Next-generation care pathways for allergic rhinitis and asthma multimorbidity

Citation for published version:

Digital Object Identifier (DOI):
10.21037/jtd.2019.08.64

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Journal of thoracic disease

Publisher Rights Statement:
The Journal of Thoracic Disease (JTD, J Thorac Dis, pISSN: 2072-1439; eISSN: 2077-6624) is an international, peer-reviewed, open-access journal, which was founded in Dec 2009. JTD is indexed by Science Citation Index Expanded (SCIE), PubMed/PubMed Central and Scopus. It is published quarterly (Dec 2009- Dec 2011), bimonthly (Jan 2012 - Dec 2013), monthly (Jan. 2014-). JTD received its impact factor of 2.027 for the year 2018. JTD publishes manuscripts that describe new findings and provide current, practical information on the diagnosis and treatment of conditions related to thoracic disease. All the submission and reviewing are conducted electronically so that rapid review is assured.

This journal provides immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge.

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Next-generation care pathways for allergic rhinitis and asthma multimorbidity: a model for multimorbid non-communicable diseases—Meeting Report (Part 1)


1University Hospital Montpellier, Montpellier, France; 2MACVIA-France, Fondation partenariale FMC VIA-LR, Montpellier, France; 3INSERM U 1168, VIMA, Ageing and Chronic Diseases Epidemiological and Public Health Approaches, Villejuif, France; 4Université Versailles St-Quentin-en-Yvelines, UMR-S 1168, Montigny le Bretonneux, France; 5Euforea, Brussels, Belgium; 6Charité, Universitätmedizin Berlin, Humboldt-Universität zu Berlin, Berlin, Germany; 7Berlin Institute of Health, Comprehensive Allergy Center, Department of Dermatology and Allergy, Berlin, Germany; 8EUFOREA, Brussels, Belgium; 9Allergy Department, Pasteur Institute, Paris, France; 10Faculty of Medicine, Transylvania University, Brasov, Romania; 11Epidemiology of Allergic and Respiratory Diseases, Department Institute Pierre Louis of Epidemiology and Public Health, INSERM and Sorbonne Universités, Medical School Saint Antoine, Paris, France; 12Department of Allergy and Immunology, Hospital Quiroánalud Bizkaia, Erandio, Spain; 13ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; 14Universitat Pompeu Fabra (UPF), Barcelona, Spain; 15CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain; 16Upper Airways Research Laboratory, ENT Dept, Ghent University Hospital, Ghent, Belgium; 17National Center of Expertise in Cognitive Stimulation (CEN STEMCO), Broca Hospital, Paris, France; 18Mines ParisTech CRI - PSL Research University, Fontainebleau, France; 19IQ4U Consultants Ltd, London, UK; 20Independent Consultant, Joensuu, Finland; 21Woolcock Institute of Medical Research, University of Sydney and Woolcock Emphysema Centre and Sydney Local Health District, Glebe, NSW, Australia; 22Allergist, La Rochelle, France; 23Dept of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium; 24Imperial College London-National Heart and Lung Institute, London, UK; 25Personalized Medicine Clinic Asthma & Allergy, Humanitas Clinical and Research Center IRCCS, Rozzano (MI), and Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI), Italy; 26Institute for Immunological Research, University of Cartagena, Campus de Zaragocilla, Edificio Biblioteca Primer piso, Cartagena, Colombia, and Foundation for the Development of Medical and Biological Sciences (Fundemeb), Cartagena, Colombia; 27Allergy Section, Department of Internal Medicine, Hospital Vall d’Hebron & ARADyAL research network, Barcelona, Spain; 28Regional Ministry of Health of Andalusia, Seville, Spain; 29College of Psychology, Nova Southeastern University and School-related Psychological Assessments and Clinical Interventions Clinic, Ft Lauderdale, Florida, USA; 30SOS Allergology and Clinical Immunology, USL Toscana Centro, Prato, Italy; 31Department of Health Research Methods, Evidence, and Impact, Division of Immunology and Allergy, Department of Medicine, McMaster University, Hamilton, Ontario, Canada; 32Department of Health, Social Services and Public Safety, Northern Ireland, Belfast, UK; 33UCIBIO, REQUIMTE, Faculty of Pharmacy, and

