicine and Pharmacy, Hochiminh City, Vietnam.  
119 58. Departments of Internal Medicine and Pediatrics (Divisions of Allergy and Immunology), University of  
120 Tennessee College of Medicine, Germantown, TN, USA.  
121 59. Oslo University Hospital, Department of Paediatrics, Oslo, and University of Oslo, Faculty of Medicine,  
122 Institute of Clinical Medicine, Oslo, Norway.  
123 60. Faculty of Health Sciences and CICS – UBI, Health Sciences Research Centre, University of Beira Interior,  
124 Covilhã, Portugal.  
125 61. EUFOREA, BRUSSELS, Belgium.  
126 62. Hospital de Dona Estefânia, Centro Hospitalar de Lisboa Central, EPE, Lisbon, Portugal and Nova Medical  
127 School, CEDOC, Integrated Pathophysiological Mechanisms Research Group, Lisbon, Portugal.  
128 63. Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm and Institute of Environmental Medicine,  
129 Karolinska Institutet, Stockholm, Sweden.  
130 64. CIRFF, Center of Pharmacoeconomics, University of Naples Federico II, Naples, Italy.  
131 65. Director of Center of Allergy, Immunology and Respiratory Diseases, Santa Fe, Argentina Center for Allergy  
132 and Immunology, Santa Fe, Argentina.  
133 66. Unité Médico-Economie, Département de l'Information Médicale, University Hospital, Montpellier, France  
134 67. Institute of Medical Statistics, and Computational Biology, Medical Faculty, University of Cologne, Germany  
135 and CRI-Clinical Research International-Ltd, Hamburg, Germany.  
136 68. Rhinology Unit & Smell Clinic, ENT Department, Hospital Clínic; Clinical & Experimental Respiratory  
137 Immunoallergy, IDIBAPS, CIBERES, University of Barcelona, Spain.  
138 69. Food Allergy Referral Centre Veneto Region, Department of Women and Child Health, Padua General  
139 University Hospital, Padua, Italy.  
140 70. Scientific Centre of Children's Health under the MoH, Moscow, Russia  
141 Russian National Research medical University named Pirogov, Moscow, Russia.  
142 71. Director of Department of Pharmacy of University of Naples Federico II, Naples, Italy.  
143 72. Department of Allergy, Immunology and Respiratory Medicine, Alfred Hospital and Central Clinical School,  
144 Monash University, Melbourne, Victoria, Australia; Department of Immunology, Monash University,  
145 Melbourne, Victoria, Australia.  
146 73. Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, South Korea.  
147 74. Department of Immunology and Allergology, Faculty of Medicine in Pilsen, Charles University in Prague,  
148 Pilsen, Czech Republic.  
149 75. Allergy and Respiratory Diseases, Ospedale Policlinico San Martino -University of Genoa, Italy.  
150 76. Allergy department, Pasteur Institute, Paris, France.  
151 77. Observational and Pragmatic Research Institute, Singapore, Singapore.  
152 78. David Hide Centre, St Mary's Hospital, Isle of Wight and University of Southampton, Southampton, UK.  
153 79. Pneumologie et Soins Intensifs Respiratoires, Hôpitaux Universitaires Paris, Centre  
154 Hôpital Cochin, France.  
155 80. Association Asthme et Allergie, Paris, France.  
156 81. Hospital de Clinicas, University of Parana, Brazil.

- 157 82. Honorary Clinical Research Fellow, Allergy and Respiratory Research Group, The University of Edinburgh,  
158 Edinburgh, UK  
159 83. Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw,  
160 Poland.  
161 84. Allergy and Clinical Immunology Department, Centro Medico-Docente La Trinidad, Caracas, Venezuela.  
162 85. The Royal National TNE Hospital, University College London, UK.  
163 86. Immunomodulation and Tolerance Group, Imperial College London, and Allergy and Clinical Immunology,  
164 Imperial College London, London, UK.  
165 87. The Usher Institute of Population Health Sciences and Informatics, The University of Edinburgh, Edinburgh,  
166 UK.  
167 88. Imunoalergologia, Centro Hospitalar Universitário de Coimbra and Faculty of Medicine, University of  
168 Coimbra, Portugal.  
169 89. Skin and Allergy Hospital, Helsinki University Hospital and University of Helsinki, Helsinki, Finland.  
170 90. Allergist, Montevideo, Uruguay.  
171 91. Vilnius University Institute of Clinical Medicine, Clinic of Children's Diseases, and Institute of Health  
172 Sciences, Department of Public Health, Vilnius, Lithuania; European Academy of Paediatrics (EAP/UEMS-SP),  
173 Brussels, Belgium.  
174 92. Department of Lung Diseases and Clinical Immunology, University of Turku and Terveystalo allergy clinic,  
175 Turku, Finland.  
176 93. University of Bari Medical School, Unit of Geriatric Immunoallergology, Bari, Italy.  
177 94. Asthma UK, Mansell street, London, UK.  
178 95. Department of Medicine, Clinical Immunology and Allergy, McMaster University, Hamilton, Ontario,  
179 Canada.  
180 96. Department of Pulmonary Diseases, Celal Bayar University, Faculty of Medicine, Manisa, Turkey  
181 97. Allergy & Asthma Center Westend, Outpatient & Clinical Research Center, Berlin, Germany.  
182 98. National Hospital Organization, Tokyo National Hospital, Tokyo, Japan  
183  
184

185 **Short title: Next-generation 2019 ARIA guidelines**

186

187 **Author for correspondence**

188 Professor Jean Bousquet  
189 CHU Arnaud de Villeneuve, 371 Avenue du Doyen Gaston Giraud, 34295 Montpellier Cedex 5,  
190 France Tel +33 611 42 88 47, Fax :+33 467 41 67 01 [jean.bousquet@orange.fr](mailto:jean.bousquet@orange.fr)

