



MACVIA-ARIA Sentinel NetworK for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation

Jean Bousquet, J. Schunemann, J. Fonseca, B. Samolinski, C. Bachert, G.
Canonica, T. Casale, A. Cruz, P. Demoly, P. Hellings, et al.

► To cite this version:

Jean Bousquet, J. Schunemann, J. Fonseca, B. Samolinski, C. Bachert, et al.. MACVIA-ARIA Sentinel NetworK for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation. *Allergy*, 2015, 70 (11), pp.1372-1392. 10.1111/all.12686 . hal-02099381

HAL Id: hal-02099381

<https://hal.science/hal-02099381>

Submitted on 24 Mar 2020

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.

MACVIA-ARIA Sentinel Network for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation

J. Bousquet^{1,2,3,243}, H. J. Schunemann⁴, J. Fonseca^{5,244,245,246}, B. Samolinski⁶, C. Bachert⁷, G. W. Canonica⁸, T. Casale⁹, A. A. Cruz^{10,247}, P. Demoly^{11,12,248}, P. Hellings¹³, A. Valiulis¹⁴, M. Wickman^{15,249}, T. Zuberbier^{16,250}, S. Bosnic-Anticevitch¹⁷, A. Bedbrook², K. C. Bergmann^{16,250}, D. Caimmi¹¹, R. Dahl¹⁸, W. J. Fokkens¹⁹, I. Grisle²⁰, K. Lodrup Carlsen^{21,251}, J. Mullol²², A. Muraro²³, S. Palkonen²⁴, N. Papadopoulos^{25,252}, G. Passalacqua⁸, D. Ryan^{26,253}, E. Valovirta²⁷, A. Yorgancioglu²⁸, W. Aberer²⁹, I. Agache³⁰, M. Adachi³¹, C. A. Akdis³², M. Akdis³², I. Annesi-Maesano^{12,248}, I. J. Ansotegui³³, J. M. Anto^{34,35,36,37}, S. Arnavielhe³⁸, H. Arshad³⁹, I. Baiardini⁸, A. K. Baigenzhin⁴⁰, C. Barbara⁴¹, E. D. Bateman⁴², B. Beghé⁴³, E. H. Bel⁴⁴, A. Ben Kheder⁴⁵, K. S. Bennoor⁴⁶, M. Benson⁴⁷, M. Bewick⁴⁸, T. Bieber⁴⁹, C. Bindslev-Jensen¹⁸, L. Bjerner⁵⁰, H. Blain^{51,52}, A. L. Boner⁵³, L. P. Boulet⁵⁴, M. Bonini⁵⁵, S. Bonini⁵⁶, I. Bosse⁵⁷, R. Bourret⁵⁸, P. J. Bousquet^{12,248}, F. Braido⁸, A. H. Briggs⁵⁹, C. E. Brightling^{60,254}, J. Brozek⁴, R. Buhl⁶¹, P. G. Burney^{62,255,256}, A. Bush⁶³, F. Caballero-Fonseca⁶⁴, M. A. Calderon⁶⁵, P. A. M. Camargos⁶⁶, T. Camuzat^{67,257}, K. H. Carlsen⁶⁸, W. Carr⁶⁹, A. M. Cepeda Sarabia^{70,258}, N. H. Chavannes⁷¹, L. Chatzi⁷², Y. Z. Chen⁷³, R. Chiron¹¹, E. Chkhartishvili⁷⁴, A. G. Chuchalin^{75,259}, G. Ciprandi⁷⁶, I. Cirule⁷⁷, J. Correia de Sousa⁷⁸, L. Cox⁷⁹, G. Crooks⁸⁰, D. J. Costa^{2,11}, A. Custovic⁸¹, S. E. Dahlen⁸², U. Darsow^{83,260}, G. De Carlo²⁴, F. De Blay⁸⁴, T. Dedeu⁸⁵, D. Deleanu⁸⁶, J. A. Denburg⁸⁷, P. Devillier⁸⁸, A. Didier⁸⁹, A. T. Dinh-Xuan⁹⁰, D. Dokic⁹¹, H. Douagui⁹², G. Dray⁹³, R. Dubakiene⁹⁴, S. R. Durham⁹⁵, M. S. Dykewicz⁹⁶, Y. El-Gamal⁹⁷, R. Emuzyte⁹⁸, A. Fink Wagner⁹⁹, M. Fletcher¹⁰⁰, A. Fiocchi¹⁰¹, F. Forastiere¹⁰², A. Gamkrelidze¹⁰³, B. Gemicioğlu¹⁰⁴, J. E. Gereda¹⁰⁵, S. González Diaz¹⁰⁶, M. Gotua¹⁰⁷, L. Grouse¹⁰⁸, M. A. Guzmán¹⁰⁹, T. Haahtela¹¹⁰, B. Hellquist-Dahl¹¹¹, J. Heinrich¹¹², F. Horak¹¹³, J. O. B. Hourihane¹¹⁴, P. Howarth¹¹⁵, M. Humbert^{116,261}, M. E. Hyland¹¹⁷, J. C. Ivancevich¹¹⁸, E. J. Jares¹¹⁹, S. L. Johnston^{120,262}, G. Joos¹²¹, O. Jonquet¹²², K. S. Jung¹²³, J. Just^{124,263}, I. Kaidashev¹²⁵, O. Kalayci¹²⁶, A. F. Kalyoncu¹²⁷, T. Keil^{128,264}, P. K. Keith¹²⁹, N. Khaltaev¹³⁰, L. Klimek¹³¹, B. Koffi N'Goran¹³², V. Kolek¹³³, G. H. Koppelman¹³⁴, M. L. Kowalski¹³⁵, I. Kull^{15,249}, P. Kuna¹³⁶, V. Kvedariene¹³⁷, B. Lambrecht¹³⁸, S. Lau¹³⁹, D. Larenas-Linnemann¹⁴⁰, D. Laune³⁸, L. T. T. Le¹⁴¹, P. Lieberman¹⁴², B. Lipworth¹⁴³, J. Li¹⁴⁴, R. Louis¹⁴⁵, Y. Magard¹⁴⁶, A. Magnan¹⁴⁷, B. Mahboub¹⁴⁸, I. Majer¹⁴⁹, M. J. Makela¹¹⁰, P. Manning¹⁵⁰, E. De Manuel Keenoy¹⁵¹, G. D. Marshall¹⁵², M. R. Masjedi¹⁵³, M. Maurer¹⁵⁴, S. Mavale-Manuel¹⁵⁵, E. Melén¹⁵⁶, E. Melo-Gomes⁴¹, E. O. Meltzer¹⁵⁷, H. Merk¹⁵⁸, N. Miculinic¹⁵⁹, F. Mihaltan¹⁶⁰, B. Milenkovic^{161,265}, Y. Mohammad¹⁶², M. Molimard¹⁶³, I. Momas^{164,165}, A. Montilla-Santana¹⁶⁶, M. Morais-Almeida¹⁶⁷, R. Mösges¹⁶⁸, L. Namazova-Baranova¹⁶⁹, R. Naclerio¹⁷⁰, A. Neou^{16,250}, H. Neffen¹⁷¹, K. Nekam¹⁷², B. Niggemann¹⁷³, T. D. Nyembue¹⁷⁴, R. E. O'Hehir^{175,266}, K. Ohta¹⁷⁶, Y. Okamoto¹⁷⁷, K. Okubo¹⁷⁸, S. Ouedraogo¹⁷⁹, P. Paggiaro¹⁸⁰, I. Pali-Schöll^{181,267}, S. Palmer²⁷⁵, P. Panzner¹⁸², A. Papi¹⁸³, H. S. Park¹⁸⁴, I. Pavord¹⁸⁵, R. Pawankar¹⁸⁶, O. Pfaar^{187,268}, R. Picard¹⁸⁸, B. Pigearias¹³², I. Pin¹⁸⁹, D. Plavec¹⁹⁰, W. Pohl¹⁹¹, T. A. Popov¹⁹², F. Portejoie², D. Postma¹⁹³, P. Potter¹⁹⁴, D. Price^{195,269}, K. F. Rabe^{196,270}, F. Raciborski⁶, F. Radier Pontal¹⁹⁷, S. Repka-Ramirez¹⁹⁸, C. Robalo-Cordeiro¹⁹⁹, C. Rolland²⁰⁰, J. Rosado-Pinto²⁰¹, S. Reitamo¹¹⁰, F. Rodenas²⁰², M. Roman Rodriguez²⁰³, A. Romano²⁰⁴, N. Rosario²⁰⁵, L. Rosenwasser²⁰⁶, M. Rottem²⁰⁷, M. Sanchez-Borges^{208,271}, G. K. Scadding²⁰⁹, E. Serrano²¹⁰, P. Schmid-Grendelmeier²¹¹, A. Sheikh²¹², F. E. R. Simons²¹³, J. C. Sisul²¹⁴, I. Skrindo^{21,251}, H. A. Smit²¹⁵, D. Solé²¹⁶, T. Sooronbaev²¹⁷, O. Spranger⁹⁹, R. Stelmach²¹⁸, T. Strandberg²¹⁹, J. Sunyer^{34,35,36,37}, C. Thijs²²⁰, A. Todo-Bom²²¹, M. Triggiani²²², R. Valenta²²³, A. L. Valero²²⁴, M. van Hage²²⁵, O. Vandenplas²²⁶, G. Vezzani^{227,272}, P. Vichyanond²²⁸, G. Viegi^{229,273}, M. Wagenmann²³⁰, S. Walker²³¹, D. Y. Wang²³², U. Wahn¹⁷³, D. M. Williams²³³, J. Wright²³⁴, B. P. Yawn²³⁵, P. K. Yiallourous^{236,274}, O. M. Yusuf²³⁷, H. J. Zar²³⁸, M. E. Zernotti²³⁹, L. Zhang²⁴⁰, N. Zhong¹⁴⁴, M. Zidarn²⁴¹ & J. Mercier²⁴²

¹University Hospital; ²MACVIA-LR, Contre les MALadies Chroniques pour un Vieillissement Actif en Languedoc – Roussillon, European Innovation Partnership on Active and Healthy Ageing Reference Site, Montpellier, France; ³INSERM, VIMA: Ageing and Chronic Diseases, Epidemiological and Public Health Approaches, Paris, France; ⁴Department of Clinical Epidemiology and Biostatistics and Medicine, McMaster University, Hamilton, ON, Canada; ⁵Center for Research in Health Technologies and Information Systems – CINTESIS,

Universidade do Porto, Porto, Portugal; ⁶Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Warsaw, Poland; ⁷Upper Airways Research Laboratory, ENT Department, Ghent University Hospital, Ghent, Belgium; ⁸Allergy and Respiratory Diseases Clinic, DIMI, University of Genoa, IRCCS AOU San Martino-IST, Genoa, Italy; ⁹Division of Allergy/Immunology, University of South Florida, Tampa, FL, USA; ¹⁰ProAR – Nucleo de Excelencia em Asma, Federal University of Bahia, Bahia, Brasil; ¹¹Department of Respiratory Diseases, Montpellier University Hospital, Montpellier, France; ¹²EPAR U707 INSERM, Paris, France; ¹³Laboratory of Clinical Immunology, Department of Microbiology and Immunology, KU Leuven, Leuven, Belgium; ¹⁴Vilnius University Clinic of Children's Diseases, Vilnius, Lithuania; ¹⁵Sachs' Children's Hospital, Stockholm, Sweden; ¹⁶Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Berlin, Germany; ¹⁷Woolcock Institute of Medical Research, University of Sydney and Sydney Local Health District, Glebe, NSW, Australia; ¹⁸Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark; ¹⁹Department of Otorhinolaryngology, Academic Medical Centre, Amsterdam, The Netherlands; ²⁰Latvian Association of Allergists, Center of Tuberculosis and Lung Diseases of Latvia, Riga, Latvia; ²¹Department of Paediatrics, Oslo University Hospital, Oslo, Norway; ²²Unitat de Rinologia i Clínica de l'Olfacte, Servei d'ORL, Hospital Clínic, Clinical & Experimental Respiratory Immunoallergy, IDIBAPS, Barcelona, Catalonia, Spain; ²³Food Allergy Referral Centre Veneto Region, Department of Women and Child Health, Padua General University Hospital, Padua, Italy; ²⁴EFA European Federation of Allergy and Airways Diseases Patients' Associations, Brussels, Belgium; ²⁵Center for Pediatrics and Child Health, Institute of Human Development, Royal Manchester Children's Hospital, University of Manchester, Manchester; ²⁶General Practitioner, Woodbrook Medical Centre, Loughborough, UK; ²⁷Department of Lung Diseases and Clinical Allergology, University of Turku, Turku, Finland; ²⁸Department of Pulmonology, Celal Bayar University, Manisa, Turkey; ²⁹Department of Dermatology, Medical University of Graz, Graz, Austria; ³⁰Transylvania University Brasov, Brasov, Romania; ³¹Department of Clinical Research Center, International University of Health and Welfare/Sanno Hospital, Tokyo, Japan; ³²Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland; ³³Department of Allergy and Immunology, Hospital Quirón Bizkaia, Erandio, Spain; ³⁴Centre for Research in Environmental Epidemiology, Barcelona, Spain; ³⁵Hospital del Mar Research Institute, Barcelona, Spain; ³⁶CIBER Epidemiología y Salud Pública, Barcelona, Spain; ³⁷Department of Experimental and Health Sciences, University of Pompeu Fabra, Barcelona, Spain; ³⁸Digi Health, Montpellier, France; ³⁹David Hide Asthma and Allergy Research Centre, Isle of Wight, UK; ⁴⁰EuroAsian Respiratory Society, Astana City, Kazakhstan; ⁴¹Faculdade de Medicina de Lisboa, Portuguese National Programme for Respiratory Diseases, Lisbon, Portugal; ⁴²Department of Medicine, University of Cape Town, Cape Town, South Africa; ⁴³Section of Respiratory Disease, Department of Oncology, Haematology and Respiratory Diseases, University of Modena and Reggio Emilia, Modena, Italy; ⁴⁴Department of Respiratory Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; ⁴⁵Service de Pneumologie IV, Hôpital Abderrahman Mami, Ariana, Tunisie; ⁴⁶Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Dhaka, Bangladesh; ⁴⁷Centre for Individualized Medicine, Department of Pediatrics, Faculty of Medicine, Linköping University, Linköping, Sweden; ⁴⁸Deputy National Medical Director, NHS England, England, UK; ⁴⁹Department of Dermatology and Allergy, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany; ⁵⁰Department of Respiratory Medicine and Allergology, University Hospital, Lund, Sweden; ⁵¹Department of Geriatrics, Montpellier University Hospital; ⁵²EA 2991 Movement To Health, Euromov, University Montpellier, Montpellier, France; ⁵³Pediatric Department, University of Verona Hospital, Verona, Italy; ⁵⁴Québec Heart and Lung Institute, Laval University, Québec City, QC, Canada; ⁵⁵Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome; ⁵⁶Second University of Naples and Institute of Translational Medicine, Italian National Research Council, Naples, Italy; ⁵⁷Allergist, La Rochelle; ⁵⁸Directeur Général Adjoint, Montpellier University Hospital, Montpellier, France; ⁵⁹Health Economics and Health Technology Assessment, Institute of Health & Wellbeing, University of Glasgow, Glasgow; ⁶⁰Institute of Lung Health, Respiratory Biomedical Unit, University Hospitals of Leicester NHS Trust, Leicestershire, UK; ⁶¹Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz, Germany; ⁶²National Heart and Lung Institute, Imperial College; ⁶³Imperial College and Royal Brompton Hospital, London, UK; ⁶⁴Centro Medico Docente La Trinidad, CaRacas, Venezuela; ⁶⁵Imperial College London – National Heart and Lung Institute, Royal Brompton Hospital NHS, London, UK; ⁶⁶Federal University of Minas Gerais, Medical School, Department of Pediatrics, Belo Horizonte, Brazil; ⁶⁷Assitant Director General, Montpellier, France; ⁶⁸Department of Paediatrics, Oslo University Hospital and University of Oslo, Oslo, Norway; ⁶⁹Allergy and Asthma Associates of Southern California, Mission Viejo, CA, USA; ⁷⁰Allergy and Immunology Laboratory, Metropolitan University, Simon Bolivar University, Barranquilla, Colombia; ⁷¹Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands; ⁷²Department of Social Medicine, Faculty of Medicine, University of Crete, Heraklion, Crete, Greece; ⁷³National Cooperative Group of Paediatric Research on Asthma, Asthma Clinic and Education Center of the Capital Institute of Pediatrics, Peking and Center for Asthma Research and Education, Beijing, China; ⁷⁴Chachava Clinic, David Tvildiani Medical University-AIETI Medical School, Grigol Robakidze University, Tbilisi, Georgia; ⁷⁵Pulmonology Research Institute FMBA, Moscow, Russia; ⁷⁶Medicine Department, IRCCS-Azienda Ospedaliera Universitaria San Martino, Genoa, Italy; ⁷⁷Latvian Association of Allergists, University Children Hospital of Latvia, Riga, Latvia; ⁷⁸Life and Health Sciences Research Institute, ICVS, School of Health Sciences, University of Minho, Braga, Portugal; ⁷⁹Department of Medicine, Nova Southeastern University, Davie, FL, USA; ⁸⁰European Innovation Partnership on Active and Healthy Ageing, Reference Site, NHS Scotland, Glasgow; ⁸¹Centre for Respiratory Medicine and Allergy, Institute of Inflammation and Repair, University of Manchester and University Hospital of South Manchester, Manchester, UK; ⁸²The Centre for Allergy Research, The Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; ⁸³Department of Dermatology and Allergy, Technische Universität München, Munich, Germany; ⁸⁴Allergy Division, Chest Disease Department, University Hospital of Strasbourg, Strasbourg, France; ⁸⁵European Regional and Local Health Association, Brussels, Belgium; ⁸⁶Allergology and Immunology Discipline, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; ⁸⁷Department of Medicine, Division of Clinical Immunology and Allergy, McMaster University, Hamilton, ON, Canada; ⁸⁸Laboratoire de Pharmacologie Respiratoire UPRES EA220, Hôpital Foch, Suresnes Université Versailles Saint-Quentin, Versailles Saint-Quentin; ⁸⁹Respiratory Diseases Department, Rangueil-Larrey Hospital, Toulouse; ⁹⁰Service de physiologie, Hôpital Cochin, Université Paris-Descartes, Assistance publique-Hôpitaux de Paris, Paris, France; ⁹¹Medical Faculty Skopje, University Clinic of Pulmology and Allergy, Skopje, R. Macedonia; ⁹²Service de Pneumo-Allergologie, Centre