* Dr. Togias’ co-authorship of this publication does not constitute endorsement by the US National Institute of Allergy and Infectious Diseases or by any other United States government agency.
Part 1

Introduction and meeting objectives

In all societies, the burden and cost of allergic and chronic respiratory diseases are increasing rapidly. Most economies are struggling to deliver modern health care effectively. There is a need to support the transformation of the health care system for integrated care with organizational health literacy. MASK (Mobile Airways Sentinel NetworK) (1), a new development of the ARIA (Allergic Rhinitis and its Impact on Asthma) initiative, and POLLAR (Impact of Air POLLution on Asthma and Rhinitis, EIT Health) (2), in collaboration with professional and patient organizations in the field of allergy and airway diseases, are proposing real-life integrated care pathways (ICPs) (3)-centred around the patient with rhinitis and using mHealth monitoring of environmental exposure (4).

An expert meeting took place at the Pasteur Institute in Paris, December 3, 2018. The aim was to discuss next-generation care pathways: (I) Patient participation, health literacy and self-care through technology-assisted “patient activation”; (II) Implementation of care pathways by pharmacists and (III) Next-generation guidelines assessing the recommendations of GRADE guidelines in rhinitis and asthma using real-world evidence (RWE) assessed by mobile technology.

The one-day meeting objectives were clear (Figure 1). The meeting was followed by a workshop. The present paper reports the background of the two-day meeting.

Organizations supporting the meeting

Impact of air POLLution on Asthma and Rhinitis (POLLAR)

The interactions between air pollution and pollen in the urban environment are potentially important for patients suffering from allergic rhinitis (AR). Urban traffic air pollutants can interact with pollen. They can trigger nasal symptoms and even impact sleep and work activity. POLLAR is a project of the European Institute of Innovation and Technology (EIT Health) (2). POLLAR is based on an application, the Allergy Diary (MASK-air®) (1), that will be combined with a new tool allowing queries on allergen, pollen, sleep quality and disorders as well as existing longitudinal and geolocalized pollution data (7).

The Reference Site Collaborative Network (RSCN) of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA)

Seventy-four Reference Sites of the EIP on AHA were recognized in 2016 by the European Commission for their commitment to excellence in investing and scaling up innovative solutions for active and healthy ageing. The RSCN brings together the EIP on AHA Reference Sites into a single forum. The goals are to promote cooperation, share and transfer good practice and solutions in the development and scaling up of health and care strategies, policies and service delivery models, while at the same time supporting the action groups in their work.

Global Alliance against Chronic Respiratory Diseases (GARD) demonstration project

GARD has approved some demonstration projects to strengthen its activities and implementation strategy. MASK is one of them (8).

Other organizations supporting the meeting

Twenty-one organizations and 3 patient’s organizations supported the meeting (Figure 2).

Planetary health

The environment quality for human health is an important paradigm of modern public health (9). During the last decades, our knowledge of the influence of the environment degradation on health has improved substantially. The last WHO assessment estimated that environmental factors caused the loss of 21% (596 million) DALYS in 2012 (1). However, this systematic assessment included neither climate change nor the related factors such as temperature increase.