191

192 **Conflicts of interest:**

193

194 *Dr. Ansotegui reports personal fees from Mundipharma, Roxall, Sanofi, MSD, Faes Farma, Hikma, UCB, Astra Zeneca, outside*  
195 *the submitted work.*

196 *Dr Bousquet reports personal fees and other from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Sanofi-*  
197 *Aventis, Takeda, Teva, Uriach, other from KYomed INNOV, outside the submitted work.*

198 *Dr Bachert reports fees from ALK, Mylan, Stallergenes, Novartis, Sanofi, GSK, Astra-Zeneca, outside the submitted work.*

199 *Dr. Bosnic Anticevich reports grants from TEVA, personal fees from TEVA, AstraZeneca, Boehringer Ingelheim, GSK, Sanofi,*  
200 *Mylan, outside the submitted work.*

201 *Dr. Boulet reports Research grants for participation to multicentre studies AIM Therapeutics, Amgen, Asmacure, AstraZeneca,*  
202 *Axikin, GlaxoSmithKline, Hoffman La Roche, Novartis, Ono Pharma, Sanofi, Takeda. Support for research projects introduced*  
203 *by the investigator AstraZeneca, Boehringer-Ingelheim, GlaxoSmithKline, Merck, Takeda. Consulting and advisory boards*  
204 *Astra Zeneca, Novartis, Methapharm. Royalties Co-author of "Up-To-Date" (occupational asthma). Nonprofit grants for*  
205 *production of educational materials AstraZeneca, Boehringer-Ingelheim, GlaxoSmithKline, Merck Frosst, Novartis. Conference*  
206 *fees AstraZeneca, GlaxoSmithKline, Merck, Novartis. Support for participation in conferences and meetings Novartis, Takeda.*  
207 *Past president and Member of the Canadian Thoracic Society Respiratory Guidelines Committee; Chair of the Board of*  
208 *Directors of the Global Initiative for Asthma (GINA). Chair of Global Initiative for Asthma (GINA) Guidelines Dissemination and*

209 *Implementation Committee;Laval University Chair on Knowledge Transfer, Prevention and Education in Respiratory and*  
210 *Cardiovascular Health; Member of scientific committees for the American College of Chest Physicians, American Thoracic*  
211 *Society, European Respiratory Society and the World Allergy Organization;1st Vice-President of the Global Asthma*  
212 *Organization «InterAsma», outside the submitted work.*  
213 *Dr. Calderon reports personal fees (advisory and/or lecture honorarium) from ALK-Abello, ALK-US, Stallergenes Greer, HAL-*  
214 *Allergy, Allergopharma, ASIT-Biotech, outside the submitted work .*  
215 *Dr. Cecchi reports personal fees from Menarini, Malesci, personal fees and non-financial support from ALK, outside the*  
216 *submitted work.*  
217 *Dr Devillier reports fees from Boehringer Ingelheim, AstraZeneca, Stallergenes Greer, ALK, Novartis, GSK, Chiesi, Menarini,*  
218 *Unither, IQVIA, Yslab, Top Pharm, outside the submitted work.*  
219 *Dr. Haahtela reports lecturing fees from Mundipharma and Orion Pharma, during the conduct of the study.*  
220 *Dr. Halken reports other from ALK-Abelló, outside the submitted work.*  
221 *Dr. Hellings reports grants and personal fees from Mylan, during the conduct of the study; personal fees from Sanofi, personal*  
222 *fees from Allergopharma, personal fees from Stallergenes, outside the submitted work.*  
223 *Dr. Ivancevich reports personal fees from Faes Farma, Eurofarma Argentina, other from Laboratorios Casasco, personal fees*  
224 *and other from Sanofi, outside the submitted work.*  
225 *Dr. Kleine-Tebbe reports personal fees from AllergenOnline (Nebraska, USA), Allergy Therapeutics, Allergopharma, Bencard,*  
226 *HAL Allergy, Dr. Pflieger, Lofarma , Merck US, AstraZeneca, Sanofi Genentech, Stallergenes-Greer, Thieme Publishers,*  
227 *ThermoFisher Scientific, Springer International Publishers, InfectoPharm, LETI, GSK, grants and personal fees from ALK-Abelló,*  
228 *Novartis, non-financial support from WHO/IUIS Allergen nomenclature subcomm, outside the submitted work.*  
229 *Dr. Lau reports personal fees from DBV, personal fees from Allergopharma, grants and personal fees from ALK, personal fees*  
230 *from Sanofi-Genzyme, outside the submitted work.*  
231 *Dr. Mösges reports personal fees from ALK, allergopharma, Allergy Therapeutics, Friulchem, Hexal, Servier, FAES, Klosterfrau,*  
232 *Bayer, GSK, Johnson&Johnson, Meda, Stada, UCB, Nuvo, Menarini Mundipharma, Pohl-Boskamp, from Hikma; grants and*  
233 *personal fees from Bencard, Stallergenes; grants from Leti, Optima, BitopAG, Hulka, Ursapharm; personal fees and non-*  
234 *financial support from Lofarma, Novartis; non-financial support from Roxall, Atmos, Bionorica, Otonomy, Ferrero,*  
235 *outside the submitted work.*  
236 *Dr. Okamoto reports personal fees from Shionogi Co., Ltd., Torii Co., Ltd., GSK, MSD, grants and personal fees from Kyorin Co.,*  
237 *Ltd., Kyowa Co., Ltd., Eizai Co., Ltd., grants and personal fees from Tiho Co., Ltd., grants from Yakuruto Co., Ltd., Yamada Bee*  
238 *Farm, personal fees from outside the submitted work. grants from ASIT biotech,*  
239 *Dr. Price reports grants from AKL Research and Development Ltd, British Lung Foundation, UK National Health Service*  
240 *personal fees from Amgen, Cipla, GlaxoSmithKline, Kyorin, Merck, grants and personal fees from AstraZeneca, Boehringer*  
241 *Ingelheim, Chiesi, Circassia, Mylan, Mundipharma, Napp, Novartis, Pfizer, Regeneron Pharmaceuticals, Respiratory*  
242 *Effectiveness Group, Sanofi Genzyme, Teva, Theravance, Zentiva (Sanofi Generics), non-financial support from Efficacy and*  
243 *Mechanism Evaluation programme, Health Technology Assessment, outside the submitted work; and stock/stock options*  
244 *from AKL Research and Development Ltd which produces phytopharmaceuticals; and owns 74% of the social enterprise*  
245 *Optimum Patient Care Ltd (Australia and UK) and 74% of Observational and Pragmatic Research Institute Pte Ltd (Singapore).*  
246 *Dr. Shamji reports grants from ALK, Regeneron, Merck, Immune Tolerance Network, personal fees from ASIT Biotech. sa, ASIT*  
247 *Biotech. Sa, Allergopharma, grants and personal fees from ALKoutside the submitted work.*  
248 *Dr. Todo-Bom reports grants and personal fees from Novartis, Mundipharma, GSK (GlaxoSmithKline), Teva Pharma, personal*  
249 *fees from AstraZeneca, grants from Boehringer Ingelheim, Sanofi, Leti, outside the submitted work.*  
250 *Dr. Tsiligianni reports personal fees from Honoraria for educational activities, speaking engagements, advisory boards from*  
251 *Boehringer Ingelheim and Novartis and a grant from GSK., outside the submitted work;*  
252 *Dr. Wallace reports and Indicates that she is the co-chair of the Joint Task Force on Practice Parameters, a task force*  
253 *composed of 12 members of the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy,*  
254 *Asthma, and Immunology.*  
255 *Dr. Wasserman reports other from CSL Behring, Shire, AstraZeneca, Teva, Meda, Merck, GSK, Novartis, Pediapharm, Aralez,*  
256 *Sanofi, Stallergenes, outside the submitted work.*  
257 *Dr Zuberbier reports Organizational affiliations: Commitee member: WHO-Initiative "Allergic Rhinitis and Its Impact on*  
258 *Asthma" (ARIA), Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI)*  
259 *Head: European Centre for Allergy Research Foundation (ECARF), Secretary General: Global Allergy and Asthma European*  
260 *Network (GA<sup>2</sup>LEN), Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO).*  
261 *The other authors have no COI to declare.*  
262  
263  
264  
265