Hospitolo-Universitaire de Béni-Messous, Algiers, Algeria; ⁹³Ecole des Mines, Alès, France; ⁹⁴Medical Faculty, Vilnius University, Vilnius, Lithuania; ⁹⁵Allergy and Clinical Immunology Section, National Heart and Lung Institute, Imperial College London, London, UK; ⁹⁶Section of Allergy and Immunology, Saint Louis University School of Medicine, Saint Louis, MI, USA; ⁹⁷Pediatric Allergy and Immunology Unit, Ain Shams University, Cairo, Egypt; ⁹⁸Clinic of Children's Diseases, Faculty of Medicine, Vilnius University, Vilnius, Lithuania; ⁹⁹Global Allergy and Asthma Platform GAAPP, Vienna, Austria; ¹⁰⁰Education for Health, Warwick, UK; ¹⁰¹Allergy Department, The Bambino Gesù Children's Research Hospital Holy see; ¹⁰²Department of Epidemiology, Regional Health Service Lazio Region, Rome, Italy; ¹⁰³National Center for Disease Control and Public Health of Georgia, Tbilisi, Georgia; ¹⁰⁴Turkish Thoracic Society Asthma-Allergy Working Group, Kocaeli, Turkey; ¹⁰⁵Allergy and Immunology Division, Clinica Ricardo Palma, Lima, Peru; ¹⁰⁶Sociedad Latinoamericana de Alergia, Asma e Immunologia, Mexico City, Mexico; ¹⁰⁷Center of Allergy and Immunology, Georgian Association of Allergology and Clinical Immunology, Tbilisi, Georgia; ¹⁰⁸Faculty of the Department of Neurology, University of Washington School of Medicine, Seattle, WA, USA; ¹⁰⁹Immunology and Allergy Division, Clinical Hospital, University of Chile, Santiago, Chile; ¹¹⁰Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland; ¹¹¹Department of Respiratory Diseases, Odense University Hospital, Odense, Denmark; ¹¹²Institute of Epidemiology I, German Research Centre for Environmental Health, Helmholtz Zentrum München, Neuherberg, Germany; ¹¹³Vienna Challenge Chamber, Vienna, Austria; ¹¹⁴Department of Paediatrics and Child Health, University College Cork, Cork, Ireland; ¹¹⁵University of Southampton Faculty of Medicine, University Hospital Southampton, Southampton, UK; ¹¹⁶Université Paris-Sud, Le Kremlin Bicêtre, France; ¹¹⁷School of Psychology, Plymouth University, Plymouth, UK; ¹¹⁸Servicio de Alergia e Immunologia, Clinica Santa Isabel; ¹¹⁹Libra Foundation, Buenos Aires, Argentina; ¹²⁰Airway Disease Infection Section, National Heart and Lung Institute, Imperial College, London, UK; ¹²¹Department of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium; ¹²²Medical Commission, Montpellier University Hospital, Montpellier, France; ¹²³Hallym University College of Medicine, Hallym University Sacred Heart Hospital, Gyeonggi-do, South Korea; ¹²⁴Allergology Department, Centre de l'Asthme et des Allergies. Hôpital d'Enfants Armand-Trousseau, Paris, France; ¹²⁵Ukrainian Medical Stomatological Academy, Poltava, Ukraine; ¹²⁶Pediatric Allergy and Asthma Unit, Hacettepe University School of Medicine; ¹²⁷School of Medicine, Department of Chest Diseases, Immunology and Allergy Division, Hacettepe University, Ankara, Turkey; ¹²⁸Institute of Social Medicine, Epidemiology and Health Economics, Charité – Universitätsmedizin Berlin, Berlin, Germany; ¹²⁹Department of Medicine, McMaster University, Health Sciences Centre 3V47, Hamilton, ON, Canada; ¹³⁰GARD Chairman, Geneva, Switzerland; ¹³¹Center for Rhinology and Allergology, Wiesbaden, Germany; ¹³²Société de Pneumologie de Langue Française et Espace Francophone de Pneumologie, Paris, France; ¹³³Department of Respiratory Medicine, Faculty of Medicine and Dentistry, University Hospital Olomouc, Olomouc, Czech Republic; ¹³⁴Department of Pediatric Pulmonology and Pediatric Allergology, Beatrix Children's Hospital, GRIAC Research Institute, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; ¹³⁵Department of Immunology, Rheumatology and Allergy, Medical University of Lodz; ¹³⁶Division of Internal Medicine, Asthma and Allergy, KUNA, Barlicki University Hospital, Medical University of Lodz, Lodz, Poland; ¹³⁷Pulmonology and Allergology Center, Vilnius University, Vilnius, Lithuania; ¹³⁸VIB Inflammation Research Center, Ghent University, Ghent, Belgium; ¹³⁹Department for Pediatric Pneumology and Immunology, Charité Medical University, Berlin, Germany; ¹⁴⁰Clinica de Alergia, Asma y Pediatría, Hospital Médica Sur, México City, México; ¹⁴¹University of Medicine and Pharmacy, Hochiminh City, Vietnam; ¹⁴²Departments of Internal Medicine and Pediatrics (Divisions of Allergy and Immunology), University of Tennessee College of Medicine, Germantown, TN, USA; ¹⁴³Scottish Centre for Respiratory Research, Cardiovascular & Diabetes Medicine, Medical Research Institute, Ninewells Hospital, University of Dundee, Dundee, UK; ¹⁴⁴State Key Laboratory of Respiratory Diseases, Guangzhou Institute of Respiratory Disease, the First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; ¹⁴⁵Department of Pulmonary Medicine, CHU Sart-Tilman, Liege, Belgium; ¹⁴⁶Service de Pneumo-allergologie, Hôpital Saint-Joseph, Paris; ¹⁴⁷Service de Pneumologie, University of Nantes, UMR INSERM, UMR1087/CNR 6291, l'Institut du Thorax, Nantes, France; ¹⁴⁸Department of Pulmonary Medicine, Rashid Hospital, Dubai, UAE; ¹⁴⁹Department of Respiratory Medicine, University Hospital, Bratislava, Slovakia; ¹⁵⁰Department of Medicine (RCSI), Bon Secours Hospital, Glasnevin, Dublin, Ireland; ¹⁵¹Kronikgune, Basque Region, Spain; ¹⁵²Division of Clinical Immunology and Allergy, Laboratory of Behavioral Immunology Research, The University of Mississippi Medical Center, Jackson, MS, USA; ¹⁵³Respiratory Disease Research, Shahid Beheshti University of Medical Sciences, Tehran, Iran; ¹⁵⁴Allergie-Centrum-Charité at the Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Berlin, Germany; ¹⁵⁵Department of Paediatrics, Maputo Central Hospital, Maputo, Mozambique; ¹⁵⁶Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; ¹⁵⁷Allergy and Asthma Medical Group and Research Center, San Diego, CA, USA; ¹⁵⁸Hautklinik – Klinik für Dermatologie & Allergologie, Universitätsklinikum der RWTH Aachen, Aachen, Deutschland; ¹⁵⁹Croatian Pulmonary Society, Zagreb, Croatia; ¹⁶⁰National Institute of Pneumology M. Nasta, Bucharest, Romania; ¹⁶¹Faculty of Medicine, University of Belgrade, Belgrade, Serbia; ¹⁶²National Center for Research in Chronic Respiratory Diseases, Tishreen University School of Medicine, Latakia, Syria; ¹⁶³Département de Pharmacologie, CHU de Bordeaux, Université Bordeaux, INSERM U657, Bordeaux Cedex; ¹⁶⁴Department of Public Health and Biostatistics, Paris Descartes University; ¹⁶⁵Paris Municipal Department of Social Action, Childhood and Health, Paris, France; ¹⁶⁶Aura Andalucia, Jaen, Spain; ¹⁶⁷Allergy and Clinical Immunology Department, Hospital CUF-Descobertas, Lisboa, Portugal; ¹⁶⁸Institute of Medical Statistics, Informatics and Epidemiology, Medical Faculty, University of Cologne, Cologne, Germany; ¹⁶⁹Scientific Centre of Children's Health under the Russian Academy of Medical Sciences, Moscow, Russia; ¹⁷⁰Section of Otolaryngology-Head and Neck Surgery, The University of Chicago Medical Center and The Pritzker School of Medicine, The University of Chicago, Chicago, IL, USA; ¹⁷¹Hospital de Niños Orlando Alassia, Santa Fe, Argentina; ¹⁷²Hospital of the Hospitaller Brothers in Buda, Budapest, Hungary; ¹⁷³Pediatric Pneumology and Immunology, Charité Universitätsmedizin Berlin, Berlin, Germany; ¹⁷⁴ENT Department, University Hospital of Kinshasa, Kinshasa, Congo; ¹⁷⁵Department of Allergy, Immunology and Respiratory Medicine, Alfred Hospital and Central Clinical School, Monash University, Melbourne, Vic., Australia; ¹⁷⁶National Hospital Organization, Tokyo National Hospital, Tokyo; ¹⁷⁷Department of Otorhinolaryngology, Chiba University Hospital, Chiba; ¹⁷⁸Department of Otolaryngology, Nippon Medical School, Tokyo, Japan; ¹⁷⁹Centre Hospitalier Universitaire Pédiatrique Charles de Gaulle, Ouagadougou, Burkina Faso; ¹⁸⁰Cardio-Thoracic and Vascular Department, University Hospital of Pisa, Pisa, Italy; ¹⁸¹Dept. of Comparative

Medicine, Messerli Research Institute of the University of Veterinary Medicine Vienna, Medical University and University Vienna, Vienna, Austria; ¹⁸²Department of Immunology and Allergology, Faculty of Medicine and Faculty Hospital in Pilsen, Charles University in Prague, Pilsen, Czech Republic; ¹⁸³Respiratory Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy; ¹⁸⁴Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, South Korea; ¹⁸⁵Nuffield Department of Medicine, University of Oxford, Oxford, UK; ¹⁸⁶Department of Pediatrics, Nippon Medical School, Tokyo, Japan; ¹⁸⁷Center for Rhinology and Allergology, Wiesbaden, Germany; ¹⁸⁸Conseil Général de l'Economie. Ministère de l'Economie, de l'Industrie et du Numérique, Paris, France; ¹⁸⁹Département de pédiatrie, CHU de Grenoble, Grenoble cedex 9, France; ¹⁹⁰Children's Hospital Srebrnjak, Zagreb, School of Medicine, University J.J. Strossmayer, Osijek, Croatia; ¹⁹¹Karl Landsteiner Institute for Clinical and Experimental Pneumology, Hietzing Hospital, Vienna, Austria; ¹⁹²Clinic of Allergy & Asthma, Medical University Sofia, Sofia, Bulgaria; ¹⁹³Department of Pulmonary Medicine and Tuberculosis, GRIAC Research Institute, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; ¹⁹⁴Allergy Diagnostic and Clinical Research Unit, University of Cape Town Lung Institute, Cape Town, South Africa; ¹⁹⁵Academic Centre of Primary Care, University of Aberdeen, Aberdeen, UK; ¹⁹⁶LungenClinic Grosshansdorf, Airway Research Center North, Member of the German Center for Lung Research, Grosshansdorf, Germany; ¹⁹⁷Conseil Départemental de l'Ordre des Pharmaciens, Maison des Professions Libérales, Montpellier, France; ¹⁹⁸SLAAI, Mexico City, Mexico; ¹⁹⁹Allergy and Clinical Immunology Department, Hospitais da Universidade de Coimbra, Coimbra, Portugal; ²⁰⁰Association Asthme et Allergie, Paris, France; ²⁰¹Serviço de Imunoalergologia, Hospital da Luz, Lisboa, Portugal; ²⁰²Polibienestar Research Institute, University of Valencia, Valencia; ²⁰³Primary Care Respiratory Research Unit, Instituto de Investigación Sanitaria de Palma IdisPa, Palma de Mallorca, Spain; ²⁰⁴Allergy Unit, Complesso Integrato Columbus, Rome, Italy; ²⁰⁵Hospital de Clínicas, University of Parana, Parana, Brazil; ²⁰⁶Department of Allergy, Asthma and Immunology, Children's Mercy Hospitals and Clinics and Pediatrics and Medicine University of Missouri-Kansas City School of Medicine, Kansas City, MI, USA; ²⁰⁷Division of Allergy Asthma and Clinical Immunology, Emek Medical Center, Afula, Israel; ²⁰⁸Allergy and Clinical Immunology Department, Centro Médico-Docente la, Trinidad, Venezuela; ²⁰⁹The Royal National TNE Hospital, University College London, London, UK; ²¹⁰Otolaryngology and Head & Neck Surgery, CHU Rangueil-Larrey, Toulouse, France; ²¹¹Allergy Unit, Department of Dermatology, University Hospital of Zurich, Zürich, Switzerland; ²¹²Allergy and Respiratory Research Group, Medical School, Centre for Population Health Sciences, The University of Edinburgh, Edinburgh, UK; ²¹³Department of Pediatrics & Child Health, Department of Immunology, Faculty of Medicine, University of Manitoba, Winnipeg, MB, Canada; ²¹⁴Sociedad Paraguaya de Alergia Asma e Inmunología, Paraguay, Paraguay; ²¹⁵Julius Center of Health Sciences and Primary Care, University Medical Center Utrecht, University of Utrecht, Utrecht, The Netherlands; ²¹⁶Division of Allergy, Clinical Immunology and Rheumatology, Department of Pediatrics, Federal University of São Paulo, São Paulo, Brazil; ²¹⁷Kyrgyzstan National Centre of Cardiology and Internal medicine, Euro-Asian respiratory Society, Bishkek, Kyrgyzstan; ²¹⁸Pulmonary Division, Heart Institute (InCor), Hospital da Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil; ²¹⁹European Union GeriatricMedicine Society, Vienna, Austria; ²²⁰Department of Epidemiology, CAPHRI School of Public Health and Primary Care, Maastricht University, Maastricht, The Netherlands; ²²¹Centre of Pneumology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal; ²²²Division of Allergy and Clinical Immunology, University of Salerno, Salerno, Italy; ²²³Division of Immunopathology, Department of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria; ²²⁴Pneumology and Allergy Department, Hospital Clinic, Clinical & Experimental Respiratory Immunoallergy, IDIBAPS, Barcelona, Spain; ²²⁵Clinical Immunology and Allergy Unit, Department of Medicine Solna, Karolinska Institutet and University Hospital, Stockholm, Sweden; ²²⁶Department of Chest Medicine, Centre Hospitalier Universitaire Dinant-Godinne, Université Catholique de Louvain, Yvoir, Belgium; ²²⁷Pulmonary Unit, Department of Cardiology, Thoracic and Vascular Medicine, Arcispedale S.Maria Nuova/IRCCS, Research Hospital, Reggio Emilia, Italy; ²²⁸Division of Allergy and Immunology, Department of Pediatrics, Siriraj Hospital, Mahidol University Faculty of Medicine, Bangkok, Thailand; ²²⁹Pulmonary Environmental Epidemiology Unit, CNR Institute of Clinical Physiology, Pisa, Italy; ²³⁰Department of Otorhinolaryngology, HNO-Klinik, Universitätsklinikum Düsseldorf, Düsseldorf, Germany; ²³¹Asthma UK, London, UK; ²³²Department of Otolaryngology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore City, Singapore; ²³³Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC; ²³⁴Bradford Institute for Health Research, Bradford Royal Infirmary, Bradford, UJ; ²³⁵Department of Research, Olmsted Medical Center, Rochester, MN, USA; ²³⁶Cyprus International Institute for Environmental & Public Health in Association with Harvard School of Public Health, Cyprus University of Technology, Limassol, Cyprus; ²³⁷The Allergy and Asthma Institute, Islamabad, Pakistan; ²³⁸Department of Paediatrics and Child Health, Red Cross Children's Hospital, MRC Unit on Child & Adolescent Health, University of Cape Town, Cape Town, South Africa; ²³⁹Universidad Católica de Córdoba, Córdoba, Argentina; ²⁴⁰Department of Otolaryngology, Head and Neck Surgery, Beijing Tongren Hospital, Capital Medical University, Beijing, China; ²⁴¹University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia; ²⁴²Vice President for Research, University Montpellier, Montpellier; ²⁴³UVSQ, UMR-S 1168, Université Versailles St-Quentin-en-Yvelines, Paris, France; ²⁴⁴Allergy Unit, Instituto CUF Porto e Hospital CUF Porto; ²⁴⁵Health Information and Decision Sciences Department – CIDES, Faculdade de Medicina, Universidade do Porto; ²⁴⁶Faculdade de Medicina da Universidade do Porto, Porto, Portugal; ²⁴⁷GARD Executive Committee, Bahia, Brasil; ²⁴⁸EPAR UMR-S UPMC, Paris, France; ²⁴⁹Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; ²⁵⁰Member of the Global Allergy and Asthma European Network (GA2LEN); ²⁵¹Faculty of Medicine, Institute of Clinical Medicine, University of Oslo, Oslo, Norway; ²⁵²Allergy Department, 2nd Pediatric Clinic, Athens General Children's Hospital "P&A Kyriakou", University of Athens, Athens, Greece; ²⁵³Honorary Clinical Research Fellow, Allergy and Respiratory Research Group, The University of Edinburgh, Edinburgh; ²⁵⁴Department of Infection, Immunity and Inflammation, University of Leicester, Leicester; ²⁵⁵Wellcome Centre for Global Health, Imperial College; ²⁵⁶MRC-PHE Centre for Environment and Health, Imperial College, London, UK; ²⁵⁷Région Languedoc Roussillon, Roussillon, France; ²⁵⁸SLAAI, Sociedad Latinoamericana de Alergia, Asma e Inmunología, Barranquilla, Colombia; ²⁵⁹GARD Executive Committee, Moscow, Russia; ²⁶⁰ZAUM-Center for Allergy and Environment, Helmholtz Center Munich, Technische Universität München, Munich, Germany; ²⁶¹Service de Pneumologie, Hôpital Bicêtre, Inserm UMR_S999, Le Kremlin Bicêtre, France; ²⁶²MRC & Asthma UK Centre in Allergic Mechanisms of