Though there are growing concerns that the health impacts of climate change will be important, there are still very limited strategies in the public health knowledge and service systems (10). This relative silent attitude is in sharp contrast to the evidence of the fast degradation of natural and climate systems. We know that today we live in a new geological period, the Anthropocene, which is functionally and stratigraphically distinct from the Holocene, and that 75% of the species will be extinguished in the next few centuries if the current tendencies continue (11). The
The need for digitally-enabled, integrated, person-centred care
Chairs: M Illario, I Annesi-Maesano
J Bousquet From guidelines to digitally-enabled, integrated, person-centred care
M Erhola Care pathways in the Finnish national programmes
JM Anto Planetary health
HJ Schünemann Next-generation guidelines

WORKING GROUPS
Group 1: Self-management
H Pinnock (chair), M Bewick, V Cardona, G Cash, M Ebisawa, D Laune, E Menditto, L Münter, J Phillips, MT Ventura
Develop a 4-page pocket guide (PG) on improved self-care (unintentional and guided) in the ICP Rhinitis, through the use of mobile technology with the development of an enhanced technology PG
Product: A 4-page paper and electronic document, translated in local languages using the ARIA approach

Group 2: ARIA in the pharmacy
O Lourenço, S Bosnic Anticevich (co-chairs), E Costa, D Laune, E Menditto
Aim and product: Develop a 4-page pocket guide on the role of the pharmacist based on the two papers already finalized (ARIA in the pharmacy, Allergy and guide for pharmacists)

Group 3: Next-generation guidelines
H Schünemann (chair), I Agache, C Bachert, L Caraballo, D Chu, T Linuma, Y Okamoto, N Pham-Thi, D Wallace
Aim: Propose a protocol and test 1-3 examples of next-generation guidelines by testing GRADE-based recommendations on real-life data obtained by MASK in order to confirm or refine the current recommendations.
Product: A paper on the examples and a guide for the development of the project

Group 4: Care pathways in allergen immunotherapy
Aim: Develop a practical guide for AIT (4 pages) including the selection of patients, patient stratification.
Product: A 4-page pocket guide

Group 5: Deployment of ICPs to other chronic respiratory diseases and sleep
G Brusselle, JL Pépin (co-chairs), I Ansotegui, JM Anto, S Bosnic Anticevich, W Fokkens, J Malva, J Mullol, U Rodts, S Salmi, O Usmani, S Williams
Aim: Initiate deployment to CRDs
- Asthma and rhinitis
- COPD
- Chronic rhinosinusitis
Product: A short paper proposing simple steps to achieve

Group 7: Deployment of ICPs to developing countries
A Cruz (chair), N Billo, E Costa, LTT Le, M Sanchez-Borges, A Yorgancioglu
Aim: Proposal to initiate deployment to low- and middle-income countries as the GARD demonstration project (MASK).
Product: A short paper proposing simple steps to achieve and launch the COPD App to be presented at the next GARD meeting

Group 8: The paediatric approach
N Papadopoulos, A Valiulis
Aim: Initiate the paediatric strategy.
Product: A draft document on the strategy

Figure 1 Programme and objectives of the meeting.
Anthropocene is characterized by an increase of the levels of climate warming for CO$_2$ in the atmosphere, the ubiquitous presence of microplastic particles in natural waters and oceans, doubling levels of nitrogen and phosphorus in our soils, and a permanent layer of airborne particles, such as carbon black from the combustion of fossil fuels. These changes are predicted to severely disrupt our natural and climate systems, increase poverty and inequalities and severely affect our society and our planet.

So why are public health related communities reacting so slowly and insufficiently to the current planetary crisis? To answer this question, a new approach called “Planetary Health” has been proposed, suggesting that our current concept of health does not consider whether past and current health gains are achieved at the cost of eroding the Earth’s underpinning natural systems and that our understanding of health is insufficient (12). Planetary health, a new concept (4,5), is the achievement of the highest attainable standard of health, wellbeing, and equity worldwide through judicious attention to the human systems - political, economic and social - that shape the limits of Earth’s natural systems within which humanity can flourish.