## 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

299

## 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).

<p>380 <b>The Ontario Chamber studies show the rapid onset of efficacy for Azelastine and its combinations. There does</b> 381 <b>not seem to be a difference between Azelastine alone or in combination. Other intranasal H<sub>1</sub>-antihistamines</b> 382 <b>have a slower onset of action. INCS (alone or with oral H<sub>1</sub>-antihistamines) are not effective before 2 hrs.</b></p> <p>383 <b>The Vienna chamber studies show that Azelastine and Levocabastine/FF are the fastest-acting medications</b> 384 <b>by comparison with oral H<sub>1</sub>-antihistamines.</b></p>
---

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 H<sub>1</sub>-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 H<sub>1</sub>-antihistamines with INCS was not found more effective than INCS  
476 alone
- 477 • The combination of intra-nasal H<sub>1</sub>-antihistamines with INCS was found more effective than INCS  
478 alone and
- 479 • Intra-nasal H<sub>1</sub>-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

492 **References**

493

- 494 1. Meltzer EO, Wallace D, Dykewicz M, Shneyer L. Minimal Clinically Important  
495 Difference (MCID) in Allergic Rhinitis: Agency for Healthcare Research and Quality or Anchor-  
496 Based Thresholds? *J Allergy Clin Immunol Pract.* 2016;4(4):682-8 e6.
- 497 2. Munoz-Cano R, Ribo P, Araujo G, Giralte E, Sanchez-Lopez J, Valero A. Severity of  
498 allergic rhinitis impacts sleep and anxiety: results from a large Spanish cohort. *Clin Transl*  
499 *Allergy.* 2018;8:23.
- 500 3. Vandenplas O, Vinnikov D, Blanc PD, Agache I, Bachert C, Bewick M, et al. Impact of  
501 Rhinitis on Work Productivity: A Systematic Review. *J Allergy Clin Immunol Pract.*  
502 2018;6(4):1274-86 e9.
- 503 4. Meltzer EO. Pharmacotherapeutic strategies for allergic rhinitis: matching treatment  
504 to symptoms, disease progression, and associated conditions. *Allergy Asthma Proc.*  
505 2013;34(4):301-11.
- 506 5. Bousquet J, Schunemann HJ, Hellings PW, Arnavielhe S, Bachert C, Bedbrook A, et al.  
507 MACVIA clinical decision algorithm in adolescents and adults with allergic rhinitis. *J Allergy*  
508 *Clin Immunol.* 2016;138(2):367-74 e2.
- 509 6. Courbis AL, Murray RB, Arnavielhe S, Caimmi D, Bedbrook A, Van Eerd M, et al.  
510 Electronic Clinical Decision Support System for allergic rhinitis management: MASK e-CDSS.  
511 *Clin Exp Allergy.* 2018;48(12):1640-53.
- 512 7. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical  
513 Devices. Guidance for Industry and Food and Drug Administration Staff Document issued on  
514 August 31, 2017. Bethesda: US Food and Drug Administration, U.S. Department of Health  
515 and Human Services Food and Drug Administration, Center for Devices and Radiological  
516 Health Center for Biologics Evaluation and Research. [CDRHClinicalEvidence@fda.hhs.gov](mailto:CDRHClinicalEvidence@fda.hhs.gov);  
517 2017.
- 518 8. Sherman RE, Anderson SA, Dal Pan GJ, Gray GW, Gross T, Hunter NL, et al. Real-World  
519 Evidence - What Is It and What Can It Tell Us? *N Engl J Med.* 2016;375(23):2293-7.
- 520 9. Briere JB, Bowrin K, Taieb V, Millier A, Toumi M, Coleman C. Meta-analyses using  
521 real-world data to generate clinical and epidemiological evidence: a systematic literature  
522 review of existing recommendations. *Curr Med Res Opin.* 2018;34(12):2125-30.
- 523 10. Brozek JL, Akl EA, Alonso-Coello P, Lang D, Jaeschke R, Williams JW, et al. Grading  
524 quality of evidence and strength of recommendations in clinical practice guidelines. Part 1 of  
525 3. An overview of the GRADE approach and grading quality of evidence about interventions.  
526 *Allergy.* 2009;64(5):669-77.
- 527 11. Brozek JL, Akl EA, Compalati E, Kreis J, Terracciano L, Fiocchi A, et al. Grading quality  
528 of evidence and strength of recommendations in clinical practice guidelines part 3 of 3. The  
529 GRADE approach to developing recommendations. *Allergy.* 2011;66(5):588-95.
- 530 12. Brozek JL, Akl EA, Jaeschke R, Lang DM, Bossuyt P, Glasziou P, et al. Grading quality of  
531 evidence and strength of recommendations in clinical practice guidelines: part 2 of 3. The  
532 GRADE approach to grading quality of evidence about diagnostic tests and strategies.  
533 *Allergy.* 2009;64(8):1109-16.
- 534 13. Oyinlola JO, Campbell J, Kousoulis AA. Is real world evidence influencing practice? A  
535 systematic review of CPRD research in NICE guidances. *BMC Health Serv Res.* 2016;16:299.
- 536 14. Bousquet J, Lund VJ, Van Cauwenberge P, Bremard-Oury C, Mounedji N, Stevens MT,  
537 et al. Implementation of guidelines for seasonal allergic rhinitis: a randomized controlled  
538 trial. *Allergy.* 2003;58(8):733-41.