Asthma, London, UK; ²⁶³Sorbonne Universités, UPMC Univ Paris 06, UMR_S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Equipe EPAR, Paris, France; ²⁶⁴Institute for Clinical Epidemiology and Biometry, University of Würzburg, Würzburg, Germany; ²⁶⁵Serbian Association for Asthma and COPD, Belgrade, Serbia; ²⁶⁶Department of Immunology, Monash University, Melbourne, Vic., Australia; ²⁶⁷Messerli Research Institute of the University of Veterinary Medicine Vienna, Medical University and University Vienna, Vienna, Austria; ²⁶⁸Department of Otorhinolaryngology, Head and Neck Surgery, Medical Faculty Mannheim, Universitätsmedizin Mannheim, Heidelberg University, Mannheim, Germany; ²⁶⁹Research in Real-Life, Cambridge, UK; ²⁷⁰Department of Medicine, Christian Albrechts University, Airway Research Center North, Member of the German Center for Lung Research, Kiel, Germany; ²⁷¹Clínica El Avila, 6a transversal Urb, Caracas, Venezuela; ²⁷²Regional Agency for Health and Social Care, Reggio Emilia; ²⁷³CNR Institute of Biomedicine and Molecular Immunology "A. Monroy", Palermo, Italy; ²⁷⁴Department of Pediatrics, Hospital "Archbishop Makarios III", Nicosia, Cyprus; ²⁷⁵Centre for Health Economics, University of York, York, UK

To cite this article: Bousquet J, Schunemann HJ, Fonseca J, Samolinski B, Bachert C, Canonica GW, Casale T, Cruz AA, Demoly P, Hellings P, Valiulis A, Wickman M, Zuberbier T, Bosnic-Anticevitch S, Bedbrook A, Bergmann KC, Caimmi D, Dahl R, Fokkens WJ, Gisle I, Lodrup Carlsen K, Mullol J, Muraro A, Palkonen S, Papadopoulos N, Passalacqua G, Ryan D, Valovirta E, Yorgancioglu A, Aberer W, Agache I, Adachi M, Akdis CA, Akdis M, Annesi-Maesano I, Ansotegui IJ, Anto JM, Arnavielhe S, Arshad H, Baiardini I, Baigenzhin AK, Barbara C, Bateman ED, Begh é B, Bel EH, Ben Kheder A, Bennoor KS, Benson M, Bewick M, Bieber T, Bindeslev-Jensen C, Bjerner L, Blain H, Boner AL, Boulet LP, Bonini M, Bonini S, Bosse I, Bourret R, Bousquet PJ, Braido F, Briggs AH, Brightling CE, Brozek J, Buhl R, Burney PG, Bush A, Caballero-Fonseca F, Calderon MA, Camargos PAM, Camuzat T, Carlsen W, Carr KH, Cepeda Sarabia AM, Chavannes NH, Chatzi L, Chen YZ, Chiron R, Chkhartishvili E, Chuchalin AG, Ciprandi G, Cirule I, Correia de Sousa J, Cox L, Crooks G, Costa DJ, Custovic A, Dahlen SE, Darsow U, De Carlo G, De Blay F, Dedeu T, Deleanu D, Denburg JA, Devillier P, Didier A, Dinh-Xuan AT, Dokic D, Douagui H, Dray G, Dubakienė R, Durham SR, Dykewicz MS, El-Gamal Y, Emuzyte R, Fink Wagner A, Fletcher M, Fiocchi A, Forastiere F, Gamkrelidze A, Gemiciglu B, Gereda JE, González Díaz S, Gotua M, Grouse L, Guzmán MA, Haahtela T, Hellquist-Dahl B, Heinrich J, Horak F, Hourihane JO'B, Howarth P, Humbert M, Hyland ME, Ivancevich JC, Jares EJ, Johnston SL, Joos G, Jonquet O, Jung KS, Just J, Kaidashev I, Kalayci O, Kalyoncu AF, Keil T, Keith PK, Khaltaev N, Klimek L, Koffi N'Goran B, Kolek V, Koppelman GH, Kowalski ML, Kull I, Kuna P, Kvedariene V, Lambrecht B, Lau S, Larenas-Linnemann D, Laune D, Le LTT, Lieberman P, Lipworth B, Li J, Louis R, Magard Y, Magnan A, Mahboub B, Majer I, Makela MJ, Manning P, De Manuel Keenoy E, Marshall GD, Masjedi MR, Maurer M, Mavale-Manuel S, Melén E, Melo-Gomes E, Meltzer EO, Merk H, Miculinic N, Mihalcan F, Milenkovic B, Mohammad Y, Molimard M, Momas I, Montilla-Santana A., Morais-Almeida M, Mösges R, Namazova-Baranova L, Naclerio R, Neou A, Neffen H, Nekam K, Niggemann B, Nyembue TD, O'Hehir RE, Ohta K, Okamoto Y, Okubo K, Ouedraogo S, Paggiaro P, Pali-Schöll I, Palmer S, Panzner P, Papi A, Park HS, Pavord I, Pawankar R, Pfaar O, Picard R, Pigearias B, Pin I, Plavec D, Pohl W, Popov TA, Portejoie F, Postma D, Potter P, Price D, Rabe KF, Raciborski F, Radier Pontal F, Repka-Ramirez S, Robalo-Cordeiro C, Rolland C, Rosado-Pinto J, Reitamo S, Rodenas F, Roman Rodriguez M, Romano A, Rosario N, Rosenwasser L, Rottem M, Sanchez-Borges M, Scadding GK, Serrano E, Schmid-Grendelmeier P, Sheikh A, Simons FER, Sisul JC, Skrinido I, Smit HA, Sol é D, Sooronbaev T, Spranger O, Stelmach R, Strandberg T, Sunyer J, Thijs C, Todo-Bom A, Triggiani M, Valenta R, Valero AL, van Hage M, Vandenplas O, Vezzani G, Vichyanond P, Vieg G, Wagenmann M, Walker S, Wang DY, Wahn U, Williams DM, Wright J, Yawn BP, Yiallourous PK, Yusuf OM, Zar HJ, Zernotti ME, Zhang L, Zhong N, Zidarn M, Mercier J. MACVIA-ARIA Sentinel Network for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation. *Allergy* 2015; **70**: 1372–1392.

Keywords

allergic rhinitis; ARIA; asthma; Information and communications technology; MACVIA-LR.

Correspondence

Jean Bousquet, CHRU Montpellier, 34295 Montpellier Cédex 5, France.
Tel.: 33 6 11 42 88 47
E-mail: jean.bousquet@orange.fr

Abstract

Several unmet needs have been identified in allergic rhinitis: identification of the time of onset of the pollen season, optimal control of rhinitis and comorbidities, patient stratification, multidisciplinary team for integrated care pathways, innovation in clinical trials and, above all, patient empowerment. MASK-rhinitis (MACVIA-ARIA Sentinel Network for allergic rhinitis) is a simple system centred around the patient which was devised to fill many of these gaps using Information and Communications Technology (ICT) tools and a clinical decision support system (CDSS) based on the most widely used guideline in allergic rhinitis and its asthma comorbidity (ARIA 2015 revision). It is one of the implementation systems of Action Plan B3 of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA). Three tools are used for the electronic monitoring of allergic diseases: a cell phone-based daily visual analogue scale (VAS) assessment of disease control, CARAT (Control of Allergic Rhinitis and Asthma Test) and e-Allergy screening (premedical system of early diagnosis of allergy and asthma based on online tools). These tools are combined with a clinical decision support system (CDSS) and are available in many languages. An e-CRF and an e-learning tool complete MASK. MASK is flexible and other tools can be added. It appears to be an advanced, global and integrated ICT answer for many unmet needs in allergic diseases which will improve policies and standards.

Allergic rhinitis (AR) is among the most common diseases globally (1) and ranks first in Europe (over 25% of the European population). It exists in all age groups, and it often starts early in life (2) and persists across the life cycle (3, 4). The burden and costs are substantial (5). It often impairs social life, work and school performance (6–8) and has a major impact on healthy ageing (9).

Several unmet needs have been identified. MASK-rhinitis is a simple system centred around the patient. It has been devised to fill many of the gaps using Information and Communications Technology (ICT) tools and a clinical decision support system (CDSS) based on the most widely used guideline in AR (ARIA) (10). It is a product of the European Innovation Partnership on Active and Healthy Ageing (11) and is currently being launched in 15 countries. Patient empowerment is essential to the project. MASK-rhinitis represents a novel tool to diagnose, stratify and manage patients with AR and to assess treatment efficacy. It has the potential to have major impact on health policies and planning. In the future, the combination with biomarkers will further improve the impact of MASK-rhinitis.

MACVIA-LR (Fighting chronic diseases for active and healthy ageing, <http://macvia.cr-languedocroussillon.fr>) is a reference site of the European Innovation Partnership on Active and Healthy Ageing (12). It initiated the project AIRWAYS ICPs, an integrated care pathway (ICP) for airway diseases (13).

Unmet needs in allergic rhinitis

Early diagnosis and management of patients with respiratory allergic diseases

Although AR is common in all age groups, it is very often overlooked and under-diagnosed, especially in preschool children and the elderly. The Polish Presidency of the EU Council (2011) targeted chronic respiratory diseases in children to promote their early recognition, prevention and management and, ultimately, to promote AHA (9).

Clinical diagnosis is difficult, and symptoms may relate to allergic and nonallergic rhinitis as well as rhinosinusitis (14). There is a need for a simple diagnostic tool.

Patient stratification

The treatment of AR is now well established. Although the majority of patients present with controlled symptoms during pharmacologic treatment, 10–20% are still uncontrolled and should be characterized as suffering from severe chronic

upper airway disease (SCUAD) (15). Patients with SCUAD have impaired quality of life, sleep, school and/or work performance (16, 17).

Many AR patients are over 65 years of age. The presentation of the disease, as well as the efficacy and safety of treatments, may differ in older adults. However, data are not yet available from RCTs.

Time of onset of the allergy season

For patients allergic to pollen, knowledge of the onset of the pollen season is of vital importance in order to start treatment as early as possible for the control of symptoms. When travelling, patients are often concerned about potential symptoms and/or bothered by symptoms outside their usual symptom ‘window’. It is therefore of importance to forecast the onset of the pollen season and to characterize seasons in different places.

Pollen counts are currently proposed to assess the exposure of pollen-allergic patients. However, counts often correlate imperfectly with symptoms (18–22) as (i) they do not represent allergen exposure alone (19, 23, 24), (ii) the number of pollen grains needed to elicit symptoms is not well defined and differs depending on the pollen species, (iii) there is a nonlinear relationship between pollen and allergic symptoms (25, 26) and (iv) interactions between pollens and atmospheric conditions or air pollution may exist (27, 28). Furthermore, for large geographical areas, pollen samplers are sparsely located. Patients may live at a distance from the sampler, and the levels of allergens in their environment may differ quite extensively from the levels detected by the sampler. Individualized pollen counts would be preferable (29) but are not feasible on a large scale. Finally, pollen counts are only available several days after onset of the season.

The assessment of allergen content in the air is feasible using antibody-based methods (18, 19, 30) or the biomolecular identification of pollen genomes (31). However, sophisticated methods are required which may not account for all of the pollen species in the ambient air, and individual measurements are not feasible.

Meteorological data may, in the future, be of interest to predict the onset of the season, but more information is needed (32–35). Combining several data sources using advanced data engineering may offer advances, but this method is still complex and not available for all pollen species in many different areas (36, 37).

Internet-based surveillance systems using search engine queries (38) and social media (39) are recent techniques with the potential to extend or even substitute the more costly dis-

Abbreviations

AHA, Active and Healthy Ageing; AIRWAYS ICPs, Integrated Care Pathways for Airway diseases; AR, Allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; CARAT, Control of Allergic Rhinitis and Asthma Test; CDSS, Clinical decision support system; EIP, European Innovation Partnership; ICP, Integrated care pathway; ICT, Information and communications technology; MACVIA-LR, Contre les MALadies Chroniques pour un Vieillessement Actif en Languedoc-Roussillon; MASK, MACVIA-ARIA Sentinel Network; MeDALL, Mechanisms of the Development of Allergy (FP7); QOL, Quality of life; RAPP, RhinAsthma Patient Perspective; RCT, Randomized control trial; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire; SCUAD, Severe Chronic Upper Airway Disease; U-BIOPRED, (IMI); VAS, Visual analogue scale.

ease surveillance systems (40). A few studies analysing online searches of pollens, rhinitis symptoms and allergies have shown associations with pollen counts (41). The analysis of online searches, in particular using Google trends, has shown potential in predicting changes in flu infections (42) and in other areas of medicine (38). Nevertheless, this type of big data analysis is just beginning (38) and more research is needed to prove its value in predicting the onset of allergic rhinitis symptoms due to the pollen season (43). Moreover, the onset of the pollen season cannot be predicted using these models.

In the meantime, other novel approaches such as a personalized pollen-related forecast (44, 45) and an ICT sentinel network based on patients' symptoms should be developed. However, these approaches need to be simple and user friendly.

Continuous management of symptoms during allergen exposure

Allergen exposure varies daily, and patients with respiratory allergic symptoms need regular monitoring of symptoms in order to optimize treatment. A clinical decision support system (CDSS) may be beneficial to optimize treatment and assess disease control after commencement of the allergy season. Moreover, such a system has the potential to improve patients' compliance to treatment. Guided management of allergic diseases including asthma was found to be effective (46, 47) with clear evidence provided by the Finnish Asthma Programme (48) and the Allergy Programme (49, 50).

Comorbidity assessment

Conjunctivitis, chronic rhinosinusitis and asthma are frequent AR comorbidities that need to be identified and treated to achieve good AR control (51). ICPs that include asthma screening and assessment, as recommended by ARIA (Allergic Rhinitis and its Impact on Asthma) (6, 7), may result in improved outcomes and should be tested. In addition, optimal AR control may facilitate the control of concomitant asthma.

Needs for a multidisciplinary team for an ICP

Integrated care pathways (ICPs) are structured multidisciplinary care plans which detail essential steps in the care of patients with a specific clinical problem (52). They promote the translation of guideline recommendations into local protocols and their subsequent application to clinical practice. An ICP forms all or part of the clinical record, documents the care given and facilitates the evaluation of outcomes for continuous quality improvement (53). ICPs can help empower patients and their care providers (health and social). They differ from clinical practice guidelines as they focus on the quality and co-ordination of care. ICPs need to have a mechanism for recording variations/deviations from planned care. Variation between recommendations and practice identified within an ICP should be noted as a variance (54, 55). In AR, there is a need for ICPs to combine the views of patients, pharmacists, primary care physicians, specialists, and other healthcare professionals.