**The need for digitally-enabled, integrated, person-centred care**

**Public health policy and the importance of next-generation pathways in non-communicable disease (NCD)**

We are all now acutely aware of the growth of NCDs and of the consequential economic and health burden on society and individuals. The rate of growth in an ageing and increasingly sedentary population threatens the viability of health systems and ‘business as usual’ is no longer viable. Self-care and health literacy remain novel approaches to disease prevention and care pathways for those with established disease, despite significant evidence of the effectiveness of such policies. Approaches, such as those developed for chronic airway diseases (13,14), act as
examples of where effective digital interactions involving the patient improve clinical outcomes. Long-term supported interventions in the UK through the Desmond and Dafne schemes (15), approved by NICE, have improved care and control in groups under care programmes. However, there has been no significant impact on overall costs and resources as had been hoped. The public health challenge requires innovative approaches to health care, evidence-based around the patient pathway, and interventions that are successfully implemented by clinicians working more closely with their patients. The current prevalent hierarchical and pedagogic approach will gradually be replaced by a patient-centred one, where the activated health literate patient becomes an active participant in his/her own care and challenges professional and dogmatic norms. The aim is to explore how we can rapidly adopt already evidence-based behaviour changes in populations at risk of the effects of NCDs. Using examples from the current practice to illustrate what can be achieved, we will explore how public health and educational systems need to adapt to a rapidly changing landscape of demand.

Rhinitis and asthma: more than co-morbidity
The Asthma Phenotypes in the Inner City (APIC) study, conducted by the NIAID-funded Inner City Asthma Consortium (ICAC), was a 1-year, prospective, observational study in children 6–17 years of age with intermittent to severe persistent asthma (16-19). The study was designed to examine phenotypes of asthma and rhinitis and included standardized, longitudinal management for both conditions with evaluations and treatment decisions at every visit. Out of the 749 children and adolescents that were enrolled in the longitudinal evaluation/management, 619 had at least 4 out of the 6 scheduled visits and were included in the phenotyping analysis.

Rhinitis was diagnosed in 93.5% of the participating children. Among 5 pre-specified rhinitis phenotypes, based on reported seasonal patterns and compatible allergic sensitizations at baseline, the most common and most severe phenotype was perennial allergic rhinitis with seasonal exacerbations (PARSE) (34.2%), whereas the least common and least severe was nonallergic rhinitis (NAR) (11.3%). During the prospective 1-year evaluation, rhinoconjunctivitis symptoms demonstrated seasonal oscillations compatible with the pre-determined phenotype, supporting the validity of history/allergic sensitization-based classification. For all phenotypes, summertime represented a clear trough in symptomatology, but in no phenotype did symptoms disappear at any time during the year. Standardized rhinitis management included 3 steps: no treatment, oral cetirizine and nasal fluticasone propionate ± cetirizine. At every study visit, around 80% of the children with PARSE required treatment with fluticasone propionate ± cetirizine, whereas less than 5% did not require any treatment. In contrast, about 50% with NAR did not require treatment at every visit. The remaining phenotypes ranged between these two extremes. In children with PARSE, 60% among those who were receiving treatment with fluticasone propionate ± cetirizine remained symptomatic at every visit. These proportions were similar for the other phenotypes except for NAR, where 80% of those prescribed nasal corticosteroids remained symptomatic. These data indicate that: (I) rhinitis is almost ubiquitous in children and adolescents with asthma; and (II) rhinitis in children and adolescents with asthma is mostly moderate to severe and difficult to control.

The study indicated a strong relationship between rhinitis and asthma. At baseline, the intensity of rhinitis symptoms and the rhinitis medication step were among the strongest variables associated with whether asthma would be characterized as easy vs. difficult-to-control during the longitudinal, 1-year evaluation. In the course of the longitudinal evaluation, the rhinoconjunctivitis symptom score and the proportion of study participants requiring fluticasone propionate ± cetirizine were consistently higher in those with difficult-to-control compared to easy-to-control asthma. In addition, causal network analysis identified the domain of “rhinitis severity” as having the strongest direct effect on the domain “asthma severity” independently of the domain “lung function”. A consistent relationship in seasonal oscillations was observed along the 12 calendar months of the prospective evaluation among participants with PARSE and seasonal allergic rhinitis (SAR) between the rhinoconjunctivitis symptom score and asthma outcomes: spring peaks of rhinoconjunctivitis occurred at the same time as peaks in asthma outcomes (particularly asthma exacerbations) whereas fall peaks in rhinoconjunctivitis preceded peaks in asthma by 2 months.