- 539 15. Bousquet J, Bodez T, Gehano P, Klossek JM, Liard F, Neukirch F, et al. Implementation  
540 of Guidelines for Allergic Rhinitis in Specialist Practices. A Randomized Pragmatic Controlled  
541 Trial. *Int Arch Allergy Immunol*. 2009;150(1):75-82.
- 542 16. Bousquet J, Hellings PW, Agache I, Amat F, Annesi-Maesano I, Ansotegui IJ, et al.  
543 Allergic Rhinitis and its Impact on Asthma (ARIA) Phase 4 (2018): Change management in  
544 allergic rhinitis and asthma multimorbidity using mobile technology. *J Allergy Clin Immunol*.  
545 2019;143(3):864-79.
- 546 17. Bousquet J, Hellings PW, Agache I, Amat F, Annesi-Maesano I, Ansotegui IJ, et al. ARIA  
547 Phase 4 (2018): Change management in allergic rhinitis and asthma multimorbidity using  
548 mobile technology. *J Allergy Clin Immunol*. 2018;pii: S0091-6749(18)31359-9. doi:  
549 10.1016/j.jaci.2018.08.049.
- 550 18. Transformation of Health and Care in the Digital Single Market is gaining more  
551 support. [https://europeaeu/digital-single-market/en/news/transformation-health-and-](https://europeaeu/digital-single-market/en/news/transformation-health-and-care-digital-single-market-gaining-more-support)  
552 [care-digital-single-market-gaining-more-support](https://europeaeu/digital-single-market/en/news/transformation-health-and-care-digital-single-market-gaining-more-support). 2018.
- 553 19. Bousquet J, Arnavielhe S, Bedbrook A, Bewick M, Laune D, Mathieu-Dupas E, et al.  
554 MASK 2017: ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma  
555 multimorbidity using real-world-evidence. *Clin Transl Allergy*. 2018;8:45.
- 556 20. Bousquet J, Anto JM, Annesi-Maesano I, Dedeu T, Dupas E, Pepin JL, et al. POLLAR:  
557 Impact of air POLLution on Asthma and Rhinitis; a European Institute of Innovation and  
558 Technology Health (EIT Health) project. *Clin Transl Allergy*. 2018;8:36.
- 559 21. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, et al.  
560 Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin*  
561 *Immunol*. 2010;126(3):466-76.
- 562 22. Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al.  
563 Allergic Rhinitis and its Impact on Asthma (ARIA) Guidelines - 2016 Revision. *J Allergy Clin*  
564 *Immunol*. 2017;140(4):950-8.
- 565 23. Dykewicz MS, Wallace DV, Baroody F, Bernstein J, Craig T, Finegold I, et al. Treatment  
566 of seasonal allergic rhinitis: An evidence-based focused 2017 guideline update. *Ann Allergy*  
567 *Asthma Immunol*. 2017;119(6):489-511 e41.
- 568 24. Bousquet J, Devillier P, Arnavielhe S, Bedbrook A, Alexis-Alexandre G, van Eerd M, et  
569 al. Treatment of allergic rhinitis using mobile technology with real-world data: The MASK  
570 observational pilot study. *Allergy*. 2018;73(9):1763-74.
- 571 25. Bedard A, Basagana X, Anto JM, Garcia-Aymerich J, Devillier P, Arnavielhe S, et al.  
572 Mobile technology offers novel insights on control and treatment of allergic rhinitis. The  
573 MASK study. *J Allergy Clin Immunol*. 2019.
- 574 26. Klimek L, Bergmann KC, Biedermann T, Bousquet J, Hellings P, Jung K, et al. Visual  
575 analogue scales (VAS): Measuring instruments for the documentation of symptoms and  
576 therapy monitoring in cases of allergic rhinitis in everyday health care: Position Paper of the  
577 German Society of Allergology (AeDA) and the German Society of Allergy and Clinical  
578 Immunology (DGAKI), ENT Section, in collaboration with the working group on Clinical  
579 Immunology, Allergology and Environmental Medicine of the German Society of  
580 Otorhinolaryngology, Head and Neck Surgery (DGHNOKHC). *Allergo J Int*. 2017;26(1):16-24.
- 581 27. Horak F, Bruttman G, Pedrali P, Weeke B, Frolund L, Wolff HH, et al. A multicentric  
582 study of loratadine, terfenadine and placebo in patients with seasonal allergic rhinitis.  
583 *Arzneimittelforschung*. 1988;38(1):124-8.