Biomarkers in respiratory allergic diseases

Biomarkers are of great importance in respiratory allergic diseases and asthma, and a large body of research is focusing on their identification and validation. Biomarker identification can be based on systems medicine approaches combining transcriptomics, proteomics, epigenetics and metabolomics in large patient cohorts. One recently completed EU project, MultiMod, resulted in a generally applicable strategy to integrate such data for diagnostic purposes using systems medicine principles (56). Two EU-funded projects are currently ongoing: U-BIOPRED (IMI) in severe asthma (57) and MeDALL (FP7) in allergy (58, 59). MeDALL has already made critical observations concerning IgE biomarkers for the diagnosis and prognosis of allergic diseases (2, 60). It is hoped that these projects will help identify biomarkers to enhance personalized medicine (61, 62) and to improve patient stratification and clinical trials. Another ongoing EU project, CASyM, has generated a road map for the implementation of systems medicine in clinical research and practice (<https://www.casym.eu/>).

Innovation in clinical trials

In randomized controlled trials (RCTs), it is essential to have clarity with regard to the definitions of disease severity and control as well as comorbidities and risk factors (e.g. smoking). RCT outcomes should be validated and standardized, so that meaningful comparisons between RCTs can be made (63). Several gaps exist in RCTs in respiratory allergy. Among them the importance of the placebo effect and the evaluation of efficacy using a single assessment tool combining symptoms, medications and quality of life (64). Novel tools for the evaluation of RCTs on AR and its common comorbidities are needed, if possible using ICT.

Climate change effects on allergic diseases

Allergy prevalence continues to grow due to novel interactions between known allergens and other environmental factors. An increase in the prevalence and severity of allergy and asthma is anticipated due to climate changes (65). Worsening ambient air pollution and altered local and regional allergen production (66) and reduction in biodiversity may play a significant role (67). This anticipated higher allergic disease burden will affect clinical practice as well as policies and public health planning.

Patient empowerment

To satisfy patient expectations, asthma and AR should be appropriately diagnosed and controlled. Patients need to be motivated to become educated and to actively increase their own health literacy to be able to take over the responsibility of their own specific condition. Patient organizations have been involved in the design, dissemination and implementation of ARIA. ICT can empower patients and thus enable them to define specific goals and to monitor disease status and control. It can also support the patient's decisions.

Tools

ARIA

ARIA was initiated during a WHO workshop in 1999 (published in 2001) (6, 7). The ultimate aim of ARIA is to achieve control of AR globally. ARIA has reclassified AR as mild/moderate-severe and intermittent/persistent. This classification closely reflects patients' needs and underlines the close relationship between rhinitis and asthma. A module devoted to the pharmacist exists (68). In its 2010 Revision, ARIA developed clinical practice guidelines for the management of AR and asthma comorbidities based on GRADE (Grading of Recommendation, Assessment, Development and Evaluation) (69). ARIA is disseminated and implemented in over 60 countries of the world (10). ARIA has been endorsed by several ministries of health.

Variance has been tested and it was found that the ARIA classification of mild vs moderate-severe and intermittent vs persistent rhinitis is valid. A modified ARIA severity classification has also recently been validated as mild, moderate and severe, both in adults (70) and children (71), although its impact on treatment stratification remains an unmet need.

The 2015 ARIA revision leading to ICPs was finalized and presented at the AIRWAYS ICPs meeting in Lisbon 1–2 July 2015 (Figure 1).

Measures of allergic rhinitis control

Concepts of disease severity, activity, control and responsiveness to treatment are linked but constitute different domains (72). Control and severity are not well delineated in AR (72).

Severity is the loss of function in the target organ(s) induced by disease (73). It is important to highlight that severity may vary over time and needs to be regularly re-evaluated (74). Control is the degree to which therapy goals are currently met (74) such as glycemic control in diabetes (75), and can be assessed in patients before or during treatment to guide therapy. However, for AR, the patients' view of severity relates to the negative impact that rhinitis has upon life; control is a measure by which their symptoms are alleviated.

Measures of AR control include (i) symptom scores, (ii) patient self-administered visual analogue scales (VAS) (16, 76–81), (iii) objective measures of nasal obstruction (such as peak nasal inspiratory flow, acoustic rhinometry and rhinomanometry) (82), (iv) a recent modification of the ARIA severity classification (83), (v) patients' reported outcomes such as quality of life (QOL) (7, 63) scores with several items (80, 84) or composite symptom-medication scores (85). However, it is important to make the score for clinical use simple and responsive to change.

VAS is a psychometric response scale for subjective characteristics or attitudes used in a large variety of diseases. The continuous (or 'analogue') aspect of VAS differentiates it from discrete scales such as the Likert scale. The sensitivity and reproducibility of VAS results are very similar, although the VAS may outperform the other scales in some cases (86, 87).

In AR, VAS for all nasal symptoms appears to be sufficient to appreciate disease control (88) and is particularly relevant to primary (89) or pharmacy care (68). VAS can be used in all age groups including preschool children (guardian evaluation) (90) and the elderly (91). Furthermore, it can be used in a wide variety of languages (81, 91–97). VAS levels vary with the ARIA classification in many languages (76, 79,

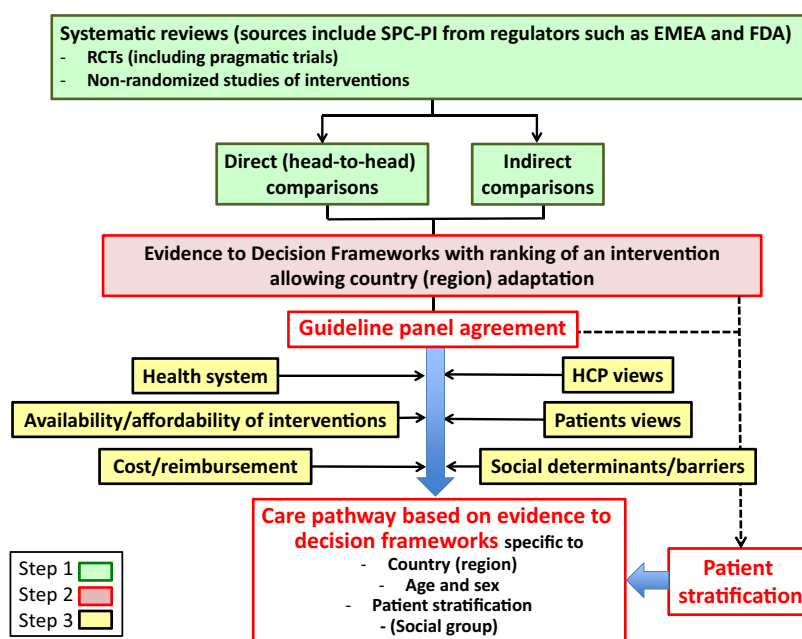


Figure 1 ARIA 2015.

81, 98). A VAS level of 50 mm is suggestive of moderate–severe AR (99–101) although in some studies the cut-off was of over 60 mm (94). VAS was used to define SCUAD (16), and patients with a low VAS level after treatment had a considerably improved Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) or work productivity (WPAI-AS). However, those with a level of over 50 mm had no improvement. VAS has been validated in cell phones (Sarah Acaster, personal communication).

VAS was found to be responsive to change in real-life cluster-randomized trials (102, 103). The minimal clinically relevant difference was set for a VAS level of 23 mm during treatment, whatever the baseline VAS level (104). A level of over 23 mm appears to be a relevant cut-off. VAS changes appear to encompass both symptoms and disease-specific QOL (88, 104).

VAS was highly responsive to change in double-blind, placebo-controlled RCTs (92, 93, 102, 105–108). These multicentre studies in Europe and Canada showed that patients easily cope with VAS in different languages.

These studies combine to indicate that VAS may be a simple and useful tool for the assessment of AR control and to follow the efficacy of treatment.

Electronic monitoring of allergic diseases

e-Allergy screening: Premedical system of early diagnosis of allergy and asthma based on online tools

The late diagnosis of allergic diseases and asthma is a serious problem. Patients with first symptoms of respiratory allergies are often misclassified in primary care. As a result, patients are either untreated or treated symptomatically, generally for a long period of time. This behaviour is detrimental to the patient, the healthcare system and the society, as it impacts on indirect costs (5).

One solution to this problem was presented in 2011 at a conference of experts during the Polish Presidency of the EU Council (109). It is an e-Allergy – premedical system capable of providing an early diagnosis of allergy and asthma on the basis of online tools. The concept is based on a screening questionnaire with built-in algorithms. It assesses individual risk of allergic diseases and includes 24 questions. The process takes about 5 minutes. The questions are selected depending on previous responses. The result is displayed in the form of risk calculation for the selected allergic diseases (asthma, allergic rhinitis, atopic dermatitis and allergy to Hymenoptera venom).

To develop the algorithm, data from the Epidemiology of Allergy in Poland (ECAP) (www.ecap.pl) were used (110). Over 20 000 people responded to the study questionnaire, and almost 5000 were subjected to additional allergological tests. Various advanced methods of statistical analysis, including an artificial neural network, have been used to develop the algorithm. The system is calibrated to maximize the effectiveness of a group of people suffering from allergic diseases.

E-allergy screening can be used both by the public with suspected allergies and physicians. The initial diagnosis can lead to an evaluation. It is performed by a primary health-

care professional and, if needed, confirmed by a specialist. The role of e-allergy is to support, not replace, the physicians and also to speed up the process of unrecognized allergic diseases by proper management.

Daily tool based on VAS using cell phones

MASK aerobiology, approved by AIRWAYS-ICPs, is a very simple IOS/Android App. It is already available and is being expanded to other systems with interoperability. Patients selected by physicians trained in allergy represent the sentinels for the onset of the season. The VAS represents a reliable and valid measure of rhinitis control (10, 72) (Figure 2). It can be used across the life cycle (90, 91, 111).

CARAT

Asthma frequently occurs in association with allergic rhinitis, and a combined management approach has been suggested. The Control of Allergic Rhinitis and Asthma Test (CARAT) is the first questionnaire to assess the control of both diseases concurrently (112–115). An overall score of more than 24 indicates good control of asthma and rhinitis, while a change of four points between two occasions indicates a clinically relevant change (115). In addition, answers to individual questions may be used to identify the specific problems of a patient (e.g. night symptoms or overuse of reliever medication). However, to have an impact on healthcare, it needs to be disseminated and adopted. At present, the adaptation of CARAT for use in different languages and cultures is being led by volunteer researchers and clinicians in 15 countries. Website and smartphone applications have been developed, and a free open model of distribution has been adopted to contribute to the dissemination of CARAT. CARAT can be used in a range of settings and circumstances in primary and secondary care for clinical, research and audit purposes, and also in ambulatory pharmacies (116). It can be used both in adults and children (117, 118) and strengthens the partnership between patients and doctors in the management of asthma and rhinitis. CARAT can be administered every 2–4 weeks both in paper and electronic forms (119) and represents an additional tool for daily assessment.

- ? Indicates a response is required
- Users touch the line to indicate response and a 'marker' appears in that location
- The marker can be moved with a finger to mark the line where intended
- Once the mark is placed the user then touches 'next' to move on to the next VAS
- Each VAS is completed once daily

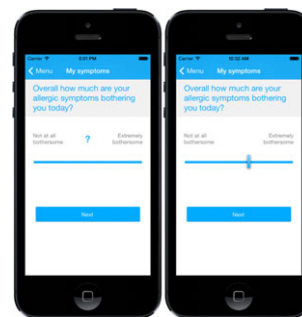


Figure 2 MASK aerobiology.

RhinAsthma Patient Perspective

'RhinAsthma Patient Perspective (RAPP)' is the first valid questionnaire to assess the individual health-related QoL of patients with asthma and rhinitis in clinical practice. It is a simple eight-question tool with good measurement properties and sensitivity to health changes. RAPP is easy to complete and score, and the results enable immediate interpretation both for the physician and for the patient. The score, calculated by summing the responses of each item, ranges from 8 (no impact on QoL) to 40 (the worst possible QoL). A cut-off point of 15 has demonstrated the best sensitivity and specificity in discriminating the achievement of an optimal health-related QoL. A change of two points in the RAPP score was found to be the minimal clinical difference that patients perceived as important, either 'beneficial or harmful.'

A new tool for the smartphone has been developed (120).

Clinical decision support system

Identifying the most suitable patients for whom an intervention is appropriate is critical for the delivery of a cost-effective health system. In many diseases, the management of patients uses ICT tools including integrated care pathways, e-health and CDSS. This has made a significant improvement and has sometimes led to a change of management in health systems. A CDSS (121, 122) immediately proposes advice for (standardized) pharmacologic treatment defined by the physician during a consultation before the pollen season. Care pathways based on AIRWAYS ICPs (13) will guide the healthcare professional. Patients with SCUAD are defined as those resistant to treatment despite optimal treatment (VAS level > 50%). Moreover, individual complaints of rhinitis, conjunctivitis or asthma are monitored by the system (123). Computer-analysed VAS responses may be measured using discrete values due to the discrete nature of computer displays, and VAS can be used in internet-based questionnaires (124).

Bias reduction, patient empowerment and identification of new markers through a Living Lab approach

Systematically collecting and mining/analysing data from patients' mobile phones where they can enter quantitative and qualitative information is indeed a promising use of innovative health technologies (125). This should allow, on an almost continuous mode, a long-term close monitoring of and connection to the patient. To our knowledge, this has not been addressed before by any other technology. However, a major requirement for the implementation of such clinical protocols is the validity of data (125, 126). In validating such protocols, bias by the degree of usage of devices by the patients and bias in information input due to the context or human factors need to be identified and eradicated; such factors are very difficult to control. The overall bias will normally be balanced by the long-term use of the application by the patient, as patients' data are always compared to their previous declarations. However, it is possible and desirable to improve the results and reduce the time necessary to obtain them. Contrary to drugs, where the administration of

medications to patients may be appropriately controlled during clinical trials, the usage of mobile phones, especially at home, is known to depend heavily on (i) the usability of such devices and supported applications, (ii) their context of use (including ongoing activities, social environment, presence of third parties), and (iii) the constraints they impose on patients, with a strong probability of weak compliance, hazardous on/off usage or even rejection and abandon by the patients (127, 128). Similarly, the adoption of these new practices, including participation and interactions from family members or professionals, is an issue (129).

Inappropriate and/or irregular use of the system – a social and behavioural bias – cannot be identified in the data analysis. This can compromise the scientific validity of the entire results. Furthermore, opportunities to address behavioural or psychological markers are not seized, even when they are already identified as possible candidates by practitioners. It is therefore both mandatory and potentially highly valuable to properly address usage problems at the patients' end and to ensure the usability of a selected mobile application.

The involvement and commitment of the patients and of the healthcare and social professionals involved from the start and during all phases of the project is the only way to address the problem. It is highly recommended to adopt a co-design/co-evaluation and user-centred design approach to the project (130). This will be a lever to gain long-term adherence of both patients and health care providers. The participation of Living Labs for Health and Autonomy will secure the many tasks to be carried out throughout the project with the users and all participants. It will ensure a proper usage validity of the collected data right from the first phases:

- Analysis of the context of use.
- Co-design of the protocol with patients and physicians.
- Evaluation/optimization of device usability, human machine interface and adoption potential.
- Follow-up of device usage during the collecting phase.

Additional tools

An e-CRF and an e-learning tool will be added to the MACVIA-ARIA suite of instruments.

MASK: the global and integrated ICT answer for unmet needs in allergic rhinitis : empowerment of patients

Electronic monitoring of the pollen season

Mobile phone messaging facilitates the management of AR (131) and chronic diseases (132, 133). Using cell phones with a touch screen, patients are geolocalized and can evaluate their symptoms daily by VAS (Figure 2). At the predicted time of the pollen season, based on local calendars and/or forecast models where available, patients receive an SMS and an E-mail indicating that they should monitor VAS daily for global symptoms on the dedicated mobile device. This information is coded and sent to a central database. Daily, 4 VAS assessments (global evaluation, nasal, ocular and bronchial

symptoms) are completed by the patient on a cell phone. The information is sent to a clinical decision support system (CDSS) for an optimal management of all the patients using the system. The system is initially being deployed in 13 countries with 14 languages (translation and back-translation, cultural adaptation and legal issues).

MASK-aerobiology is monitored daily and will be completed with CARAT at the onset of the pollen season and thereafter every 2 weeks (Figure 3).

Applications include information to patients and to the media with regard to the pollen season, optimal management of the patients with allergic symptoms, clinical trials, research and climate evaluation (Figure 4).

CDSS based on ARIA 2015 to optimize control during allergen exposure and stratification of patients

The chronic respiratory diseases CDSS (AIRWAYS-CDSS) is based on the ARIA 2015 revision (in preparation) and will

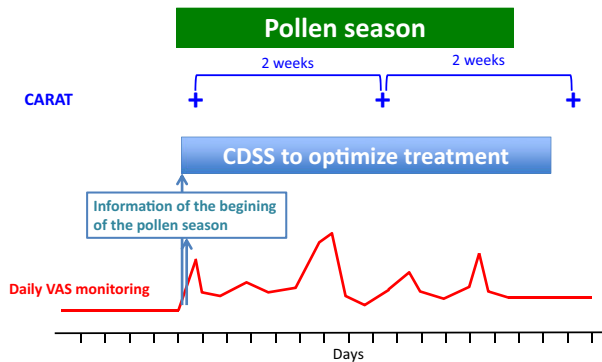


Figure 3 Combination of MASK-aerobiology, CARAT and CDSS.

enable the standardization of patient management. Patients with uncontrolled disease based on VAS e-health despite optimal treatment according to guidelines will be considered as SCUAD (severe chronic upper airway diseases) (15) (Figures 4–6). However, the physicians will determine the strategy to be used for their individual patients. All medications available in the given country are listed in the App according to the IMS list of drugs. The CDSS will be available at the end of 2015.

