

Transfer of innovation on allergic rhinitis and asthma multimorbidity in the elderly (MACVIA-ARIA) - EIP on AHA Twinning Reference Site (GARD research demonstration project)

J. Bousquet^{1,2,3} | I. Agache⁴ | M. R. Aliberti⁵ | R. Angles⁶ | I. Annesi-Maesano^{7,8} | J. M. Anto^{9,10,11} | S. Arnavielhe¹² | E. Asayag¹³ | E. Bacci¹⁴ | A. Bedbrook¹ | C. Bachert¹⁵ | I. Baroni¹⁶ | B. A. Barreto¹⁷ | M. Bedolla-Barajas¹⁸ | K. C. Bergmann^{19,20} | L. Bertorello¹⁴ | M. Bewick²¹ | T. Bieber²² | S. Birov²³ | C. Bindslev-Jensen²⁴ | A. Blua²⁵ | M. Bochenska Marciniak²⁶ | I. Bogus-Buczynska²⁶ | S. Bosnic-Anticevich²⁷ | I. Bosse²⁸ | R. Bourret²⁹ | C. Bucca³⁰ | R. Buonaiuto³¹ | M. T. Burguete Cabanas³² | D. Caillaud³⁴ | D. P. Caimmi³⁵ | D. Caiazza³¹ | P. Camargos³⁶ | G. Canfora³⁷ | V. Cardona³⁸ | A. M. Carriazo³⁹ | C. Cartier⁴⁰ | G. Castellano⁴¹ | N. H. Chavannes⁴² | L. Cecci⁴³ | M. M. Ciaravolo⁴⁴ | C. Cingi⁴⁵ | A. Ciceran⁴⁶ | L. Colas⁴⁷ | E. Colgan⁴⁸ | J. Coll⁴⁹ | D. Conforti⁵⁰ | J. Correia de Sousa⁵¹ | R. M. Cortés-Grimaldo⁵² | F. Corti⁵³ | E. Costa⁵⁴ | A. L. Courbis⁵⁵ | E. Cousein⁵⁶ | A. A. Cruz^{57,58} | A. Custovic⁵⁹ | B. Cvetkovski²⁷ | C. Dario⁶⁰ | J. da Silva⁶¹ | Y. Dauvilliers⁶² | F. De Blay⁶³ | T. Dedeu⁶⁴ | G. De Feo⁶⁵ | B. De Martino⁶⁶ | P. Demoly³⁵ | G. De Vries⁶⁷ | S. Di Capua Ercolano⁶⁸ | N. Di Carluccio³¹ | M. Doulapsi⁶⁹ | G. Dray⁵⁵ | R. Dubakiene⁷⁰ | E. Eller²⁴ | R. Emuzyte⁷¹ | J. G. Espinoza-Contreras⁷² | A. Estrada-Cardona⁷³ | J. Farrell⁴⁸ | A. Farsi⁴³ | J. Ferrero⁷⁴ | W. J. Fokkens⁷⁵ | J. Fonseca^{76,77} | J. F. Fontaine⁷⁸ | S. Forti⁵⁰ | J. L. Gálvez-Romero⁷⁹ | C. I. García-Cobas⁸⁰ | M. H. Garcia Cruz⁸¹ | B. Gemicioğlu⁸² | R. Gerth van Wijk⁸³ | M. Guidacci⁸⁴ | J. Gómez-Vera⁸⁵ | N. A. Guldmond⁸⁶ | Z. Gutter⁸⁷ | T. Haahtela⁸⁸ | J. Hajjam⁸⁹ | P. W. Hellings⁹⁰ | L. Hernández-Velázquez⁹¹ | M. Illario⁹² | J. C. Ivancevich⁹³ | E. Jares⁹⁴ | G. Joos⁹⁵ | J. Just^{96,97} | O. Kalayci⁹⁸ | A. F. Kalyoncu⁹⁹ | J. Karjalainen¹⁰⁰ | T. Keil¹⁰¹ | N. Khaltaev¹⁰² | L. Klimek¹⁰³ | V. Kritikos²⁷ | I. Kull¹⁰⁴ | P. Kuna²⁶ | V. Kvedariene¹⁰⁵ | V. Kolek¹⁰⁶ |