- 584 28. Hampel FC, Ratner PH, Van Bavel J, Amar NJ, Daftary P, Wheeler W, et al. Double-  
585 blind, placebo-controlled study of azelastine and fluticasone in a single nasal spray delivery  
586 device. *Ann Allergy Asthma Immunol.* 2010;105(2):168-73.
- 587 29. Carr W, Bernstein J, Lieberman P, Meltzer E, Bachert C, Price D, et al. A novel  
588 intranasal therapy of azelastine with fluticasone for the treatment of allergic rhinitis. *J*  
589 *Allergy Clin Immunol.* 2012;129(5):1282-9 e10.
- 590 30. Kaszuba SM, Baroody FM, deTineo M, Haney L, Blair C, Naclerio RM. Superiority of an  
591 intranasal corticosteroid compared with an oral antihistamine in the as-needed treatment of  
592 seasonal allergic rhinitis. *Arch Intern Med.* 2001;161(21):2581-7.
- 593 31. Glacy J, Putnam K, Godfrey S, Falzon L, Mauger B, Samson D, et al. Treatments for  
594 Seasonal Allergic Rhinitis. AHRQ Comparative Effectiveness Reviews. Rockville (MD)2013.
- 595 32. "Draft Guidance for Industry: Allergic Rhinitis: Clinical Development Programs for  
596 Drug Products", Food and Drug Administration, CDER.  
597 <http://www.fda.gov/cder/guidance/index.htm>. 2000.
- 598 33. Allergic Rhinitis: developing drug products for treatment. Guidance for industry.U.S.  
599 Department of Health and Human Services Food and Drug Administration Center for Drug  
600 Evaluation and Research (CDER) February 2016 Clinical/Medical Revision 1.  
601 <https://www.fda.gov/downloads/drugs/guidances/ucm071293.pdf>. 2016.
- 602 34. Katial RK, Salapatek AM, Patel P. Establishing the onset of action of intranasal  
603 corticosteroids: is there an ideal study design? *Allergy Asthma Proc.* 2009;30(6):595-604.
- 604 35. Pfaar O, Calderon MA, Andrews CP, Angjeli E, Bergmann KC, Bonlokke JH, et al.  
605 Allergen exposure chambers: harmonizing current concepts and projecting the needs for the  
606 future - an EAACI Position Paper. *Allergy.* 2017;72(7):1035-42.
- 607 36. Ellis AK, Jacobs RL, Tenn MW, Steacy LM, Adams DE, Walker TJ, et al. Clinical  
608 standardization of two controlled allergen challenge facilities - The Environmental Exposure  
609 Unit and the Biogenics Research Chamber. *Ann Allergy Asthma Immunol.* 2019.
- 610 37. mHealth. New horizons for health through mobile technologies. Global Observatory  
611 for eHealth series- Vol 3 WHO Library Cataloguing-in-Publication Data.  
612 2011;[http://www.who.int/goe/publications/goe\\_mhealth\\_web.pdf](http://www.who.int/goe/publications/goe_mhealth_web.pdf).
- 613 38. Sleurs K, Seys S, Bousquet J, Fokkens W, Gorris S, Pugin B, et al. Mobile health tools  
614 for the management of chronic respiratory diseases. *Allergy.* 2019.
- 615 39. Bousquet J, Hellings PW, Agache I, Bedbrook A, Bachert C, Bergmann KC, et al. ARIA  
616 2016: Care pathways implementing emerging technologies for predictive medicine in rhinitis  
617 and asthma across the life cycle. *Clin Transl Allergy.* 2016;6:47.
- 618 40. Bousquet J, Agache I, Aliberti MR, Angles R, Annesi-Maesano I, Anto JM, et al.  
619 Transfer of innovation on allergic rhinitis and asthma multimorbidity in the elderly (MACVIA-  
620 ARIA) - EIP on AHA Twinning Reference Site (GARD research demonstration project). *Allergy.*  
621 2018;73(1):77-92.
- 622 41. Bousquet J, Bedbrook A, Czarlewski W, Onorato GL, Arnavielhe S, Laune D, et al.  
623 Guidance to 2018 good practice: ARIA digitally-enabled, integrated, person-centred care for  
624 rhinitis and asthma. *Clin Transl Allergy.* 2019;9:16.
- 625 42. Menditto E, Costa E, Midao L, Bosnic-Anticevich S, Novellino E, Bialek S, et al.  
626 Adherence to treatment in allergic rhinitis using mobile technology. The MASK Study. *Clin*  
627 *Exp Allergy.* 2019;49(4):442-60.
- 628 43. Bousquet J, Murray R, Price D, Somekh D, Munter L, Phillips J, et al. The allergic  
629 allergist behaves like a patient. *Ann Allergy Asthma Immunol.* 2018;121(6):741-2.