These two innovative tools (allergy sentinel network and AIRWAYS-CDSS) will be combined in MASK-rhinitis and will make it possible to assess some of the unmet needs of clinical trials in allergic diseases. They will allow optimal management of the patients, assessment of control, compliance to treatment as well as patient stratification.

Validation of ARIA guidelines

There is a need to validate guidelines using cluster-randomized trials to define whether the new strategy is more effective than a free treatment choice. The International Consensus of Rhinitis (102) and ARIA 2001 (103) were both validated. MASK will also be validated using the same methodology (Figure 7).

MASK-rhinitis, a single tool for the ICP

An ICP has a focus on an interactive and multidisciplinary pathway (Figure 8). MASK can be used by:

- Patients, to screen for allergic diseases (in a later stage, biomarkers will help to confirm the allergic origin of the symptoms).
- Pharmacists, to guide them in the prescription of OTC medications and direct the uncontrolled patients to physicians.

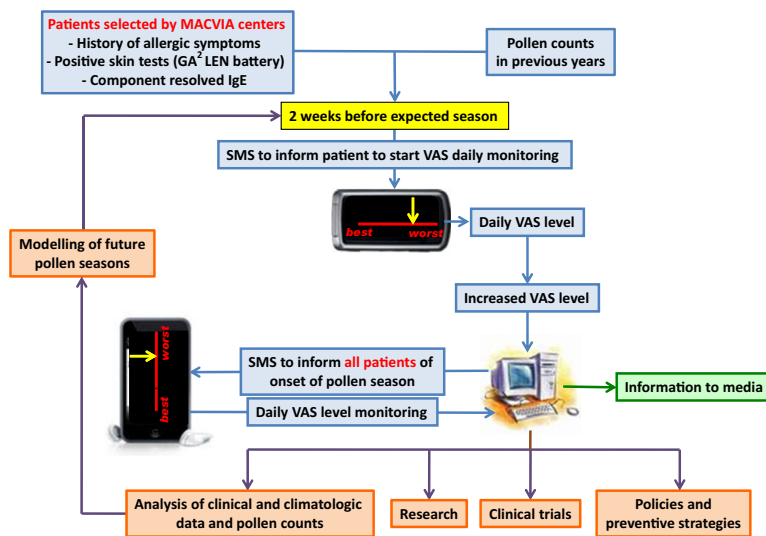


Figure 4 The MASK ICT strategy and usage.

- The primary care physician, to prescribe appropriate treatment and to follow up with the patient according to the physician's instructions (CDSS) and assessment of control.
- The specialist, if there is failure to gain control by the primary physician.

These tools should be customized to be applicable globally.

Clinical trials

These three innovative tools (CARAT, allergy sentinel network and AIRWAYS-CDSS) are combined in MASK-rhinitis and will make it possible to perform innovative clinical trials in AR (Figure 9) including trials of allergen-specific immunotherapy (64, 134).

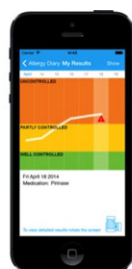
- Phenotypic characterization of allergic patients with stratification of patient severity, characterization of patients with SCUAD and characterization of patients to be treated.
- Randomized controlled trials (placebo-controlled or real-life cluster-randomized trials).
- Follow-up of patients in clinical settings during treatment.
- Follow-up of patients in clinical settings after treatment has been stopped (persistent effects).
- Assessment of side-effects due to treatment.

Implementation and application of MASK-rhinitis

Promotion of active and healthy ageing

The developmental origin of ageing is on the EU political agenda. The Polish Priority of the EU Council (2011) promoted the recognition, prevention and management of CRDs in children to ultimately impact AHA (1095). The developmental determinants of chronic diseases in ageing were reinforced during the Cyprus Presidency of the EU Council (2012), which proposed to fight against NCDs across the life cycle (135). A meeting at the European Parliament organized by the Region Languedoc Roussillon under the auspices of the Cyprus EU Priority (November 2012) was focused on CRDs (136). MASK-rhinitis will help to detect symptomatic

- In case of continued high scores the feedback message will display an appropriate message in red type and a warning icon will mark the graph
- Prompts users to discuss their diary data with their health care provider



Aim: get to 'green' and stay there

Figure 5 Screen of the App.

patients early, to improve management, to increase school and work productivity and, ultimately, to promote AHA.

Early detection of symptomatic patients

One of the major problems of patients suffering from pollen allergy is the identification of the onset of the pollen season at home as well as alertness when pollen peaks are to be expected. Another problem is when travelling to regions where the seasons of pollens eliciting symptoms may differ compared to home (Table 1). As patients will be geolocalized, they will be informed about the level of the pollen season and will also be able to determine the season when travelling using MASK-rhinitis.

Stratification of patients with severe allergic diseases

Patient stratification is needed to identify patients with SCUAD, those for whom specific immunotherapy or other interventions are appropriate. This is critical for the delivery of a cost-effective health system. Although all studies are not consistent, in many diseases, ICT tools, ICPs, e-health and CDSS are likely to define the phenotypes of allergic patients. The main challenge for allergic diseases in the 21st century is to understand their complexity. The vast majority of AR patients can be treated using a simple algorithm. However, a substantial number of these patients are uncontrolled despite treatment (16) and require a personalized (tailored) approach.

Clinical trials

In specific immunotherapy RCTs, it is recommended to monitor pollen counts in order to determine the onset of the season and to correlate counts with symptoms. As discussed earlier, pollen counts alone may misrepresent exposure, especially if performed at a locality that is remote to that of a particular patient. As a result of such potential confounders, unconvincing data have been produced and a placebo-based

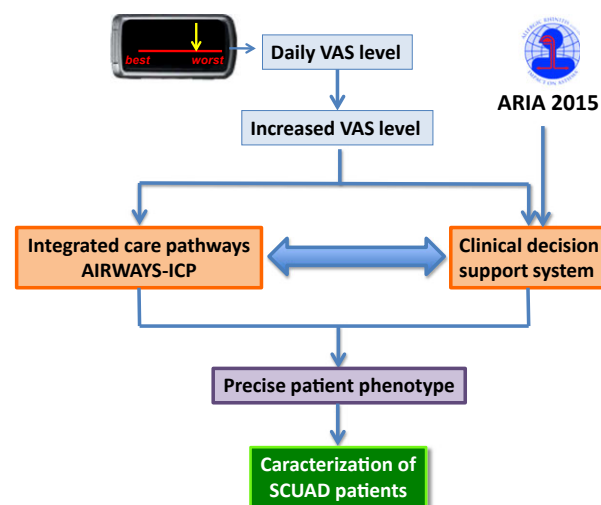


Figure 6 MASK CDSS.

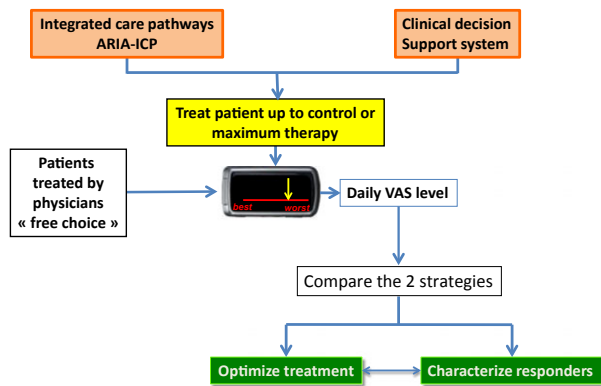


Figure 7 Validation of MASK in a cluster-randomized trial to evaluate guidelines.

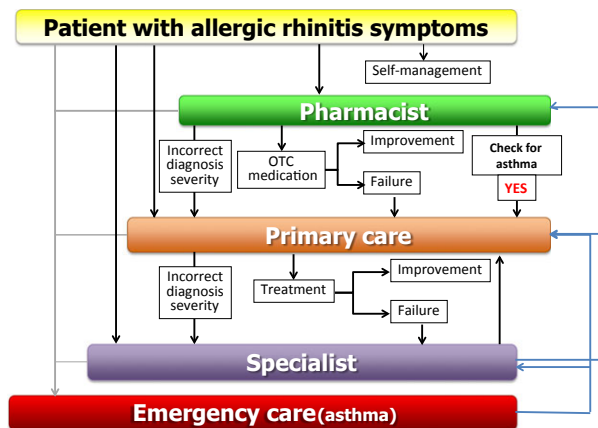


Figure 8 ICP for MASK-rhinitis.

method was found to be more effective (137). Moreover, there is a need to define the peak pollen season. MASK-rhinitis is suitable for this approach (64).

Scientific studies

Not all patients respond to pharmacologic treatment and/or immunotherapy. Research is needed in well-phenotyped patients to find novel therapeutic approaches. MASK-rhinitis can help characterize patients so that they can be stratified in further analyses. Global partnerships and platforms should ensure the application of standard methodology and protocols in the collection and sharing of samples and data (138).

Assessment of the effects of climate change and land use

Climate change impacts aeroallergens, particularly pollen (139) and moulds (140). The potential effect of land-use changes on pollen release may interact with climate change (141). Allergenic pollens are well known in Europe (66), but climate change can exert a range of effects on pollen (142–146). Pollination may start earlier in the future due to climate change (147, 148). The duration of the pollen season

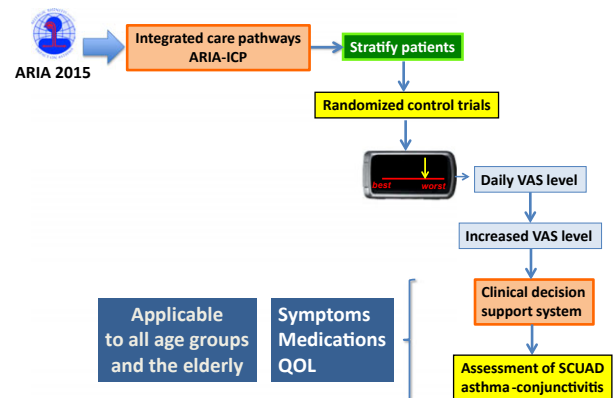


Figure 9 Clinical trials using MASK-rhinitis.

Table 1 Implications of MASK-rhinitis in early detection of pollen allergy

Early premedical diagnosis
Optimal treatment proposed to control symptoms and prevent severe disease (e.g. asthma exacerbations)
Optimal duration of the treatment
Reduction in costs incurred by pollen allergy

is extended in some species. Some plants produce a greater quantity of pollen (149–151) or pollen with stronger allergenicity (152–155) under modified climatic conditions. New allergenic pollen types can appear and result in patients developing new allergies (e.g. ragweed pollen). The pattern of change will vary regionally depending on latitude, altitude, rainfall and storms, land-use patterns, urbanization, transportation and energy production (156).

An integrated approach is needed to anticipate a higher allergic disease burden that will affect clinical practice and public health planning. A number of practical prevention strategies need to be proposed to meet this unprecedented public health challenge and to combat inequities. Both adaptation and mitigation will be needed to counteract the effects of climate change in allergy (Table 2).

Implementation of the European Environment and Health

Continued support will be provided to research addressing the aims of the major policy initiatives such as the European

Table 2 Implications of MASK-rhinitis in climate change and land use

To detect new sensitizations using pollen counts or derived methods
To detect changes in pollen seasons
To develop policies for prevention

Environment and Health Action Plan (2004–2010), the Fifth Ministerial Conference on Environment and Health and the EU Sustainable Development Strategy with its environment and public health components. MASK-rhinitis also includes strong socio-economic perspectives. In the medium term, it will ensure the engagement of relevant stakeholders (e.g., user groups, civil society organizations, policymakers) and it will cultivate a multidisciplinary approach (including researchers from social sciences and humanities).

Policies and public health planning

In clinical epidemiology and public health, a uniform definition of AR and severity is needed to identify prevalence, burden and costs, to improve quality of care and to optimize healthcare planning and policies.

MASK: from the ARIA 2015 guideline to an integrated health system for allergic rhinitis and its asthma comorbidity

There is an urgent need to propose an innovative health system for one of the most common global diseases. Around 20% of the EU population suffers from AR and the costs are very high, particularly the indirect costs. Although most patients can self-manage their symptoms, many need OTC drugs from the pharmacists and a few (but still in millions of subjects) need medical advice. Fewer, but still in millions, will need specialist advice. It is very important that a common language is used between patients and pharmacists, primary care and specialists. MASK is able to provide this common language using e-health and a very simple tool (VAS). Moreover, the CDSS will help patients to self-manage under the control of their physicians. Adding CARAT or other tools, an economic evaluation can be provided to assess the benefits and cost savings (indirect and direct costs) of interventions (5). A warning on asthma is in place in MASK allowing the assessment of this important comorbidity in AR patients. Reimbursement patterns can also be monitored and health system stratification made possible (157). MASK based on ARIA 2015 appears to be in a unique position to make the links between all stakeholders.

Conflicts of interest

Elisabeth Bel: reports grants from Chiesi and GSK outside the submitted work, and personal fees from Cipla, Sanofi/Regeneron, GSK, and Novartis, outside the submitted work; Jean Bousquet: has received honoraria for: Scientific and advisory boards – Almirall, Meda, Merck, MSD, Novartis, Sanofi-Aventis, Takeda, Teva, Uriach. Lectures during meetings – Almirall, AstraZeneca, Chiesi, GSK, Meda, Menarini, Merck, MSD, Novartis, Sanofi-Aventis, Takeda, Teva, Uriach. Board of Directors – Stallergènes; Warner Carr: Clinical Research, Merck, Mylan, Regeneron, Genentech, Novartis, Oriel, Afferent, Teva- Consultant, Teva, Meda, AstraZeneca, Alcon, Allergan, Merck, Boehringer Ingelheim – Honorarium and Speakers Bureau, Teva, Meda, AstraZe-

neca, Mylan, Alcon, Allergan; Thomas Casale: reports personal fees from Circassia, grants from Merck, grants from Stallergènes, outside the submitted work; Adnan Custovic: reports grants from Medical Research Council, grants from The JP Moulton Charitable Foundation, grants from North West Lung Research Centre Charity, grants from European Union 7th Framework Programme, grants from National Institute of Health Research, personal fees from Novartis, personal fees from Thermo Fisher, personal fees from AstraZeneca, personal fees from ALK, personal fees from GlaxoSmithKline, outside the submitted work; Ronald Dahl: Consulting, given lectures for: Boehringer-Ingelheim, Novartis, TEVA, MEDA, Pfizer, ALK-Abello, Vectura, AZ, GSK, CIPLA; Ulf Darsow: has been speaker, investigator and/or been a member of advisory boards for Allergopharma, ALK Abello', Bencard, GSK, Hermal, MEDA, Novartis Pharma, Stallergènes, Stiefel; Pascal Demoly: consultant (and speaker) for Stallergènes, ALK, Circassia and Chiesi and a speaker for Allergopharma, Merck, AstraZeneca, Menarini and GlaxoSmithKline. Investigator for Menarini, Pierre Fabre Médicaments, Stallergènes and ALK; Judah Denburg: is CEO and Scientific Advisor of the Allergy, Genes and Environment Network of Centres of Excellence (AllerGen NCE Inc); Alain Didier: have received honorarium for talks from Astra Zeneca, GSK, MSD, Novartis, Stallergènes and has consulting arrangement with GSK, Novartis, Stallergènes and Allergo (ALK); Anh Tuan Dinh Xuan: has received honoraria from Aerocrine, Chiesi and Stallergènes for invited lectures during satellite scientific symposia of national and international meetings during the last 3 years; Stephen Durham: consultancy fees from ALK Abello, Circassia, Merck USA, Biomay and Leti, manufacturers of allergy vaccines. Research funding via Imperial College from Merck, ALK Abello and Biotech Tools; Mark Dykewicz: Merck (Consultant) and Novartis (research funding); Joao Fonseca: a member of advisory boards for Boehringer Ingelheim and Novartis, has received payment for lectures and services from A. Menarini, Aerocrine, AstraZeneca, Merck Sharp Dohme, Novartis, Teva; Carlos Ivancevich: Chief Editor of the WAO website, Interasma website and the Latin American Society of Allergy, Asthma and Immunology website. Collaborate with the laboratory Faes Pharma of Spain as scientific advisor on social media and speaker at symposiums of Sanofi-Aventis; Tari Haatela: reports personal fees from Boehringer Ingelheim, MSD and OrionPharma, outside the submitted work; Marc Humbert: has relationships with drug companies including Astrazeneca, Chiesi, GSK, Merck, Novartis, Pfizer, Roche, Sanofi and TEVA. In addition to being an investigator in trials involving these companies, relationships include consultancy service and membership of scientific advisory boards; Michael Hyland: reports grants and personal fees from Novartis, during the conduct of the study; personal fees from GSK, outside the submitted work; Sebastian Johnston: reports grants and personal fees from Centocor, grants and personal fees from Sanofi Pasteur, grants and personal fees from GSK, grants and personal fees from Chiesi, grants and personal fees from Boehringer Ingelheim, personal fees from Grünenthal, grants and personal fees from Novartis, grants,