Abbreviations: AHA, Active and Healthy Aging; AIT, specific immunotherapy; AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; CARAT, Control of Allergic Rhinitis and Asthma Test; EIP, European Innovation Partnership; EU, European Union; HIT, Health information technology; ICT, information and communications technology; MACVIA, Contre les MALadies Chroniques pour un Vieillessement Actif; MASK, MACVIA-ARIA Sentinel Network; NAR, non allergic rhinitis; SCUAD, Severe chronic upper airways disease; VAS, visual analogue scale.

E. Krzych-Fała¹⁰⁷ | **M. Kupczyk**²⁶ | **P. Lacwik**²⁶ | **S. La Grutta**¹⁰⁸ | **D. Larenas-Linnemann**¹⁰⁹ | **D. Laune**¹² | **D. Lauri**¹¹⁰ | **J. Lavrut**¹¹¹ | **M. Lessa**¹¹² | **G. Levato**¹¹³ | **L. Lewis**¹¹⁴ | **I. Lieten**¹¹⁵ | **A. Lipiec**¹⁰⁷ | **R. Louis**¹¹⁶ | **J. A. Luna-Pech**¹¹⁷ | **A. Magnan**⁴⁷ | **J. Malva**^{118,119} | **J. F. Maspero**¹²⁰ | **J. J. Matta-Campos**¹²¹ | **O. Mayora**⁵⁰ | **M. A. Medina-Ávalos**¹²² | **E. Melén**¹²³ | **E. Menditto**¹²⁴ | **J. Millot-Keurinck**¹²⁵ | **G. Moda**¹²⁶ | **M. Morais-Almeida**¹²⁷ | **R. Mösges**¹²⁸ | **A. Mota-Pinto**^{119,129,130} | **J. Mulla**¹³¹ | **A. Muraro**¹³² | **R. Murray**¹³³ | **M. Noguès**¹²⁵ | **M. Nalin**¹⁶ | **L. Napoli**¹³⁴ | **H. Neffen**¹³⁵ | **R. E. O'Hehir**¹³⁶ | **G. L. Onorato**¹ | **S. Palkonen**¹³⁷ | **N. G. Papadopoulos**^{138,139} | **G. Passalacqua**¹⁴⁰ | **J. L. Pépin**¹⁴¹ | **A. M. Pereira**¹⁴² | **M. Persico**¹⁴³ | **O. Pfaar**^{144,145} | **A. C. Pozzi**¹⁴⁶ | **E. Prokopakis**⁶⁹ | **B. Pugin**⁹⁰ | **F. Raciborski**¹⁰⁷ | **J. Rimmer**¹⁴⁷ | **J. A. Rizzo**¹⁴⁸ | **C. Robalo-Cordeiro**¹⁴⁹ | **M. Rodríguez-González**¹⁵⁰ | **G. Rolla**¹⁵¹ | **R. E. Roller-Wirnsberger**¹⁵² | **A. Romano**^{153,154} | **M. Romano**¹⁶ | **M. R. Romano**⁵ | **J. Salimäki**¹⁵⁵ | **B. Samolinski**¹⁰⁷ | **F. S. Serpa**¹⁵⁶ | **S. Shamai**¹²⁸ | **M. Sierra**⁴⁹ | **M. Sova**¹⁵⁷ | **M. Sorlini**¹⁵⁸ | **C. Stellato**⁶⁵ | **R. Stelmach**¹⁵⁹ | **T. Strandberg**¹⁶⁰ | **V. Stroetmann**²³ | **R. Stukas**¹⁶¹ | **A. Szylling**¹⁰⁷ | **R. Tan**²⁷ | **V. Tibaldi**¹⁵¹ | **A. Todo-Bom**¹⁶² | **S. Toppila-Salmi**⁸⁸ | **P. Tomazic**¹⁶³ | **U. Trama**¹⁶⁴ | **M. Triggiani**⁶⁵ | **A. Valero**¹⁶⁵ | **E. Valovirta**^{166,167} | **A. Valiulis**^{168,169} | **M. van Eerd**⁶⁷ | **T. Vasankari**¹⁷⁰ | **A. Vatrella**⁶⁵ | **M. T. Ventura**¹⁷¹ | **M. T. Verissimo**^{118,119} | **F. Viart**⁴⁰ | **S. Williams**¹⁷² | **M. Wagenmann**¹⁷³ | **C. Wanscher**¹⁷⁴ | **M. Westman**¹⁷⁵ | **M. Wickman**¹⁷⁶ | **I. Young**¹⁷⁷ | **A. Yorgancioglu**¹⁷⁸ | **E. Zernotti**¹⁷⁹ | **T. Zuberbier**^{19,20} | **A. Zurkühlen**³³ | **B. De Oliveira**¹⁸⁰ | **A. Senn**¹⁸⁰