- 630 44. Nagarajan N, Jalal D. Resistant Hypertension: Diagnosis and Management. *Adv*  
631 *Chronic Kidney Dis.* 2019;26(2):99-109.
- 632 45. Bousquet J, Bachert C, Canonica GW, Casale TB, Cruz AA, Lockey RJ, et al. Unmet  
633 needs in severe chronic upper airway disease (SCUAD). *J Allergy Clin Immunol.*  
634 2009;124(3):428-33.
- 635 46. Bousquet J, Caimmi DP, Bedbrook A, Bewick M, Hellings PW, Devillier P, et al. Pilot  
636 study of mobile phone technology in allergic rhinitis in European countries: the MASK-  
637 rhinitis study. *Allergy.* 2017;72(6):857-65.
- 638 47. Caimmi D, Baiz N, Tanno LK, Demoly P, Arnavielhe S, Murray R, et al. Validation of the  
639 MASK-rhinitis visual analogue scale on smartphone screens to assess allergic rhinitis control.  
640 *Clin Exp Allergy.* 2017;47(12):1526-33.
- 641 48. Bousquet J, Arnavielhe S, Bedbrook A, Fonseca J, Morais Almeida M, Todo Bom A, et  
642 al. The Allergic Rhinitis and its Impact on Asthma (ARIA) score of allergic rhinitis using mobile  
643 technology correlates with quality of life: The MASK study. *Allergy.* 2018;73(2):505-10.
- 644 49. Bousquet J, Devillier P, Anto JM, Bewick M, Haahtela T, Arnavielhe S, et al. Daily  
645 allergic multimorbidity in rhinitis using mobile technology: a novel concept of the MASK  
646 study. *Allergy.* 2018;73(9):1763-74.
- 647 50. Bousquet J, VandenPlas O, Bewick M, Arnavielhe S, Bedbrook A, Murray R, et al. The  
648 Work Productivity and Activity Impairment Allergic Specific (WPAI-AS) Questionnaire Using  
649 Mobile Technology: The MASK Study. *J Investig Allergol Clin Immunol.* 2018;28(1):42-4.
- 650 51. Bonini M. Electronic health (e-Health): emerging role in asthma. *Curr Opin Pulm Med.*  
651 2017;23(1):21-6.
- 652 52. Pizzulli A, Perna S, Florack J, Pizzulli A, Giordani P, Tripodi S, et al. The impact of  
653 telemonitoring on adherence to nasal corticosteroid treatment in children with seasonal  
654 allergic rhinoconjunctivitis. *Clin Exp Allergy.* 2014;44(10):1246-54.
- 655 53. Miller TA. Health literacy and adherence to medical treatment in chronic and acute  
656 illness: A meta-analysis. *Patient Educ Couns.* 2016;99(7):1079-86.
- 657 54. Batterham RW, Hawkins M, Collins PA, Buchbinder R, Osborne RH. Health literacy:  
658 applying current concepts to improve health services and reduce health inequalities. *Public*  
659 *Health.* 2016;132:3-12.
- 660 55. Hellings PW, Borrelli D, Pietikainen S, Agache I, Akdis C, Bachert C, et al. European  
661 Summit on the Prevention and Self-Management of Chronic Respiratory Diseases: report of  
662 the European Union Parliament Summit (29 March 2017). *Clin Transl Allergy.* 2017;7:49.
- 663 56. Bousquet J, Meltzer EO, Couroux P, Koltun A, Kopietz F, Munzel U, et al. Onset of  
664 Action of the Fixed Combination Intranasal Azelastine-Fluticasone Propionate in an Allergen  
665 Exposure Chamber. *J Allergy Clin Immunol Pract.* 2018;6(5):1726-32.
- 666 57. Patel P, D'Andrea C, Sacks HJ. Onset of action of azelastine nasal spray compared  
667 with mometasone nasal spray and placebo in subjects with seasonal allergic rhinitis  
668 evaluated in an environmental exposure chamber. *Am J Rhinol.* 2007;21(4):499-503.
- 669 58. Patel P, Roland PS, Marple BF, Benninger PJ, Margalias H, Brubaker M, et al. An  
670 assessment of the onset and duration of action of olopatadine nasal spray. *Otolaryngol Head*  
671 *Neck Surg.* 2007;137(6):918-24.
- 672 59. Patel P, Patel D, Kunjibettu S, Hall N, Wingertzahn MA. Onset of action of ciclesonide  
673 once daily in the treatment of seasonal allergic rhinitis. *Ear Nose Throat J.* 2008;87(6):340-  
674 53.
- 675 60. Salapatek AM, Lee J, Patel D, D'Angelo P, Liu J, Zimmerer RO, Jr., et al. Solubilized  
676 nasal steroid (CDX-947) when combined in the same solution nasal spray with an

677 antihistamine (CDX-313) provides improved, fast-acting symptom relief in patients with  
678 allergic rhinitis. *Allergy Asthma Proc.* 2011;32(3):221-9.

679 61. Patel P, Patel D. Efficacy comparison of levocetirizine vs montelukast in ragweed  
680 sensitized patients. *Ann Allergy Asthma Immunol.* 2008;101(3):287-94.

681 62. Horak F, Jager S, Toth J, Berger U. Efficacy and tolerability of astemizole-D and  
682 Loratadine-D during prolonged, controlled allergen challenge in the Vienna Challenge  
683 Chamber. *Arzneimittelforschung.* 1996;46(11):1077-81.

684 63. Horak F, Jager S, Berger U. Onset and duration of the effects of three antihistamines  
685 in current use--astemizole, loratadine and terfenadine forte--studied during prolonged,  
686 controlled allergen challenges in volunteers. *J Int Med Res.* 1992;20(5):422-34.

687 64. Horak F, Zieglmayer UP, Zieglmayer R, Kavina A, Marschall K, Munzel U, et al.  
688 Azelastine nasal spray and desloratadine tablets in pollen-induced seasonal allergic rhinitis: a  
689 pharmacodynamic study of onset of action and efficacy. *Curr Med Res Opin.* 2006;22(1):151-  
690 7.

691 65. Horak F, Zieglmayer P, Zieglmayer R, Lemell P. The effects of bilastine compared with  
692 cetirizine, fexofenadine, and placebo on allergen-induced nasal and ocular symptoms in  
693 patients exposed to aeroallergen in the Vienna Challenge Chamber. *Inflamm Res.*  
694 2010;59(5):391-8.

695 66. Zieglmayer UP, Horak F, Toth J, Marks B, Berger UE, Burtin B. Efficacy and safety of an  
696 oral formulation of cetirizine and prolonged-release pseudoephedrine versus budesonide  
697 nasal spray in the management of nasal congestion in allergic rhinitis. *Treat Respir Med.*  
698 2005;4(4):283-7.