personal fees and Shareholding from Synairgen, outside the submitted work; In addition, Dr. Johnston has a patent Blair ED, Killington RA, Rowlands DJ, Clarke NJ, Johnston SL. Transgenic animal models of HRV with human ICAM-1 sequences. UK patent application No. 02 167 29.4, 18 July 2002 and International patent application No. PCT/EP2003/007939, 17 July 2003. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. Anti-virus therapy for respiratory diseases. UK patent application No. GB 0405634.7, 12 March 2004. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. Interferon-Beta for Anti-Virus Therapy for Respiratory Diseases. International Patent Application No. PCT/GB05/50031, 12 March 2004. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. The use of Interferon Lambda for the treatment and prevention of virally-induced exacerbation in asthma and chronic pulmonary obstructive disease. UK patent application No. 0518425.4, 9 September 2005. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. Anti-Virus Therapy for Respiratory Diseases. US Patent Application – 11/517,763, Patent No. 7569216, National Phase of PCT/GB2005/050031, 04 August 2009. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. Interferon-beta for Anti-Virus Therapy for Respiratory Diseases. European Patent Number 1734987, 5 May 2010. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. Anti-Virus Therapy for Respiratory Diseases (IFNb therapy) Hong Kong Patent Number 1097181, 31 August 2010. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. Anti-Virus Therapy for Respiratory Diseases (IFNb therapy). Japanese Patent Number 4807526, 26 August 2011. licensed, a patent Wark PA, Johnston SL, Holgate ST, Davies DE. Interferon-beta for Anti-Virus Therapy for Respiratory Diseases. New Hong Kong – Divisional Patent Application No. 11100187.0, 10 January 2011. licensed, and a patent Burdin N, Almond J, Lecouturier V, Girerd-Chambaz Y, Guy, B, Bartlett N, Walton R, McLean G, Glanville N, Johnston SL. Induction of cross-reactive cellular response against rhinovirus antigens European Patent Number 13305152, 4 April 2013. Pending; Jocelyne Just: on the advisory board for Novartis, ALK, and Thermofischer; is a speaker for AstraZeneca, Novartis, ALK, Stallergens, Teva; and has received grants from Novartis and Stallergens; Ludger Klimek: has received research grants for his institution from ALK Abelló (Germany/Denmark), Allergopharma (Germany), Stallergenes (Germany/ France), HAL Allergy (Germany/the Netherlands), Artu Biologicals (the Netherlands), Allergy Therapeutics/Bencard (UK/Germany), Hartington (Spain), Lofarma (Italy), Novartis/Leti (Germany/Spain), GlaxoSmithKline (UK/Germany), Essex Pharma (Germany), Cytos (Switzerland), Curalogic (Denmark), Roxall (Germany), Biomay (Austria), Thermo Fisher (Germany), Circasia (UK), Biotech Tools s.a. (Belgium), and Meda Pharma GmbH (Germany); and/or he has served as an advisor and on speakers' bureaus for some of the aforementioned companies. LK has received travel grants from HAL Allergy (the Netherlands/Germany), Meda (Germany/Sweden) and Allergopharma (Germany), and he is a consultant for Bencard

(Germany), Novartis/Leti (Germany), Meda (Germany), ALK Abelló (Germany/Denmark), Allergopharma (Germany) and Boehringer Ingelheim (Germany). LK is Board Member of the ENT Section of the European Academy of Allergy and Clinical Immunology (EAACI), Vice-President of the German Academy of Allergology and Clinical Immunology, Vice-President German Union of Allergologists, Member of the Board of Directors of the German Society for Otorhinolaryngology HNS. He is co-editor and author of different chapters of the textbook 'Allergien bei Kindern und Jugendlichen' (publisher: Schattauer-Verlag, Germany), author of one chapter in 'Allergologie' (publisher: Springer, Germany) and author of different chapters in 'Allergologie' (publisher: Schattauer-Verlag); Gerard Koppelman: grants outside this work from Dutch Lung Foundation, Ubbo Emmius Foundation and Stichting Astma Bestrijding; Piotr Kuna: reports personal fees from Adamed, personal fees from Allergopharma, personal fees from Almirall, personal fees from AstraZeneca, personal fees from Boehringer Ingelheim, personal fees from Celon Pharma, personal fees from Chiesi, personal fees from FAES, personal fees from GSK, personal fees from HAL, personal fees from Meda, personal fees from MSD, personal fees from Novartis, personal fees from Pfizer, personal fees from Polfarmex, personal fees from Polpharma, personal fees from Stallergens, personal fees from Teva, personal fees from Lekam, outside the submitted work; Désirée Larenas: Speaker para: Astrazeneca, Pfizer, MIT, Glenmark, MEDA, MSD, Novartis, UCB. Advisory board: Boehringer-Ingelheim, Novartis, Astrazeneca, MEDA, Mit, Glenmark, MSD, Pfizer. Grants from development of guidelines: TEVA, Pfizer, Novartis, UCB, Sanofi, GSK, Carnot, Senosiain, MEDA, MSD, Astrazeneca; Brian Lipworth: unrestricted grant support from Meda, Teva, Chiesi, Almirall. Multi centre grants from Jansen, Pearl, Roche, AZ, Teva. Consulting for Meda, Chiesi, Neopharma, Cipla, Sandoz. Ad boards for Teva, Meda, Chiesi. Support to attend educational meetings from Boehringer, Teva, Chiesi; Renaud Louis: research grants from GSK, Novartis, Chiesi over the last 2 years – in national Aboard of GSK, AstraZeneca and Mundipharma; Le Ltt: honorarium for lectures, funding for investigation, support to attend symposium of Astra Zeneca, Boehringer- Ingelheim, Glaxo Smith kline, Novartis, Pfizer and MSD. Consultant of Astra -Zeneca and Boehringer- Ingelheim; Antoine Magnan: Investigator: GSK Novartis Astra Zeneca Roche SANOFI Amgen Boehringer. Consultant: Novartis, MSD, AstraZeneca, ALK, TEVA, Mundipharma, Takeda, GSK, Boehringer. Symposia: ALK, Stallergènes, Novartis, MSD, Chiesi, GSK, Astra-Zeneca, Roche. Research Grants: MSD, Astellas, Sanofi, Novartis, Stallergènes; P Manning: Personal Benefits <\$10 000: A. Menarrini, Shares: none, Non-Personal Interests/benefits >\$10 000: none; Marcus Maurer: Grant/Research/Clinical Trial Support: Novartis; Genentech; Uriach; Abbott Laboratories; FAES; UCB; Moxie. Consultant/Advisory Boards: Novartis Genentech; Uriach; Abbott Laboratories; FAES; MSD; Almirall; UCB; Moxie; Sanofi; Ralf Mosges: reports personal fees from ALK-Abello, Ohropax, Meda, Servier, Stada, Menarini, Allergy Therapeutics,

Novartis, Leti, Allergopharma, Bayer, Faes, GSK, Johnson+Johnson, MSD, grants and personal fees from Arthrocare, Bencard, Stallergenes, BiotechTools, Lofarma, grants from Ursapharm, Bitop, HAL, AIPreven, Optima, non-financial support from Greer, Roxall, personal fees and non-financial support from UCB, non-financial support from Atmos, outside the submitted work; member of the guidelines task force of the German Academy of Otorhinolaryngology, chairman of the International Standardisation Committee of the European Rhinologic Society (ERS) and chairman of the ENT-Section of the European Academy of Allergy, Asthma and Clinical Immunology (EAACI); Robert Naclerio: Advisory Board: GSK, Merck, Sanofi, Teva – Speaker: Merck, Teva; Ken Ohta: honoraria for lectures and advisory meetings from Kyorin, GSK, Boehringer Ingelheim, AstraZeneca and Astellas; Yoshitaka Okamoto: Research grant from Torii Co. Ltd., Shionogi Co. Ltd., – Lecture fee from Torii Co. LTD., MSD Co. Ltd; Kimihio Okubo: Lecture Fee:GSK, MSD, Tanabe-Mitsubishi, Sanofi, Ono, Torii, Kyowa-Kirin – Consultancy: MSD, Tanabe-Mitsubishi, Sanofi, Ono, Torii, Taiho, Astellas, Teikoku; Pier Luigi Paggiaro: personal support for education and research from: AstraZeneca, Almirall, Boehringer Ingelheim, Chiesi, Guidotti-Malesci, GSK, Menarini, MSD, Mundipharma, Novartis, Takeda, Zambon; Nikos Papadopoulos: grant from GSK, Nestlé, Merck – Fees from: Abbvie, Sanofi, Meda, GSK, Novartis, Menarini, ALK-Abello, Allergopharma, Uriach, Stallergenes, MSD; Alberto Papi: has received grants, personal fees, and non-financial support from AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline, Boehringer Ingelheim, Merck Sharp & Dohme, Menarini, Novartis, Zambon, TEVA, Pfizer, Takeda, and Mundipharma; O Pfaar: has received research grants for his institution from ALK Abelló (Germany/Denmark), Allergopharma (Germany), Stallergenes (Germany/France), HAL Allergy (Germany/the Netherlands), Artu Biologicals (the Netherlands), Allergy Therapeutics/Bencard (UK/Germany), Hartington (Spain), Lofarma (Italy), Novartis/Leti (Germany/Spain), GlaxoSmithKline (UK/Germany), Essex Pharma (Germany), Cytos (Switzerland), Curalogic (Denmark), Roxall (Germany), Biomay (Austria), Thermo Fisher (Germany), Circassia (UK), European Union (FP-7 Health-2013 Innovation 1), Biotech Tools s.a. (Belgium), and Meda Pharma GmbH (Germany); and/or he has served as an advisor and on speakers' bureaus for some of the aforementioned companies. OP has received travel grants from HAL Allergy (the Netherlands/Germany) and Allergopharma (Germany), and he is a consultant for Bencard (Germany), HAL Allergy (the Netherlands), Novartis/Leti (Germany), Meda (Germany), ALK Abelló (Germany/Denmark), Allergopharma (Germany), Biotech Tools s.a. (Belgium), GfK Bridgehead (UK), Navigant Consulting (USA), Sanofi (USA), Guidepoint Global Advisors (USA), Thermo Fisher (Germany) and Stallergenes (Germany/France); he is Scientific Board Member of Mobile Chamber Experts (MCX), a GA2LEN Partner. OP is the current chairman of the Immunotherapy Interest Group (IT IG) of the European Academy of Allergy and Clinical Immunology (EAACI) and is the secretary of the ENT section of the German Society

for Allergy and Clinical Immunology (DGAKI). He has received grants for the 'Spezifische Immuntherapie'-award 2014 and the 'Nachwuchsförderpreis'-award 2010 of the DGAKI. He is co-editor and an author of the textbook 'Allergien bei Kindern und Jugendlichen' (publisher: Schattauer-Verlag, Germany), 'Allergologie' (publisher: Schattauer-Verlag) and author of different chapters of 'Allergologie- Handbuch' (publisher: Schattauer-Verlag, Germany) and has received payment for development of educational presentations from GlaxoSmithKline (Germany), Bencard (Germany), and Novartis (Germany); Davor Plavec: reports grants from Ministry of Science, Education and Sports of Republic of Croatia, grants and personal fees from GlaxoSmithKline, grants and personal fees from MSD, personal fees from Sandoz, personal fees from Salveo, grants from Schering-Plough, outside the submitted work; Dirkje Postma: The University of Groningen has received money for Professor Postma regarding an unrestricted educational grant for research from Astra Zeneca. Travel to ERS and/or ATS has been partially funded by Astra Zeneca, Chiesi, GSK, Takeda. Fees for consultancies were given to the University of Groningen by Astra Zeneca, Boehringer Ingelheim, Chiesi, GSK, Takeda and TEVA. Travel and lectures in China paid by Chiesi; David Price: Board Membership with Aerocrine, Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, and Teva. Consultancy: A Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda, Mundipharma, Napp, Novartis, Pfizer, and Teva; Grants and unrestricted funding for investigator-initiated studies from UK National Health Service, British Lung Foundation, Aerocrine, AKL Ltd, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Eli Lilly, GlaxoSmithKline, Meda, Merck, Mundipharma, Napp, Novartis, Orion, Pfizer, Respiratory Effectiveness Group, Takeda, Teva, and Zentiva; Payments for lectures/speaking: Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Meda, Merck, Mundipharma, Novartis, Pfizer, SkyePharma, Takeda, and Teva; Payment for manuscript preparation: Mundipharma and Teva; Patents (planned, pending or issued): AKL Ltd.; Payment for the development of educational materials: GlaxoSmithKline, Novartis; Stock/Stock options: Shares in AKL Ltd which produces phytopharmaceuticals and owns 80% of Research in Real Life Ltd and its subsidiary social enterprise Optimum Patient Care; received Payment for travel/accommodations/meeting expenses from Aerocrine, Boehringer Ingelheim, Mundipharma, Napp, Novartis, and Teva; Funding for patient enrolment or completion of research: Almirall, Chiesi, Teva, and Zentiva; and Peer reviewer for grant committees: Medical Research Council (2014), Efficacy and Mechanism Evaluation programme (2012), HTA (2014); Dermot Ryan: Board member URIACH and Stallergenes. received payments from GSK and MEDA to deliver lectures on their behalf. Chair of the Primary Care Interest Group of EAACI; Miguel Roman-Rodriguez: has provided consultancy to or lectured on behalf of AstraZeneca, GlaxoSmithKline, Novartis, Almirall, Chiesi, Mundipharma, Boehringer-Ingel-

heim, Rovi and Teva; Glenis Scadding: Research grants from GSK, ALK. Honoraria for articles, consulting, lectures/ chairing and/or advisory boards: ALK, Astra Zeneca, Britannia Pharmaceuticals, Capnia, Church & Dwight, Circassia, GSK, Groupo Uriach, Meda, Merck, MSD, Ono Pharmaceuticals, Oxford Therapeutics, Sanofi-Aventis, Shionogi, UCB. Travel funding from Bayer, GSK; Estelle Simons: Uriach Medical Advisory Board, UpToDate, The Medical Letter; Rafael Stelmach: AstraZeneca; Boehringer Ingelheim; Bayer; Chiesi; Eurofarma; Glaxo Smith Kline; Mantecorp-Farmasa; Novartis; MSD; Nycomed; Reckitt Bekinser, related to sponsorship for achievement/participation of clinical trials, conferences or consultancy activities;

Ana Todo Bom: Fee for speaking, reimbursement for attending or organising a symposium) from Novartis Farma, Faes Farma, Astrazeneca, Bial Aristegui, Thermo Fisher, Boehringer; Rudolf Valenta: has received research grants from Biomay AG, Vienna, Austria, Thermo Fisher, Uppsala, Sweden. He serves as a consultant for Biomay AG, Vienna, Austria, Thermofisher, Uppsala, Sweden and Frese- nius Medical Care, Bad Homburg, Germany; Ulrich Wahn: received fees for lectures and consultation within the last 5 years from: Stallergenes, Allergopharma, ALK, Novartis, Merck, and MEDA; All the other authors declare that they have no conflicts of interest.