¹MACVIA-France, Contre les MAladies Chroniques pour un Vleillissement Actif en France European Innovation Partnership on Active and Healthy Ageing Reference Site, Montpellier, France

²VIMA, INSERM U 1168, VIMA: Ageing and Chronic Diseases, Epidemiological and Public Health Approaches, Villejuif, France

³Université Versailles St-Quentin-en-Yvelines, UMR-S 1168, Montigny le Bretonneux, France

⁴Faculty of Medicine, Transylvania University, Brasov, Romania

⁵Municipality of Salerno, Salerno, Italy

⁶Innovación y nuevas tecnologías, Salud Sector sanitario de Barbastro, Barbastro, Spain

⁷EPAR U707 INSERM, Paris, France

⁸EPAR UMR-S UPMC, Paris VI, Paris, France

⁹ISGLoBAL, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain

¹⁰IMIM (Hospital del Mar Research Institute), Universitat Pompeu Fabra (UPF), Barcelona, Spain

¹¹CIBER Epidemiología y Salud Pública (CIBERESP), Universitat Pompeu Fabra (UPF), Barcelona, Spain

¹²Kyomed, Montpellier, France

¹³Argentine Society of Allergy and Immunopathology, Buenos Aires, Argentina

¹⁴Regione Liguria, Genoa, Italy

¹⁵Upper Airways Research Laboratory, ENT Department, Ghent University Hospital, Ghent, Belgium