699 67. Stubner UP, Toth J, Marks B, Berger UE, Burtin B, Horak F. Efficacy and safety of an  
700 oral formulation of cetirizine and prolonged-release pseudoephedrine versus xylometazoline  
701 nasal spray in nasal congestion. *Arzneimittelforschung.* 2001;51(11):904-10.

702 68. Horak F, Stubner UP, Zieglmayer R, Harris AG. Effect of desloratadine versus placebo  
703 on nasal airflow and subjective measures of nasal obstruction in subjects with grass pollen-  
704 induced allergic rhinitis in an allergen-exposure unit. *J Allergy Clin Immunol.*  
705 2002;109(6):956-61.

706 69. Murdoch RD, Bareille P, Ignar D, Miller SR, Gupta A, Boardley R, et al. The improved  
707 efficacy of a fixed-dose combination of fluticasone furoate and levocabastine relative to the  
708 individual components in the treatment of allergic rhinitis. *Clin Exp Allergy.* 2015;45(8):1346-  
709 55.

710 70. Stubner P, Zieglmayer R, Horak F. A direct comparison of the efficacy of  
711 antihistamines in SAR and PAR: randomised, placebo-controlled studies with levocetirizine  
712 and loratadine using an environmental exposure unit - the Vienna Challenge Chamber (VCC).  
713 *Curr Med Res Opin.* 2004;20(6):891-902.

714 71. Stuebner P, Horak F, Zieglmayer R, Arnaiz E, Leuratti C, Perez I, et al. Effects of  
715 rupatadine vs placebo on allergen-induced symptoms in patients exposed to aeroallergens in  
716 the Vienna Challenge Chamber. *Ann Allergy Asthma Immunol.* 2006;96(1):37-44.

717  
718

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 GA<sup>2</sup>LEN: 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

729

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

739

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*

746

747

748

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

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

750

751

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 $\geq 12$ years of age, clinicians:                    |
| 766 | • Should routinely prescribe monotherapy with an INCS rather than a combination of INCS and oral H <sub>1</sub> - |
| 767 | antihistamine.  |
| 768 | • Should recommend an INCS over LTRA (for $\geq 15$ 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)

776

777

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

	<b>GRADE recommendation</b>	<b>mHealth RWE</b>	<b>Chamber studies</b>
<b>Oral H<sub>1</sub>-antihistamines are less potent than INCS BUT many patients prefer oral drugs</b>	(21) No information on patient's preference	(24)(25) No information on patient's preference	
<b>Intra-nasal H<sub>1</sub>-antihistamines are less effective than INCS</b>	(21)		
<b>Intra-nasal H<sub>1</sub>-antihistamines are effective within minutes</b>	(21)		(57, 64)
<b>INCS should continue being prescribed as first line therapy in moderate-severe rhinitis</b>	(21, 23)	(24, 25)	
<b>The onset of action of INCS takes a few hours to a few days (ciclesonide has a faster onset)</b>	(21)		(59, 60)
<b>The combination of INCS and oral H<sub>1</sub>-antihistamines offers no advantage over INCS</b>	(22, 23)	(24, 25)	
<b>The combination of INCS and intra-nasal H<sub>1</sub>-antihistamines is more effective than INCS</b>	YES in moderate-severe patients: (23) With restriction: (22)	(24, 25)	
<b>The combination of INCS and intra-nasal H<sub>1</sub>-antihistamines is effective within minutes</b>			(56, 60, 69)
<b>Leukotriene antagonists are less potent than INCS</b>	(23)		(56, 60, 69)