Care pathways in the Finnish national programmes
Finland has been pioneering in implementing national public health programmes for respiratory diseases. Starting from 1994 with the asthma programme (20), the Finnish Lung Health Association (Filha) as the main organizer has continued the work with programmes for COPD 1998 (21,22), sleep-apnoea 2002 (23), allergy 2008 (24), tuberculosis 2013, and indoor air 2018. All programmes have shared: (I)
political commitment on national and regional levels; (II) broad consensus of opinion leaders both on specialist and GP levels; (III) simple and measurable goals, predefined activities and indicators for monitoring the result; (IV) focus on regional educational activities; and (V) involvement of multidisciplinary working groups and patient organizations from the outset.

In asthma, health care costs, emergency visits and hospitalizations have reduced markedly (20,25). Mortality is almost non-existent in those under the age of 60 years. The patients have less and milder symptoms and use medication more rationally. Knowledge of asthma and COPD has increased among professionals, as shown by an improved quality of asthma referral letters and lung function measurements with dynamic spirometry. In COPD, the increasing trend of hospital days has been halted by the programme activities. During the last 20 years, sleep apnoea has appeared as a significant public health problem, but is now treated more actively in primary health care, as guided by the programme.

National programmes have been a framework for systematic improvements in management. At patient level, the development of current care guidelines has given a solid platform for the everyday work of clinicians, nurses and pharmacists in health centres, specialist care and rehabilitation. The evidence-based guidelines have been produced by Duodecim, an independent and transparent Finnish Medical Society, working closely with medical experts. Currently, the guidelines are introduced to everyday practice by an electronic decision support system. This platform can also be integrated to any electronic health record containing structured patient data.

Finland has been active in planning and implementing new protocols for digital services in health care. Those are Virtual Hospital 2.0, led by the University Hospital of Helsinki. The Digital health village includes an entry point for patients with respiratory symptoms/diagnosis. Implementation and adoption of the second phase of the national Kanta health information services were carried out step-by-step from May 2010 to December 2017 (26,27). Currently, the Kanta services include integrated, interoperable information from electronic medical and health records, personal health records, electronic prescribing and social welfare sources that can benefit patients, care providers and policy makers.

Finland has a long systematic history in the development of national respiratory programmes and comprehensive digital services that enable new openings and possibilities for better health support and disease management in the country.

MASK-air (The Allergy Diary)
mHealth, such as apps running on consumer smart devices, is becoming increasingly popular and has the potential to profoundly affect health care and health outcomes. However, it may be disruptive and results achieved are not always reaching the goals. Allergic Rhinitis and its Impact on Asthma (ARIA) has evolved from a guideline using the best evidence-based approach to care pathways suited to real-life using mobile technology in allergic rhinitis (AR) and asthma multimorbidity. Patients largely use over-the-counter (OTC) medications dispensed in pharmacies. Shared decision making (SDM) centred around the patient and based on self-management should be the norm. MASK (Mobile Airways Sentinel NetworK), the Phase 3 ARIA initiative, is based on the freely available MASK app (the Allergy Diary, Android and iOS platforms). MASK is available in 17 languages and deployed in 23 countries. The potential usefulness of MASK will be further explored by POLLAR (Impact of Air POLLution on Asthma and Rhinitis), a new Horizon 2020 project using the Allergy Diary.