¹⁶Telbios SRL, Milan, Italy

¹⁷Alergologo, Belem, Brazil

- ¹⁸Hospital Civil de Guadalajara Dr. Juan I. Menchaca, Guadalajara, Mexico
- ¹⁹Comprehensive Allergy-Centre-Charité, Department of Dermatology and Allergy, Charité-Universitätsmedizin Berlin, Berlin, Germany
- ²⁰Global Allergy and Asthma European Network (GA²LEN), Berlin, Germany
- ²¹iQ4U Consultants Ltd, London, UK
- ²²Department of Dermatology and Allergy, Rheinische Friedrich-Wilhelms-University, Bonn, Germany
- ²³Empirica Communication and Technology Research, Bonn, Germany
- ²⁴Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark
- ²⁵Argentine Association of Respiratory Medicine, Buenos Aires, Argentina
- ²⁶Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz, Lodz, Poland
- ²⁷Woolcock Institute of Medical Research, University of Sydney and Sydney Local Health District, Glebe, NSW, Australia
- ²⁸Allergist, La Rochelle, France
- ²⁹Centre Hospitalier Valenciennes, Valenciennes, France
- ³⁰Chief of the University Pneumology Unit- AOU Molinette, Hospital City of Health and Science of Torino, Torino, Italy
- ³¹Pharmacist of COFASER - Consorzio Farmacie Servizi-Salerno, Salerno, Italy
- ³²Centro Médico Zambrano Hellion, Monterrey, Mexico
- ³³Gesundheitsregion KölnBonn - HRCB Projekt GmbH, Köln, Germany
- ³⁴Service de pneumologie, CHU et université d'Auvergne, Clermont-Ferrand, France
- ³⁵Department of Respiratory Diseases, Montpellier University Hospital, Montpellier, France
- ³⁶Department of Pediatrics, Medical School, Federal University of Minas Gerais, Belo Horizonte, Brazil
- ³⁷Mayor of Sarno and President of Salerno Province, Anesthesiology Service, Sarno "Martiri del Villa Malta" Hospital, Sarno, Italy
- ³⁸S. Allergologia, S. Medicina Interna, Hospital Vall d'Hebron, Barcelona, Spain
- ³⁹Regional Ministry of Health of Andalusia, Seville, Spain
- ⁴⁰ASA - Advanced Solutions Accelerator, Clapiers, France
- ⁴¹Celentano Pharmacy, Massa Lubrense, Italy
- ⁴²Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands
- ⁴³S.O.S Allergology and Clinical Immunology, USL Toscana Centro, Prato, Italy
- ⁴⁴Specialist Social Worker, Sorrento, Italy
- ⁴⁵ENT Department, Medical Faculty, Eskisehir Osmangazi University, Eskisehir, Turkey
- ⁴⁶Argentine Federation of Otorhinolaryngology Societies, Buenos Aires, Argentina
- ⁴⁷Service de Pneumologie, UMR INSERM, UMR1087and CNR 6291, l'institut du thorax, University of Nantes, Nantes, France
- ⁴⁸Department of Health, Social Services and Public Safety, Belfast, UK
- ⁴⁹Innovación y nuevas tecnologías, Salud Sector sanitario de Barbastro, Barbastro, Spain
- ⁵⁰Fondazione Bruno Kessler (FBK), Trento, Italy
- ⁵¹Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal
- ⁵²Alergologa, Guadalajara, Mexico
- ⁵³FIMMG (Federazione Italiana Medici di Medicina Generale), Milan, Italy
- ⁵⁴UCIBIO, REQYULTE, Faculty of Pharmacy and Competence Center on Active and Healthy Ageing of University of Porto (AgeUPNetWork), Porto, Portugal
- ⁵⁵Ecole des Mines, Alès, France
- ⁵⁶Vice Président de la CME - Centre Hospitalier, Valenciennes, France
- ⁵⁷ProAR – Nucleo de Excelencia em Asma, Federal University of Bahia, Bahia, Brazil
- ⁵⁸GARD/WHO Executive Committee and Federal University of Bahia, Bahia, Brazil
- ⁵⁹Department of Pediatric, Imperial College London, London, UK
- ⁶⁰Azienda Provinciale per i Servizi Sanitari di Trento (APSS-Trento), Trento, Italy
- ⁶¹Allergy Service, University Hospital of Federal University of Santa Catarina (HU-UFSC), Florianópolis, Brazil
- ⁶²Sleep Unit, Department of Neurology, Hôpital Gui-de-Chauliac Montpellier, Inserm U1061, Montpellier, France
- ⁶³Allergy Division, Chest Disease Department, University Hospital of Strasbourg, Strasbourg, France
- ⁶⁴AQuAS, Barcelona, Spain & EUREGHA, European Regional and Local Health Association, Brussels, Belgium
- ⁶⁵Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
- ⁶⁶Social Workers Coordinator, Sorrento, Italy
- ⁶⁷Peercode DV, Gerdermalsen, The Netherlands
- ⁶⁸Farmacie Dei Golfi Group, Massa Lubrense, Italy
- ⁶⁹Department of Otolaryngology, University of Crete School of Medicine, Heraklion, Greece
- ⁷⁰Medical Faculty, Vilnius University, Vilnius, Lithuania