779

780



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

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

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

782

783

784

785

786

787

788

789

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



Partner of  Health



EIT Health is supported by the EIT, a body of the European Union



European Innovation Partnership on Active and Healthy Ageing



American College of Allergy, Asthma & Immunology



EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY



European Federation of Allergy and Airways Diseases Patients' Associations



ERS EUROPEAN RESPIRATORY SOCIETY



European Rhinologic Society Founded 1963



Global Allergy and Asthma European Network Network of Excellence

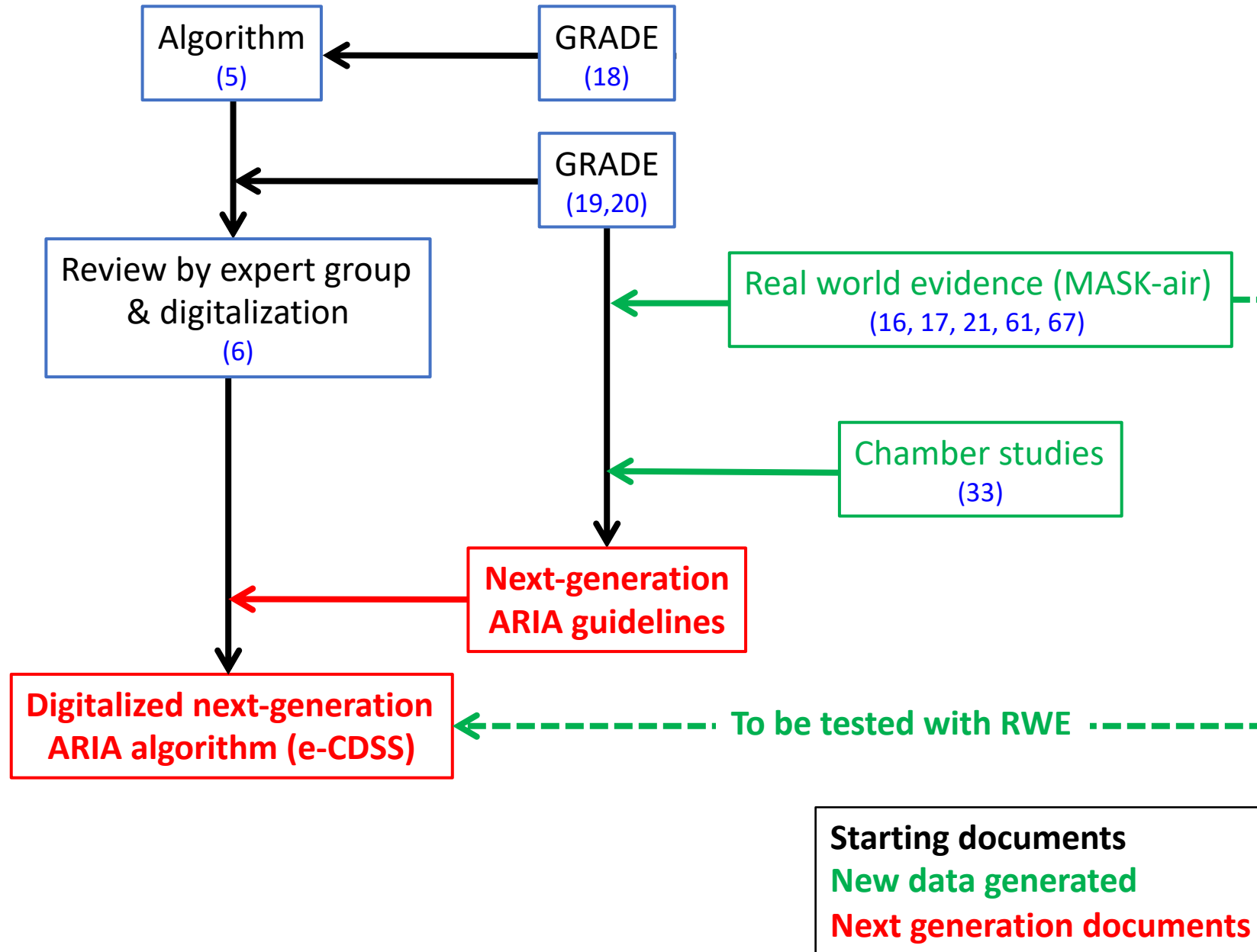


A world where all people breathe freely

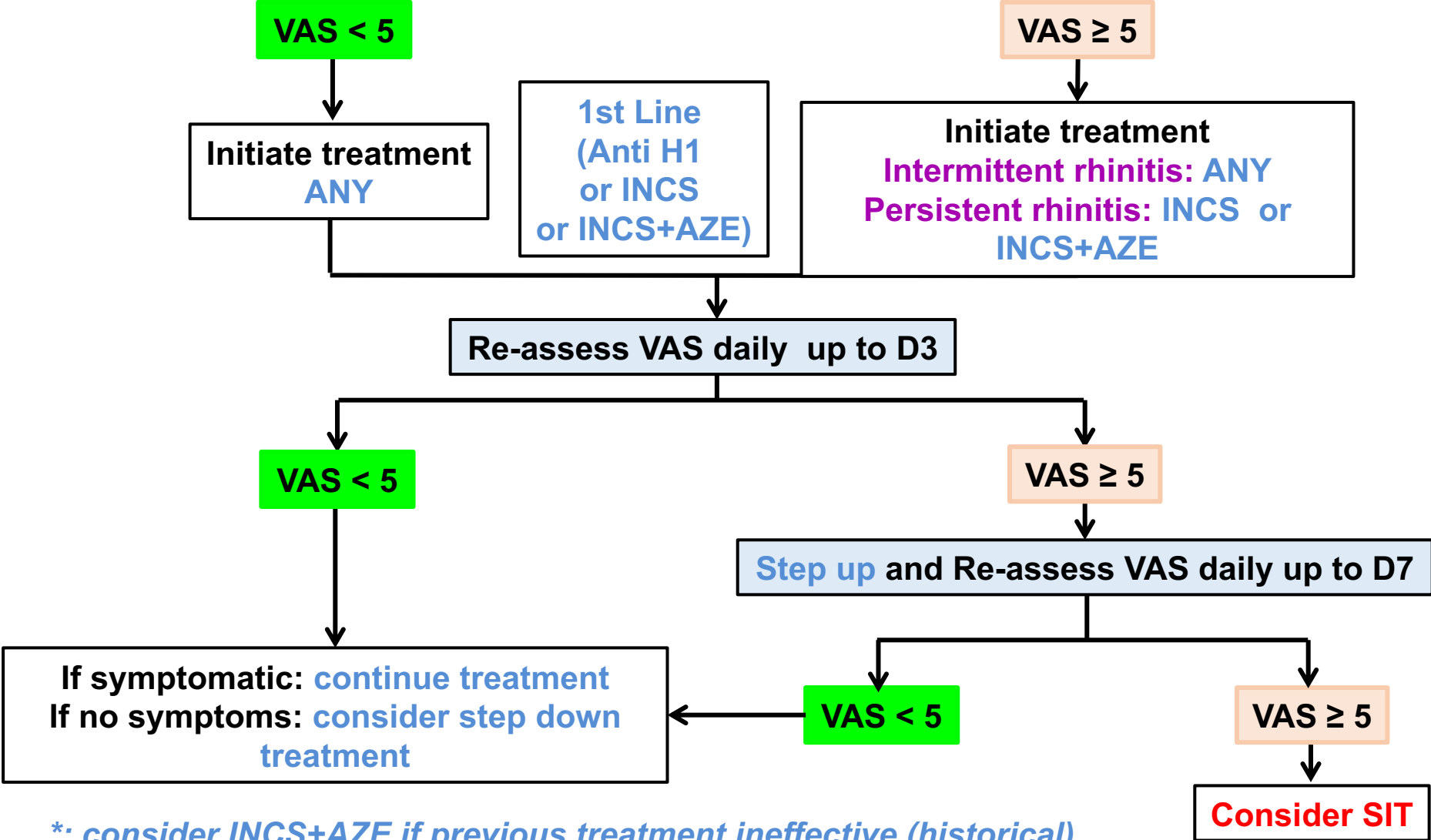


SOCIÉTÉ DE PNEUMOLOGIE DE LANGUE FRANÇAISE





# Assessment of control in untreated symptomatic patient



# Assessment of control in treated symptomatic patient