The scientific evidence of MASK-air is based on a validated “research” tool (The Allergy Diary up to 2018) that has led to large scale deployment (MASK-air, 2019–):
- Validation of the App using COSMIN guidelines (28);
- Baseline characteristics informed (29);
- Work productivity associated with the control of allergic diseases (30,31);
- EQ-5D is available and was found to correlate with baseline characteristics (32);
- Novel phenotypes of allergic diseases were discovered (33);
- Adherence to treatment is extremely low and novel approaches to inform the efficacy of treatment have been proposed (34) leading to novel studies to better understand guidelines (35-37).

From guidelines to digitally-enabled, integrated, person-centred care

MASK and POLLAR, with the help of three EU projects (DigitalHealthEurope, Eurifi and Vigour) recently accepted on the digital transformation of health, are proposing a second change management strategy following the ARIA change management (4).

In the context of implementing communication on the digital transformation of health and care, specifically in relation to chapter 5 “digital tools for citizen empowerment
and for person-centred care”, DG SANTE took steps to support the scaling-up and wider implementation of good practices in the field of digitally-enabled, integrated, person-centred care. This work was carried out in collaboration with the newly-established Commission Expert Group “Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases”.

For this purpose, DG SANTE—in collaboration with the Commission’s Joint Research Centre—organized a “marketplace” workshop with the Joint Research Centre in Ispra, the third biggest European Commission site after Brussels and Luxembourg. The aim of this workshop was for representatives from Member States and other countries participating in the 3rd Health Programme to learn more about the eight good practices and key policy initiatives in the domain of digitally-enabled, integrated, person-centred care, with a view to possible transfer and replication of the presented practices. The ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma multimorbidity using real-world-evidence was presented. This practice is a GARD demonstration project.

Acknowledgments
None.