- ⁷¹Clinic of Children's Diseases, Faculty of Medicine, Vilnius University, Vilnius, Lithuania
- ⁷²University of Aguascalientes, Chihuahua, Mexico
- ⁷³Alergologo, Playa del Carmen, Mexico
- ⁷⁴Andalusian Agency for Healthcare Quality, Seville, Spain
- ⁷⁵Department of Otorhinolaryngology, Academic Medical Centre, Amsterdam, The Netherlands
- ⁷⁶Center for Health Technology and Services Research- CINTESIS, Faculdade de Medicina, Universidade do Porto, Porto, Portugal
- ⁷⁷Allergy Unit, CUF Porto Instituto & Hospital, Porto, Portugal
- ⁷⁸Allergist, Reims, France
- ⁷⁹Regional Hospital of ISSSTE, Puebla, Mexico
- ⁸⁰Alergologo, Guadalajara, Mexico
- ⁸¹Allergy Clinic, National Institute of Respiratory Diseases, Mexico City, Mexico
- ⁸²Department of Pulmonary Diseases, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, Turkey
- ⁸³Department of Internal Medicine, Section of Allergology, Erasmus MC, Rotterdam, The Netherlands
- ⁸⁴Member of the Brazilian Society of Pediatrics and Society of Immunization, Representative of GINA (Global Initiative Against Asthma), Brasilia, Brazil
- ⁸⁵Allergy Clinic, Hospital Regional del ISSSTE 'Lic. López Mateos', Mexico City, Mexico
- ⁸⁶Institute of Health Policy and Management iBMG, Erasmus University, Rotterdam, The Netherlands
- ⁸⁷University Hospital Olomouc – National eHealth Centre, Olomouk, Czech Republic
- ⁸⁸Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland
- ⁸⁹Centich: centre d'expertise national des technologies de l'information et de la communication pour l'autonomie, GÉrontopôle autonomie longévité des Pays de la Loire, Conseil régional des Pays de la Loire, Centre d'expertise Partenariat Européen d'Innovation pour un vieillissement actif et en bonne santé, Nantes, France
- ⁹⁰Laboratory of Clinical Immunology, Department of Microbiology and Immunology, KU Leuven, Leuven, Belgium
- ⁹¹Alergologo, Ensenada, Mexico
- ⁹²Division for Health Innovation, Campania Region and Federico II University Hospital Naples (R&D and DISMET), Naples, Italy
- ⁹³Servicio de Alergia e Inmunología, Clínica Santa Isabel, Buenos Aires, Argentina
- ⁹⁴Libra Foundation, Buenos Aires, Argentina
- ⁹⁵Department of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium
- ⁹⁶Allergology Department, Centre de l'Asthme et des Allergies, Hôpital d'Enfants Armand-Trousseau (APHP, Paris), Paris, France
- ⁹⁷Sorbonne Universités, UPMC Univ Paris 06, UMR_S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Equipe EPAR, Paris, France
- ⁹⁸Pediatric Allergy and Asthma Unit, Hacettepe University School of Medicine, Ankara, Turkey
- ⁹⁹Immunology and Allergy Division, Department of Chest Diseases, School of Medicine, Hacettepe University, Ankara, Turkey
- ¹⁰⁰Allergy Centre, Tampere University Hospital, Tampere, Finland
- ¹⁰¹Institute of Social Medicine, Epidemiology and Health Economics, Charité - Universitätsmedizin Berlin, Berlin, and Institute for Clinical Epidemiology and Biometry, University of Wuerzburg, Wuerzburg, Germany
- ¹⁰²GARD, Geneva, Switzerland
- ¹⁰³Center for Rhinology and Allergology, Wiesbaden, Germany
- ¹⁰⁴Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden
- ¹⁰⁵Clinic of Infectious, Chest Diseases, Dermatology and Allergology, Vilnius University, Vilnius, Lithuania
- ¹⁰⁶Department of Respiratory Medicine, Faculty of Medicine and Dentistry, University Hospital, Olomouc, Czech Republic
- ¹⁰⁷Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Warsaw, Poland
- ¹⁰⁸Institute of Biomedicine and Molecular Immunology (IBIM), National Research Council (CNR), Palermo, Italy
- ¹⁰⁹Clínica de Alergia, Asma y Pediatría, Hospital Médica Sur, México City, Mexico
- ¹¹⁰Presidente CMMC, Milano, Italy
- ¹¹¹Head of the Allergy Department of Pedro de Elizalde Children's Hospital, Buenos Aires, Argentina
- ¹¹²Faculdade de Medicina da Universidade Federal da Bahia, Salvador de Bahia, Brazil
- ¹¹³Sifmed, Milano, Italy
- ¹¹⁴Promotor B3 Action Group EIP on AHA and Senior Fellow, International Foundation for Integrated Care, Aberystwyth, UK
- ¹¹⁵Tech Life Valley, Diepenbeek, Belgium
- ¹¹⁶Department of Pulmonary Medicine, CHU Sart-Tilman, Liege, Belgium
- ¹¹⁷University of Guadalajara, Guadalajara, Mexico
- ¹¹⁸Faculty of Medicine, Institute of Biomedical Imaging and Life Sciences (IBILI), University of Coimbra, Coimbra, Portugal
- ¹¹⁹Ageing@Coimbra EIP-AHA Reference Site, Coimbra, Portugal
- ¹²⁰Argentine Association of Allergy and Clinical Immunology, Buenos Aires, Argentina