References

- Bousquet J, Khaltaev N. *Global surveillance, prevention and control of Chronic Respiratory Diseases. A comprehensive approach. Global Alliance against Chronic Respiratory Diseases*. Geneva, Switzerland: World Health Organization. ISBN 978 92 4 156346 8. 2007:148.
- Westman M, Lupinek C, Bousquet J, Andersson N, Pahr S, Baar A et al. Early childhood IgE reactivity to pathogenesis-related class 10 proteins predicts allergic rhinitis in adolescence. *J Allergy Clin Immunol* 2015;**135**:1199–1206.
- Bousquet J, Anto JM, Berkouk K, Gergen P, Pinto AJ, Auge P et al. Developmental determinants in non-communicable chronic diseases and ageing. *Thorax*. 2015; **70**:595–597.
- Bousquet J, Gern JE, Martinez FD, Anto JM, Johnson CC, Holt PG et al. Birth cohorts in asthma and allergic diseases: report of a NIAID/NHLBI/MeDALL joint workshop. *J Allergy Clin Immunol* 2014;**133**:1535–1546.
- Zuberbier T, Lotvall J, Simoens S, Subramanian SV, Church MK. Economic burden of inadequate management of allergic diseases in the European Union: a GA(2) LEN review. *Allergy* 2014;**69**:1275–1279.
- Bousquet J, Van CP, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;**5**(Suppl):S147–S334.
- Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2) LEN and AllerGen). *Allergy* 2008;**63**(Suppl 86):8–160.
- Walker S, Khan-Wasti S, Fletcher M, Cullinan P, Harris J, Sheikh A. Seasonal allergic rhinitis is associated with a detrimental effect on examination performance in United Kingdom teenagers: case-control study. *J Allergy Clin Immunol* 2007;**120**: 381–387.
- Samolinski B, Fronczak A, Wlodarczyk A, Bousquet J. Council of the European Union conclusions on chronic respiratory diseases in children. *Lancet* 2012;**379**: e45–e46.
- Bousquet J, Schunemann HJ, Samolinski B, Demoly P, Baena-Cagnani CE, Bachert C et al. Allergic Rhinitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. *J Allergy Clin Immunol* 2012;**130**:1049–1062.
- Bousquet J, Michel J, Standberg T, Crooks G, Iakovidis I, Gomez M. The european innovation partnership on active and healthy ageing: the european geriatric medicine introduces the EIP on AHA column. *Eur Geriatr Med* 2014;**5**:361–362.
- Bousquet J, Hajjam J, Piette F, Jean-Bart B, Wlosik C, Robine JM et al. The French reference sites of the European Innovation Partnership on active and healthy ageing. *Presse Med* 2013;**42**:1558–1561.
- Bousquet J, Addis A, Adcock I, Agache I, Agusti A, Alonso A et al. Integrated care pathways for airway diseases (AIRWAYS-ICPs). *Eur Respir J*. 2014;**44**:304–323.
- Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinol Suppl* 2012;**23**:3–p.
- Bousquet J, Bachert C, Canonica GW, Casale TB, Cruz AA, Lockey RJ et al. Unmet needs in severe chronic upper airway disease (SCUAD). *J Allergy Clin Immunol* 2009;**124**:428–433.
- Bousquet PJ, Bachert C, Canonica GW, Casale TB, Mullol J, Klossek JM et al. Uncontrolled allergic rhinitis during treatment and its impact on quality of life: a cluster randomized trial. *J Allergy Clin Immunol* 2010;**126**:666–668.
- Hellings PW, Fokkens WJ, Akdis C, Bachert C, Cingi C, Dietz dLD et al. Uncontrolled allergic rhinitis and chronic rhinosinusitis: where do we stand today? *Allergy* 2013;**68**:1–7.
- Marsh D, Dechamp C, Cour P, Bousquet J, Deviller P. Correlation between the atmospheric level of antigen Amb-al (AgE) and the number of Ambrosia artemisiaefolia pollen grains in Lyon and neighboring regions. *Allerg Immunol (Paris)* 1987;**1**:43.
- Buters JT, Weichenmeier I, Ochs S, Pusch G, Kreyling W, Boere AJ et al. The allergen Bet v 1 in fractions of ambient air deviates from birch pollen counts. *Allergy*. 2010;**65**:850–858.
- Agarwal MK, Swanson MC, Reed CE, Yunginger JW. Airborne ragweed allergens: association with various particle sizes and short ragweed plant parts. *J Allergy Clin Immunol* 1984;**74**:687–693.
- Frenz DA. Interpreting atmospheric pollen counts for use in clinical allergy: spatial variability. *Ann Allergy Asthma Immunol* 2000;**84**:481–489.
- Caillaud DM, Martin S, Segala C, Vidal P, Lecadet J, Pellier S et al. Airborne pollen levels and drug consumption for seasonal allergic rhinoconjunctivitis: a 10-year study in France. *Allergy* 2015;**70**:99–106.
- Galan C, Antunes C, Brandao R, Torres C, Garcia-Mozo H, Caeiro E et al. Airborne olive pollen counts are not representative of exposure to the major olive allergen Ole e 1. *Allergy* 2013;**68**: 809–812.
- Frenguelli G, Passalacqua G, Bonini S, Fiocchi A, Incorvaia C, Marcucci F et al. Bridging allergologic and botanical knowledge in seasonal allergy: a role for phenology. *Ann Allergy Asthma Immunol* 2010;**105**:223–227.
- Caillaud D, Martin S, Segala C, Besancenot JP, Clot B, Thibaudon M. Effects of

- airborne birch pollen levels on clinical symptoms of seasonal allergic rhinoconjunctivitis. *Int Arch Allergy Immunol* 2014;**163**:43–50.
26. Caillaud DM, Martin S, Segala C, Besancenot JP, Clot B, Thibaudon M. Nonlinear short-term effects of airborne Poaceae levels on hay fever symptoms. *J Allergy Clin Immunol* 2012;**130**:812–814.
27. Annesi-Maesano I, Rouve S, Desqueyroux H, Jankovski R, Klossek JM, Thibaudon M et al. Grass pollen counts, air pollution levels and allergic rhinitis severity. *Int Arch Allergy Immunol* 2012;**158**:397–404.
28. Lubitz S, Schober W, Pusch G, Effner R, Klopp N, Behrendt H et al. Polycyclic aromatic hydrocarbons from diesel emissions exert proallergic effects in birch pollen allergic individuals through enhanced mediator release from basophils. *Environ Toxicol* 2010;**25**:188–197.
29. Boehm G, Leuschner RM. Experiences with the 'Individual Pollen Collector' developed by G. Boehm. *Experientia Suppl* 1987;**51**:87–88.
30. Agarwal MK, Swanson MC, Reed CE, Yunginger JW. Immunochemical quantitation of airborne short ragweed, *Alternaria*, antigen E, and Alt-I allergens: a two-year prospective study. *J Allergy Clin Immunol* 1983;**72**:40–45.
31. Longhi S, Cristofori A, Gatto P, Cristofolini F, Grando MS, Gottardini E. Biomolecular identification of allergenic pollen: a new perspective for aerobiological monitoring? *Ann Allergy Asthma Immunol* 2009;**103**:508–514.
32. Cassagne E, Caillaud PD, Besancenot JP, Thibaudon M. Forecasting the onset of an allergic risk to poaceae in Nancy and Strasbourg (France) with different methods. *Eur Ann Allergy Immunol* 2007;**39**:262–268.
33. Estrella N, Menzel A, Kramer U, Behrendt H. Integration of flowering dates in phenology and pollen counts in aerobiology: analysis of their spatial and temporal coherence in Germany (1992–1999). *Int J Biometeorol* 2006;**51**:49–59.
34. Laaidi K. Predicting days of high allergenic risk during *Betula* pollination using weather types. *Int J Biometeorol* 2001;**45**:124–132.
35. Myszkowska D, Majewska R. Pollen grains as allergenic environmental factors—new approach to the forecasting of the pollen concentration during the season. *AAEM* 2014;**21**:681–688.
36. Voukantsis D, Berger U, Tzima F, Karatzas K, Jaeger S, Bergmann KC. Personalized symptoms forecasting for pollen-induced allergic rhinitis sufferers. *Int J Biometeorol*. 2015;**59**:889–897.
37. de Weger LA, Beerthuizen T, Hiemstra PS, Sont JK. Development and validation of a 5-day-ahead hay fever forecast for patients with grass-pollen-induced allergic rhinitis. *Int J Biometeorol* 2014;**58**:1047–1055.
38. Nuti SV, Wayda B, Ranasinghe I, Wang S, Dreyer RP, Chen SI et al. The use of google trends in health care research: a systematic review. *PLoS ONE* 2014;**9**:e109583.
39. Broniatowski DA, Paul MJ, Dredze M. National and local influenza surveillance through Twitter: an analysis of the 2012–2013 influenza epidemic. *PLoS ONE* 2013;**8**:e83672.
40. Bernardo TM, Rajic A, Young I, Robiadek K, Pham MT, Funk JA. Scoping review on search queries and social media for disease surveillance: a chronology of innovation. *J Med Internet Res* 2013;**15**:e147.
41. Mosges R, Adrian M, El HE, Konig V. What Google(R) knows about the pollen season. *Allergy* 2011;**66**:707–708.
42. Dugas AF, Jalalpour M, Gel Y, Levin S, Torcaso F, Igusa T et al. Influenza forecasting with Google Flu Trends. *PLoS ONE* 2013;**8**:e56176.
43. Konig V, Mosges R. A model for the determination of pollen count using google search queries for patients suffering from allergic rhinitis. *J Allergy* 2014;**2014**:381983.
44. Berger U, Kmenta M, Bastl K. Individual pollen exposure measurements: are they feasible? *Curr Opin Allergy Clinical Immunol* 2014;**14**:200–205.
45. Kmenta M, Bastl K, Jager S, Berger U. Development of personal pollen information—the next generation of pollen information and a step forward for hay fever sufferers. *Int J Biometeorol* 2014;**58**:1721–1726.
46. Lahdensuo A, Haahtela T, Herrala J, Kava T, Kiviranta K, Kuusisto P et al. Randomised comparison of guided self management and traditional treatment of asthma over one year. *BMJ* 1996;**312**:748–752.
47. Lahdensuo A, Haahtela T, Herrala J, Kava T, Kiviranta K, Kuusisto P et al. Randomised comparison of cost effectiveness of guided self management and traditional treatment of asthma in Finland. *BMJ* 1998;**316**:1138–1139.
48. Haahtela T, Tuomisto LE, Pietinalho A, Klaukka T, Erhola M, Kaila M et al. A 10 year asthma programme in Finland: major change for the better. *Thorax* 2006;**61**:663–670.
49. von Hertzen LC, Savolainen J, Hannuksela M, Klaukka T, Lauerma A, Makela MJ et al. Scientific rationale for the Finnish Allergy Programme 2008–2018: emphasis on prevention and endorsing tolerance. *Allergy* 2009;**64**:678–701.
50. Haahtela T, von Hertzen L, Makela M, Hannuksela M. Finnish Allergy Programme 2008–2018—time to act and change the course. *Allergy* 2008;**63**:634–645.
51. Deliu M, Belgrave D, Simpson A, Murray CS, Kerry G, Custovic A. Impact of rhinitis on asthma severity in school-age children. *Allergy* 2014;**69**:1515–1521.
52. Campbell H, Hotchkiss R, Bradshaw N, Porteous M. Integrated care pathways. *BMJ* 1998;**316**:133–137.
53. Overill S. A practical guide to care pathways. *J Integr Care* 1998;**2**:93–98.
54. Integrated Care Pathways users in Scotland (ICPUS). A workbook for people starting to develop integrated care pathways. <http://www.icpus.org.uk2007>.
55. How to produce and evaluate an integrated care pathway (ICP): information for staff. Great Ormond Street Hospital for Children. www.goshnhs.uk. 2010.
56. Bruhn S, Fang Y, Barrenas F, Gustafsson M, Zhang H, Konstantinell A et al. A generally applicable translational strategy identifies S100A4 as a candidate gene in allergy. *Sci Translat Med* 2014;**6**:218ra4.
57. Auffray C, Adcock IM, Chung KF, Djukanovic R, Pison C, Sterk PJ. An integrative systems biology approach to understanding pulmonary diseases. *Chest* 2010;**137**:1410–1416.
58. Bousquet J, Anto J, Auffray C, Akdis M, Cambon-Thomsen A, Keil T et al. MeDALL (Mechanisms of the Development of ALLergy): an integrated approach from phenotypes to systems medicine. *Allergy* 2011;**66**:596–604.
59. Anto JM, Pinart M, Akdis M, Auffray C, Bachert C, Basagana X et al. Understanding the complexity of IgE-related phenotypes from childhood to young adulthood: a Mechanisms of the Development of Allergy (MeDALL) seminar. *J Allergy Clin Immunol* 2012;**129**:943–954.
60. Lupinek C, Wollmann E, Baar A, Banerjee S, Breiteneder H, Broecker BM et al. Advances in allergen-microarray technology for diagnosis and monitoring of allergy: the MeDALL allergen-chip. *Methods* 2014;**66**:106–119.
61. Bousquet J, Anto JM, Sterk PJ, Adcock IM, Chung KF, Roca J et al. Systems medicine and integrated care to combat chronic noncommunicable diseases. *Genome Med* 2011;**3**:43.
62. Skrindo I, Lupinek C, Valenta R, Hovland V, Pahr S, Baar A et al. The use of the MeDALL-chip to assess IgE sensitization, a new diagnostic tool for allergic disease? *Pediatr Allergy Immunol* 2015;**26**:239–246.

63. Baiardini I, Bousquet PJ, Brzoza Z, Canonica GW, Compalati E, Fiocchi A et al. Recommendations for assessing patient-reported outcomes and health-related quality of life in clinical trials on allergy: a GA(2) LEN taskforce position paper. *Allergy* 2010;**65**:290–295.
64. Pfaar O, Demoly P, Gerth van Wijk R, Bonini S, Bousquet J, Canonica GW et al. Recommendations for the standardization of clinical outcomes used in allergen immunotherapy trials for allergic rhinoconjunctivitis: an EAACI Position Paper. *Allergy* 2014;**69**:854–867.
65. Ayres JG, Forsberg B, Annesi-Maesano I, Dey R, Ebi KL, Helms PJ et al. Climate change and respiratory diseases: European Respiratory Society position statement. *Eur Respir J* 2009;**34**:295–302.
66. D'Amato G, Cecchi L, Bonini S, Nunes C, Annesi-Maesano I, Behrendt H et al. Allergenic pollen and pollen allergy in Europe. *Allergy* 2007;**62**:976–990.
67. Haahtela T. Allergy is rare where butterflies flourish in a biodiverse environment. *Allergy* 2009;**64**:1799–1803.
68. Members of the Workshops. ARIA in the pharmacy: management of allergic rhinitis symptoms in the pharmacy. Allergic rhinitis and its impact on asthma. *Allergy* 2004;**59**:373–387.
69. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin Immunol* 2010;**126**:466–476.
70. Valero A, Ferrer M, Baro E, Sastre J, Navarro AM, Marti-Guadano E et al. Discrimination between moderate and severe disease may be used in patients with either treated or untreated allergic rhinitis. *Allergy* 2010;**65**:1609–1613.
71. Montoro J, Del CA, Mullol J, Molina X, Bartra J, Davila I et al. Validation of the modified allergic rhinitis and its impact on asthma (ARIA) severity classification in allergic rhinitis children: the PEDRIAL study. *Allergy* 2012;**67**:1437–1442.
72. Bousquet J, Anto JM, Demoly P, Schunemann HJ, Togias A, Akdis M et al. Severe chronic allergic (and related) diseases: a uniform approach—a MeDALL–GA2LEN–ARIA position paper. *Int Arch Allergy Immunol* 2012;**158**:216–231.
73. Expert panel report 3: Guidelines for the diagnosis and management of asthma. National Asthma Education and Prevention Program. National Heart, Lung and Blood Institute. US Department of Health and Human Services. 440 pages. 2007.
74. Vestbo J, Rennard S. Chronic obstructive pulmonary disease biomarker(s) for disease activity needed—urgently. *Am J Respir Crit Care Med* 2010;**182**:863–864.
75. Vijan S. Type 2 diabetes. *Ann Intern Med* 2010;**152**:ITC31–15.
76. Bousquet PJ, Bousquet-Rouanet L, Co Minh HB, Urbinelli R, Allaert FA, Demoly P. ARIA (Allergic Rhinitis and Its Impact on Asthma) classification of allergic rhinitis severity in clinical practice in France. *Int Arch Allergy Immunol* 2007;**143**:163–169.
77. Di Lorenzo G, Pacor ML, Amodio E, Leto-Barone MS, La Piana S, D'Alcamo A et al. Differences and similarities between allergic and nonallergic rhinitis in a large sample of adult patients with rhinitis symptoms. *Int Arch Allergy Immunol* 2011;**155**:263–270.
78. Lu D, Zhao Y, Zheng Y, An P, Wang L, Qiao X et al. Evaluation of quality of life questionnaires for adult patients with moderate to severe allergic rhinitis. *Am J Otolaryngol* 2011;**32**:494–498.
79. del Cuvillo A, Montoro J, Bartra J, Valero A, Ferrer M, Jauregui I et al. Validation of ARIA duration and severity classifications in Spanish allergic rhinitis patients – The ADRIAL cohort study. *Rhinology* 2010;**48**:201–205.
80. Demoly P, Jankowski R, Chassany O, Besah Y, Allaert FA. Validation of a self-questionnaire for assessing the control of allergic rhinitis. *Clin Exp Allergy* 2011;**41**:860–868.
81. Ohta K, Bousquet PJ, Aizawa H, Akiyama K, Adachi M, Ichinose M et al. Prevalence and impact of rhinitis in asthma. SACRA, a cross-sectional nation-wide study in Japan. *Allergy* 2011;**66**:1287–1295.
82. Ragab SM, Lund VJ, Saleh HA, Scadding G. Nasal nitric oxide in objective evaluation of chronic rhinosinusitis therapy. *Allergy* 2006;**61**:717–724.
83. Valero A, Ferrer M, Sastre J, Navarro AM, Monclus L, Marti-Guadano E et al. A new criterion by which to discriminate between patients with moderate allergic rhinitis and patients with severe allergic rhinitis based on the Allergic Rhinitis and its Impact on Asthma severity items. *J Allergy Clin Immunol* 2007;**120**:359–365.
84. Schatz M, Meltzer EO, Nathan R, Derebery MJ, Mintz M, Stanford RH et al. Psychometric validation of the rhinitis control assessment test: a brief patient-completed instrument for evaluating rhinitis symptom control. *Ann Allergy Asthma Immunol* 2010;**104**:118–124.
85. Devillier P, Chassany O, Vicaud E, de Beaumont O, Robin B, Dreyfus JF et al. The minimally important difference in the Rhinoconjunctivitis Total Symptom Score in grass-pollen-induced allergic rhinoconjunctivitis. *Allergy* 2014;**69**:1689–1695.
86. Grant S, Aitchison T, Henderson E, Christie J, Zare S, McMurray J et al. A comparison of the reproducibility and the sensitivity to change of visual analogue scales, Borg scales, and Likert scales in normal subjects during submaximal exercise. *Chest* 1999;**116**:1208–1217.
87. Pfennings L, Cohen L, van der Ploeg H. Preconditions for sensitivity in measuring change: visual analogue scales compared to rating scales in a Likert format. *Psychol Rep* 1995;**77**:475–480.
88. Bousquet PJ, Combescure C, Klossek JM, Daires JP, Bousquet J. Change in visual analog scale score in a pragmatic randomized cluster trial of allergic rhinitis. *J Allergy Clin Immunol* 2009;**123**:1349–1354.
89. Ryan D, van Weel C, Bousquet J, Toskala E, Ahlstedt S, Palkonen S et al. Primary care: the cornerstone of diagnosis of allergic rhinitis. *Allergy* 2008;**63**:981–989.
90. Morais-Almeida M, Santos N, Pereira AM, Branco-Ferreira M, Nunes C, Bousquet J et al. Prevalence and classification of rhinitis in preschool children in Portugal: a nationwide study. *Allergy* 2013;**68**:1278–1288.
91. Morais-Almeida M, Pite H, Pereira AM, Todo-Bom A, Nunes C, Bousquet J et al. Prevalence and classification of rhinitis in the elderly: a nationwide survey in Portugal. *Allergy* 2013;**68**:1150–1157.
92. Bousquet J, Bachert C, Canonica GW, Mullol J, Van Cauwenberge P, Bindsløv JC et al. Efficacy of desloratadine in intermittent allergic rhinitis: a GALEN study. *Allergy* 2009;**64**:1516–1523.
93. Bousquet J, Bachert C, Canonica GW, Mullol J, Van Cauwenberge P, Jensen CB et al. Efficacy of desloratadine in persistent allergic rhinitis – a GA(2)LEN study. *Int Arch Allergy Immunol* 2010;**153**:395–402.
94. Larenas-Linnemann D, Dinger H, Shah-Hosseini K, Michels A, Mosges R. Over diagnosis of persistent allergic rhinitis in perennial allergic rhinitis patients: a nationwide study in Mexico. *Am J Rhinol Allergy* 2013;**27**:495–501.
95. Shao J, Cui YX, Zheng YF, Peng HF, Zheng ZL, Chen JY et al. Efficacy and safety of sublingual immunotherapy in children aged 3–13 years with allergic rhinitis. *Am J Rhinol Allergy* 2014;**28**:131–139.
96. Wei H, Zhang Y, Shi L, Zhang J, Xia Y, Zang J et al. Higher dosage of HIFU treatment may lead to higher and longer efficacy for moderate to severe perennial allergic rhinitis. *Int J Med Sci* 2013;**10**:1914–1920.
97. Tatar EC, Surenglu UA, Saylam G, Isik E, Ozdek A, Korkmaz H. Is there any correlation between the results of skin-prick test and the severity of symptoms in allergic