Footnote

Conflicts of Interest: Dr. Ansotegui reports personal fees from Mundipharma, Roxall, Sanofi, MSD, Faes Farma, Hikma, UCB, Astra Zeneca, outside the submitted work. Dr. Bachert reports personal fees from ALK, Stallergen, during the conduct of the study; personal fees from ALK, Stallergen, outside the submitted work. Dr. Bousquet reports personal fees from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Purina, Sanofi-Aventis, Takeda, Teva, Uriach, other from KYomed-Innov, outside the submitted work. Dr. Calderon reports personal fees from ALK-Abello, ALK-US, Stallergenes Greer, HAL-Allergy, Allergopharma, ASIT-Biotech, outside the submitted work. Dr. Canonica reports grants from ALK ABELLO, Allergy Therapeutics, Anallergo, Hal Allergy, Stallergenes Greer, outside the submitted work. Dr. Cardona reports personal fees from ALK, Allergopharma, Allergy Therapeutics, Diater, LETI, Thermofisher, Stallergenes, outside the submitted work. Dr. Cecchi reports personal fees from Menarini, Malesci ALK, outside the submitted work. Dr. Cruz reports grants from National Institutes for Health Research (UK), National Institutes of Health (USA), grants and other from National Research Council (Brazil), other from Federal University of Bahia (Brazil), non-financial support from Fundacao ProAR, grants and personal fees from GSK, personal fees from AstraZeneca, Boehringer Ingelheim, CHIESI, Eurofarma, MEDA Pharma. Dr. Durham reports personal fees from Adiga, personal fees from ALK, personal fees from Allergopharma, MedicalUpdate GmBC, UCB, outside the submitted work. Dr. Ebisawa reports personal fees from Mylan, DBV Technologies, Thermofisher, outside the submitted work. Dr. Fokkens reports grants from Mylan, Allergy Therapeutics, GSK, ALK. Dr. Fonseca being a partner in a company developing mobile technologies for monitoring airways diseases. Dr. Klimmek reports grants and personal fees from ALK Abelló, Denmark, grants and personal fees from Novartis, Switzerland, Allergopharma, Germany, Bionorica, Sweden, GSK, Great Britain, Lofarma, Italy, personal fees from MEDA, Sweden, Boehringer Ingelheim, Germany, grants from Biomay, Austria, grants from HAL, Netherlands, grants from LETI, Spain, Roxall, Germany, Bencard, Great Britain, outside the submitted work. Dr. Kuna reports personal fees from Adamed, AstraZeneca, Boehringer Ingelheim, Hal, Chiesi, Novartis, Berlin Chemie Menarini, outside the submitted work. Dr. Kvedariene reports personal fees from GSK, non-financial support from StallergenGreer, Mylan, AstraZeneca, Dimuna, Norameda, outside the submitted work. D Larenas Linnemann reports personal fees from GSK, Astrazeneca, MEDA, Boehringer Ingelheim, Novartis, Grunenthal, UCB, Amstrong, Siegfried, DBV Technologies, MSD, Pfizer. grants from Sanofi, AstraZeneca, Novartis, UCB, GSK, TEVA, Chiesi, Boehringer Ingelheim, outside the submitted work. Dr. MULLOL reports personal fees from SANOFI-Genzyme-Regeneron, ALK-Abelló AS, Menarini Group, MSD, GlaxoSmithKline, Novartis, GENENTECH-Roche, grants and personal fees from UCB Pharma, MYLAN-MEDA Pharma, URIAGH Group, outside the submitted work. Y Okamoto reports personal fees from Shionogi Co. Ltd., Torii Co. Ltd., GSK, MSD, Kyowa Co. Ltd., from Eizai Co. Ltd., grants and personal fees from Kyorin Co. Ltd., Tiho Co. Ltd., grants from Yakuruto Co. Ltd., Yamada Bee Farm, outside the submitted work. N Papadopoulos reports personal fees from Novartis, Faes Farma, BIOMAY, HAL, Nutricia Research, Menarini, Novartis, MEDA, Abbvie, Novartis, MSD, Omega Pharma Danone, grants from Menarini outside the submitted work. O Pfäar reports grants and personal fees from ALK-Abelló, Allergopharma,
Stallergenes Greer, HAL Allergy Holding B.V./HAL Allergie GmbH, Bencard Allergie GmbH/Allergy Therapeutics, Lofarma, Biotech Tools S.A, LETI/LETI Pharma, Anergis S.A. grants from Biomay, Nuvo, Circassia, Glaxo Smith Kline, personal fees from Novartis Pharma, MEDA Pharma, Mobile Chamber Experts (a GA2LEN Partner), Pohl-Boskamp, Indoor Biotechnologies, grants from, outside the submitted work. Dr. Samolinski reports non-financial support from Mylan, during the conduct of the study. Dr. Shamji reports grants and personal fees from ALK, ASIT Biotech, sa, Allergopharma, grants from Regeneron, Merck, Immune Tolerance Network, outside the submitted work. Dr. Tsiligianni reports personal fees from Novartis, GSK, Boehringer Ingelheim, Astra Zeneca, grants from GSK Hellas, outside the submitted work. Dr. Wallace is co-chair of the Joint Task Force on Practice Parameters of the AAAAI/ACAAI. However, it does not feel that this causes any conflict of interest in the writing/review of the document. Zuberdier reports fees from Bayer Health Care, FAES, Novartis, Henkel, Astra Zeneca, AbbVie, ALK, Almirall, Astellas, Bayer Health Care, Bencard, Berlin Chemie, HAL, Leti, Media, Menarini, Merck, MSD, Pfizer, Sanofi, Stallergenes, Takeda, Teva, UCB, Henkel, Kryolan, l'Oreal; Commitee member: WHO-Initiative “Allergic Rhinitis and Its Impact on Asthma” (ARIA). Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI). Head: European Centre for Allergy Research Foundation (ECARF). Secretary General: Global Allergy and Asthma European Network (GA2LEN). Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO). The other authors have no conflicts of interest to declare.

**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**References**