- ¹²¹Hospital Regional Siglo XXI, Mexico City, Mexico
- ¹²²Alergologo, Veracruz, Mexico
- ¹²³Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm and Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
- ¹²⁴CIRFF, Federico II University, Naples, Italy
- ¹²⁵Caisse d'assurance retraite et de la santé au travail du Languedoc-Roussillon (CARSAT-LR), Montpellier, France
- ¹²⁶Regione Piemonte, Torino, Italy
- ¹²⁷Allergy and Clinical Immunology Department, Hospital CUF-Descobertas, Lisboa, Portugal
- ¹²⁸Institute of Medical Statistics, Informatics and Epidemiology, Medical Faculty, University of Cologne, Cologne, Germany
- ¹²⁹Laboratory of General Pathology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal
- ¹³⁰Institute of Biomedical Imaging and Life Sciences (IBILI), Faculty of Medicine, University of Coimbra, Coimbra, Portugal
- ¹³¹Clinical & Experimental Respiratory Immunoallergy, ENT Department, Hospital Clínic, IDIBAPS, Universitat de Barcelona, Barcelona, Spain
- ¹³²Department of Women and Child Health, Food Allergy Referral Centre Veneto Region, Padua General University Hospital, Padua, Italy
- ¹³³MedScript Ltd, Dundalk, Co. Louth, Ireland
- ¹³⁴Consortium of Pharmacies and Services COSAFER, Salerno, Italy
- ¹³⁵Head of Respiratory Medicine, Alassia Children's Hospital, Center for Allergy and Immunology, Santa Fe, Argentina
- ¹³⁶Department of Allergy, Immunology and Respiratory Medicine, Alfred Hospital and Central Clinical School, Monash University, Melbourne, Vic., Australia
- ¹³⁷EFA European Federation of Allergy and Airways Diseases Patients' Associations, Brussels, Belgium
- ¹³⁸Center for Pediatrics and Child Health, Institute of Human Development, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK
- ¹³⁹Allergy Department, 2nd Pediatric Clinic, Athens General Children's Hospital "P&A Kyriakou", University of Athens, Athens, Greece
- ¹⁴⁰Allergy and Respiratory Diseases, IRCCS San Martino Hospital-IST-University of Genoa, Genoa, Italy
- ¹⁴¹Department of Pneumology, CHU Grenoble, Grenoble, France
- ¹⁴²Allergy Unit, CUF-Porto Hospital and Institute, Center for Research in Health Technologies and Information Systems, CINTESIS, Universidade do Porto, Porto, Portugal
- ¹⁴³Sociologist, Municipality, Sorrento, Italy
- ¹⁴⁴Department of Otorhinolaryngology, Head and Neck Surgery, Universitätsmedizin Mannheim, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany
- ¹⁴⁵Center for Rhinology and Allergy, Wiesbaden, Germany
- ¹⁴⁶Vice-Presidente of IML, Milano, Italy
- ¹⁴⁷Woolcock Institute of Medical Research, University of Sydney and Sydney Local Health District, Glebe, NSW, Australia
- ¹⁴⁸Alergista, Recife, Brazil
- ¹⁴⁹Centre of Pneumology, Coimbra University Hospital, Coimbra, Portugal
- ¹⁵⁰Alergologo, Mexico City, Mexico
- ¹⁵¹Regione Piemonte, Torino, Italy
- ¹⁵²Medical University of Graz, Graz, Austria
- ¹⁵³Allergy Unit, Presidio Columbus, Rome, Catholic University of Sacred Heart, Rome, Italy
- ¹⁵⁴IRCCS Oasi Maria S.S., Troina, Italy
- ¹⁵⁵Association of Finnish Pharmacists, Helsinki, Finland
- ¹⁵⁶Allergist, Vitoria, Brazil
- ¹⁵⁷Departement of Internal Medicine, University Hospital, Olomouc, Czech Republic
- ¹⁵⁸IML (Lombardy Medical Initiative), Bergamo, Italy
- ¹⁵⁹Pulmonary Division, Heart Institute (InCor), Hospital da Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil
- ¹⁶⁰Center for Life Course Health Research, Helsinki University Hospital, Helsinki University, University of Oulu, Oulu, Finland
- ¹⁶¹Public Health Institute of Vilnius University, Vilnius, Lithuania
- ¹⁶²Imunoalergologia, Centro Hospitalar Universitário de Coimbra and Faculty of Medicine, University of Coimbra, Coimbra, Portugal
- ¹⁶³Department of ENT, Medical University of Graz, Graz, Austria
- ¹⁶⁴Division on Pharmacy and Devices Policy, Campania Region, Naples, Italy
- ¹⁶⁵Pneumology and Allergy Department, Hospital Clínic, Clinical & Experimental Respiratory Immunoallergy, IDIBAPS, CIBERES, University of Barcelona, Barcelona, Spain
- ¹⁶⁶Department of Lung Diseases and Clinical Allergy, University of Turku, Turku, Finland
- ¹⁶⁷Allergy Clinic, Terveystalo, Turku, Finland
- ¹⁶⁸Vilnius University Clinic of Children's Diseases and Public Health Institute, Vilnius, Lithuania
- ¹⁶⁹European Academy of Paediatrics (EAP/UEMS-SP), Brussels, Belgium
- ¹⁷⁰FILHA, Finnish Lung Association, Helsinki, Finland