- rhinitis? *Am J Rhinol Allergy* 2012;**26**:e37–e39.
98. Rouve S, Didier A, Demoly P, Jankowsky R, Klossek JM, Anessi-Maesano I. Numeric score and visual analog scale in assessing seasonal allergic rhinitis severity. *Rhinology* 2010;**48**:285–291.
 99. Baiardini I, Braidò F, Brandi S, Tarantini F, Bonini S, Bousquet PJ et al. The impact of GINA suggested drugs for the treatment of asthma on Health-Related Quality of Life: a GA(2)LEN review. *Allergy* 2008;**63**:1015–1030.
 100. Bousquet PJ, Demoly P, Devillier P, Mesbah K, Bousquet J. Impact of allergic rhinitis symptoms on quality of life in primary care. *Int Arch Allergy Immunol* 2013;**160**:393–400.
 101. Yamamoto H, Yamada T, Sakashita M, Kubo S, Susuki D, Tokunaga T et al. Efficacy of prophylactic treatment with montelukast and montelukast plus add-on loratadine for seasonal allergic rhinitis. *Allergy Asthma Proc* 2012;**33**:e17–e22.
 102. Bousquet J, Lund VJ, Van Cauwenberge P, Bremard-Oury C, Mounedji N, Stevens MT et al. Implementation of guidelines for seasonal allergic rhinitis: a randomized controlled trial. *Allergy* 2003;**58**:733–741.
 103. Bousquet J, Bodez T, Gehano P, Klossek JM, Liard F, Neukirch F et al. Implementation of guidelines for allergic rhinitis in specialist practices. a randomized pragmatic controlled trial. *Int Arch Allergy Immunol* 2009;**150**:75–82.
 104. Demoly P, Bousquet PJ, Mesbah K, Bousquet J, Devillier P. Visual analogue scale in patients treated for allergic rhinitis: an observational prospective study in primary care: asthma and rhinitis. *Clin Exp Allergy* 2013;**43**:881–888.
 105. Ciprandi G, Cirillo I, Pistorio A, Di Gioacchino M, Fenoglio D. Ebasine increases IFN-gamma production in patients with persistent allergic rhinitis. *J Biol Regul Homeost Agents* 2009;**23**:31–36.
 106. Davies RJ, Lund VJ, Harten-Ash VJ. The effect of intranasal azelastine and beclomethasone on the symptoms and signs of nasal allergy in patients with perennial allergic rhinitis. *Rhinology* 1993;**31**:159–164.
 107. Henauer S, Hugonot L, Hugonot R, Kurzeja A, Gastpar H, Rauch-Riedelsheimer B et al. Multi-centre double-blind comparison of terfenadine once daily versus twice daily in patients with hay fever. *J Int Med Res* 1987;**15**:212–223.
 108. Newson-Smith G, Powell M, Baehre M, Garnham SP, MacMahon MT. A placebo controlled study comparing the efficacy of intranasal azelastine and beclomethasone in the treatment of seasonal allergic rhinitis. *Eur Arch Otorhinolaryngol* 1997;**254**:236–241.
 109. Samolinski B, Fronczak A, Kuna P, Akdis CA, Anto JM, Bialoszewski AZ et al. Prevention and control of childhood asthma and allergy in the EU from the public health point of view: Polish Presidency of the European Union. *Allergy* 2012;**67**:726–731.
 110. Samolinski B, Sybilski AJ, Raciborski F, Tomaszewska A, Samel-Kowalik P, Walkiewicz A et al. Prevalence of rhinitis in Polish population according to the ECAP (Epidemiology of Allergic Disorders in Poland) study. *Otolaryngol Pol.* 2009;**63**:324–330.
 111. Klimek L, Bachert C, Mosges R, Munzel U, Price D, Virchow JC et al. Effectiveness of MP29-02 for the treatment of allergic rhinitis in real-life: results from a noninterventional study. *Allergy Asthma Proc* 2015;**36**:40–47.
 112. Azevedo P, Correia dSJ, Bousquet J, Bugalho-Almeida A, Del GS, Demoly P et al. Control of Allergic Rhinitis and Asthma Test (CARAT): dissemination and applications in primary care. *Prim Care Respir J.* 2013;**22**:112–116.
 113. Fonseca JA, Nogueira-Silva L, Morais-Almeida M, Azevedo L, Sa-Sousa A, Branco-Ferreira M et al. Validation of a questionnaire (CARAT10) to assess rhinitis and asthma in patients with asthma. *Allergy* 2010;**65**:1042–1048.
 114. Nogueira-Silva L, Martins SV, Cruz-Correia R, Azevedo LF, Morais-Almeida M, Bugalho-Almeida A et al. Control of allergic rhinitis and asthma test—a formal approach to the development of a measuring tool. *Respir Res* 2009;**10**:52.
 115. van der Leeuw S, van der Molen T, Dekhuijzen PN, Fonseca JA, van Gemert FA, Gerth van Wijk R et al. The minimal clinically important difference of the control of allergic rhinitis and asthma test (CARAT): cross-cultural validation and relation with pollen counts. *NPJ Prim Care Respir Med* 2015;**25**:14107.
 116. Lourenco O, Calado S, Sa-Sousa A, Fonseca J. Evaluation of allergic rhinitis and asthma control in a Portuguese community pharmacy setting. *J Managed Care Special Pharm* 2014;**20**:513–522.
 117. Borrego LM, Fonseca JA, Pereira AM, Pinto VR, Linhares D, Morais-Almeida M. Development process and cognitive testing of CARATkids – Control of Allergic Rhinitis and Asthma Test for children. *BMC Pediatr* 2014;**14**:34.
 118. Linhares DV, da Fonseca JA, Borrego LM, Matos A, Pereira AM, Sa-Sousa A et al. Validation of control of allergic rhinitis and asthma test for children (CARATKids)—a prospective multicenter study. *Pediatr Allergy Immunol* 2014;**25**:173–179.
 119. Burnay E, Cruz-Correia R, Jacinto T, Sousa AS, Fonseca J. Challenges of a mobile application for asthma and allergic rhinitis patient enablement-interface and synchronization. *Telemed J e-health* 2013;**19**:13–18.
 120. Braidò F, Baiardini I, Stagi E, Scichilone N, Rossi O, Lombardi C et al. RhinAsthma patient perspective: a short daily asthma and rhinitis QoL assessment. *Allergy* 2012;**67**:1443–1450.
 121. Bright TJ, Wong A, Dhurjati R, Bristow E, Bastian L, Coeytaux RR et al. Effect of clinical decision-support systems: a systematic review. *Ann Intern Med* 2012;**157**:29–43.
 122. Jaspers MW, Smeulders M, Vermeulen H, Peute LW. Effects of clinical decision-support systems on practitioner performance and patient outcomes: a synthesis of high-quality systematic review findings. *J Am Med Inform Assoc* 2011;**18**:327–334.
 123. lavel R, Bousquet J, Andre C. Clinical efficacy of sublingual-swallow immunotherapy: a double-blind, placebo-controlled trial of a standardized five-grass-pollen extract in rhinitis. *Allergy* 1998;**53**:493–498.
 124. Reips UD, Funke F. Interval-level measurement with visual analogue scales in Internet-based research: VAS Generator. *Behav Res Methods* 2008;**40**:699–704.
 125. Dunton GF, Dzibur E, Kawabata K, Yanez B, Bo B, Intille S. Development of a smartphone application to measure physical activity using sensor-assisted self-report. *Front Publ Health* 2014;**2**:12.
 126. Shiffman S, Stone AA, Hufford MR. Ecological momentary assessment. *Ann Rev Clin Psychol* 2008;**4**:1–32.
 127. Radzuweit M, Lechner U. Introducing tablet computers into medical practice: design of mobile apps for consultation services. *Health Technol Assess* 2014;**4**:31–41.
 128. Lluch M. Strategic Intelligence Monitor on Personal Health Systems phase 2 (SIMPHS 2) Evidence consolidation Report on best practices and key drivers of success, JRC-IPTS. 2012. Available from: <https://ec.europa.eu/jrc/sites/default/files/jrc73069.pdf>.
 129. Dubey G. Les nouvelles technologies en autonomie et santé: un déplacement des frontières de la connaissance Ann Mines. 2014(82-88).
 130. Beusart-Zéphir M, Eklin P, Pelayo S, Beuscart R. The human factors engineering approach to biomedical informatics projects: state of the art, results, benefits and challenges. *Yearb Med Inform* 2007: 109–27.
 131. Wang K, Wang C, Xi L, Zhang Y, Ouyang Y, Lou H et al. A randomized controlled

- trial to assess adherence to allergic rhinitis treatment following a daily short message service (SMS) via the mobile phone. *Int Arch Allergy Immunol* 2014;**163**:51–58.
132. de Jongh T, Gurol-Urganci I, Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging for facilitating self-management of long-term illnesses. *Cochrane Database Syst Rev* 2012;**12**:CD007459.
 133. Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V, Atun R, Car J. Mobile phone messaging reminders for attendance at healthcare appointments. *Cochrane Database Syst Rev* 2013;**12**:CD007458.
 134. Canonica GW, Cox L, Pawankar R, Baena-Cagnani CE, Blaiss M, Bonini S et al. Sublingual immunotherapy: World Allergy Organization position paper 2013 update. *World Allergy Organ J* 2014;**7**:6.
 135. Council conclusions on Healthy Ageing across the Lifecycle. 3206th Employment, social policy, health and consumer affairs Council meeting. Brussels, 7 December 2012. http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/lsa/134097.pdf. 2012.
 136. Bousquet J, Tanasescu CC, Camuzat T, Anto JM, Blasi F, Neou A et al. Impact of early diagnosis and control of chronic respiratory diseases on active and healthy ageing. A debate at the European Union Parliament. *Allergy* 2013;**68**:555–561.
 137. Frew AJ, Dubuske L, Keith PK, Corrigan CJ, Aberer W, Fischer vW-DK. Assessment of specific immunotherapy efficacy using a novel placebo score-based method. *Ann Allergy Asthma Immunol* 2012;**109**:342–347.
 138. Bousquet J, Mantzouranis E, Cruz AA, Ait-Khaled N, Baena-Cagnani CE, Bleecker ER et al. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol* 2010;**126**:926–938.
 139. Beggs PJ, Bambrick HJ. Is the global rise of asthma an early impact of anthropogenic climate change? *Environ Health Perspect* 2005;**113**:915–919.
 140. Hollins PD, Kettlewell PS, Atkinson MD, Stephenson DB, Corden JM, Millington WM et al. Relationships between airborne fungal spore concentration of *Cladosporium* and the summer climate at two sites in Britain. *Int J Biometeorol* 2004;**48**:137–141.
 141. Deak AJ, Makra L, Matyasovszky I, Csepe Z, Muladi B. Climate sensitivity of allergenic taxa in Central Europe associated with new climate change related forces. *Sci Total Environ* 2012;**442C**:36–47.
 142. de WL, Hiemstra PS. The effect of climate change on pollen allergy in the Netherlands. *Ned Tijdschr Geneesk* 2009;**153**:A1410.
 143. Emberlin J, Detandt M, Gehrig R, Jaeger S, Nolard N, Rantio-Lehtimäki A. Responses in the start of *Betula* (birch) pollen seasons to recent changes in spring temperatures across Europe. *Int J Biometeorol* 2002;**46**:159–170.
 144. Fitter AH, Fitter RS. Rapid changes in flowering time in British plants. *Science* 2002;**296**:1689–1691.
 145. Stach A, Emberlin J, Smith M, Adams-Groom B, Myszkowska D. Factors that determine the severity of *Betula* spp. pollen seasons in Poland (Poznan and Krakow) and the United Kingdom (Worcester and London). *Int J Biometeorol* 2008;**52**:311–321.
 146. Smith M, Emberlin J, Stach A, Czarnecka-Operacz M, Jenerowicz D, Silny W. Regional importance of *Alnus* pollen as an aeroallergen: a comparative study of *Alnus* pollen counts from Worcester (UK) and Poznan (Poland). *AAEM* 2007;**14**:123–128.
 147. Garcia-Mozo H, Galan C, Jato V, Belmonte J, de IGC, Fernandez D et al. *Quercus* pollen season dynamics in the Iberian peninsula: response to meteorological parameters and possible consequences of climate change. *AAEM* 2006;**13**:209–224.
 148. Emberlin J, Mullins J, Corden J, Jones S, Millington W, Brooke M et al. Regional variations in grass pollen seasons in the UK, long-term trends and forecast models. *Clin Exp Allergy* 1999;**29**:347–356.
 149. Wayne P, Foster S, Connolly J, Bazzaz F, Epstein P. Production of allergenic pollen by ragweed (*Ambrosia artemisiifolia* L.) is increased in CO₂-enriched atmospheres. *Ann Allergy Asthma Immunol* 2002;**88**:279–282.
 150. Ziska LH, Gebhard DE, Frenz DA, Faulkner S, Singer BD, Straka JG. Cities as harbingers of climate change: common ragweed, urbanization, and public health. *J Allergy Clin Immunol* 2003;**111**:290–295.
 151. Frei T, Gassner E. Climate change and its impact on birch pollen quantities and the start of the pollen season an example from Switzerland for the period 1969–2006. *Int J Biometeorol* 2008;**52**:667–674.
 152. Ahlholm JU, Helander ML, Savolainen J. Genetic and environmental factors affecting the allergenicity of birch (*Betula pubescens* ssp. *czerepanovii* [Orl.] Hamet-ahti) pollen. *Clin Exp Allergy* 1998;**28**:1384–1388.
 153. Molino NA, Slutsky AS, Zamel N. The effects of air pollution on allergic bronchial responsiveness. *Clin Exp Allergy* 1992;**22**:667–672.
 154. Behrendt H, Becker WM, Fritzsche C, Sliwa-Tomczok W, Tomczok J, Friedrichs KH et al. Air pollution and allergy: experimental studies on modulation of allergen release from pollen by air pollutants. *Int Arch Allergy Immunol* 1997;**3**:69–74.
 155. D'Amato G. Environmental urban factors (air pollution and allergens) and the rising trends in allergic respiratory diseases. *Allergy* 2002;**57**(Suppl 72):30–33.
 156. Shea KM, Truckner RT, Weber RW, Peden DB. Climate change and allergic disease. *J Allergy Clin Immunol* 2008;**122**:443–453.
 157. de-Manuel-Keenoy E, David M, Mora J, Prieto L, Domingo C, Orueta J et al. Activation of Stratification Strategies and Results of the interventions on frail patients of Healthcare Services (ASSEHS) DG Sanco Project No. 2013 12 04. *Eur Geriatr Med* 2014;**5**:342–346.