¹⁷¹Unit of Geriatric Immunoallergy, University of Bari Medical School, Bari, Italy

¹⁷²International Primary Care Respiratory Group IPCRG, Aberdeen, UK

¹⁷³Department of Otorhinolaryngology, HNO-Klinik, Universitätsklinikum Düsseldorf, Düsseldorf, Germany

¹⁷⁴EIP on AHA Coordinator, Region of Southern Denmark, Odense, Denmark

¹⁷⁵Department of Medicine Solna, Immunology and Allergy Unit, Karolinska Institutet and Department of ENT Diseases, Karolinska University Hospital, Stockholm, Sweden

¹⁷⁶Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm and Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

¹⁷⁷Queen's University, Belfast, UK

¹⁷⁸Celal Bayar University Department of Pulmonology, GARD Executive Committee, Manisa, Turkey

¹⁷⁹Universidad Católica de Córdoba, Córdoba, Argentina

¹⁸⁰EC-CNECT-H2, European Commission, Brussels, Belgium

Correspondence

Jean Bousquet, CHU Arnaud de Villeneuve, Montpellier Cédex 5, France.
Email: jean.bousquet@orange.fr

Funding information

This study received an unrestricted educational grant from Meda (Bad Homburg, Germany) and Structural Development Funds from the European Union (Région Languedoc Roussillon). The app belongs to the Région Occitanie (formerly Languedoc-Roussillon, Midi-Pyrénées, France). MASK is a project of the B3 Action Plan of the European Innovation Partnership on Active and Healthy Ageing—EIP on AHA (European Commission DG Santé and DG CONNECT) and of the “Twinning” (Transfer of Innovation, 2016 Pilot Twinning Support Scheme of the EIP on AHA) of the app in 22 EIP on AHA Reference Sites.

Edited by: Hans-Uwe Simon

[Correction added on 28 November 2017 after first online publication: One of the author names was previously incorrect and has been corrected in this version.]

Abstract

The overarching goals of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA) are to enable European citizens to lead healthy, active and independent lives whilst ageing. The EIP on AHA includes 74 Reference Sites. The aim of this study was to transfer innovation from an app developed by the MACVIA-France EIP on AHA reference site (*Allergy Diary*) to other reference sites. The phenotypic characteristics of rhinitis and asthma multimorbidity in adults and the elderly will be compared using validated information and communication technology (ICT) tools (i.e. the *Allergy Diary* and CARAT: Control of Allergic Rhinitis and Asthma Test) in 22 Reference Sites or regions across Europe. This will improve the understanding, assessment of burden, diagnosis and management of rhinitis in the elderly by comparison with an adult population. Specific objectives will be: (i) to assess the percentage of adults and elderly who are able to use the *Allergy Diary*, (ii) to study the phenotypic characteristics and treatment over a 1-year period of rhinitis and asthma multimorbidity at baseline (cross-sectional study) and (iii) to follow-up using visual analogue scale (VAS). This part of the study may provide some insight into the differences between the elderly and adults in terms of response to treatment and practice. Finally (iv) work productivity will be examined in adults.

KEYWORDS

Allergy, *Allergy Diary*, asthma, European Innovation Partnership on Active and Healthy Ageing, rhinitis

1 | INTRODUCTION

Rhinitis, the most common chronic disease in Europe, often starts early in life, persists across the life cycle and causes a high disease burden in all age groups.¹ Rhinitis and asthma multimorbidity is common¹ and the two diseases should be considered jointly. The symptoms of allergic rhinitis (AR) can cause considerable morbidity in terms of physical and emotional comfort and functional capacity. Work productivity is one of the major societal impacts of AR.^{2,3} Sleep impairment is common in AR^{4,5} and is associated with severe nasal symptoms.⁶

By 2020, rhinitis will affect at least 20% of the old-age population.^{7–11} Rhinitis in this age group has phenotypic specificities and treatment modalities including poly-medication. The effects of

polypharmacy may contribute to congestion and dryness.¹² Sex may also be a confounding factor in the elderly. The phenotypic characteristics and treatment of rhinitis in the elderly depend on ageing (physiology, immunology), socio-cultural barriers, environmental factors (urban vs rural), allergic and non-allergic multi-morbidities,^{13,14} drug availability and affordability, specific side effects to drugs in this age group,¹⁵ and health systems as well as type of care. However, rhinitis burden in the elderly is an under-recognized and under-treated problem.⁸ Important demographic changes are expected in the European population. It is therefore crucial to study the phenotype and treatment of rhinitis-asthma multimorbidity in this age group in different European regions in order to (i) provide new concepts and hypotheses and (ii) offer new diagnosis and management strategies to reduce health and social inequalities.

Measures of AR control include symptom scores, control scores and patients' self-administered visual analogue scales (VAS).^{11,16-23} VAS, a psychometric response scale for subjective characteristics or attitudes, has been successfully used in many diseases including AR. Severe chronic upper airway disease (SCUAD) defines uncontrolled AR patients despite optimal pharmacotherapy.²⁴ The Control of Allergic Rhinitis and Asthma Test (CARAT)²⁵⁻²⁸ is the only self-administered questionnaire to quantify the control of both AR and asthma concurrently. It consists of 10 questions on upper and lower airway symptoms, sleep interference, activity limitation, and the need to increase medication over a 4-week period. CARAT meets all items of the COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) checklist.²⁹⁻³¹ CARAT was developed and validated in Portugal and has been translated and culturally adapted in over 25 languages and nine countries (Belgium, Brazil, France, Germany, Greece, India, Italy, the Netherlands and Ukraine). Web and smartphone versions have been developed, and an open model of distribution contributes to its dissemination.

European Innovation Partnerships (EIPs) bring together all relevant actors at European Union (EU), national and regional levels to: (i) step up research and development efforts; (ii) coordinate investments in demonstration and pilots; (iii) anticipate and fast-track any necessary regulation and standards; and (iv) ensure that any breakthroughs are quickly brought to the market. The goals of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA) are to enable European citizens to lead healthy, active and independent lives whilst ageing. The EIP on AHA includes 74 Reference Sites.

MACVIA-France (Fighting chronic diseases for active and healthy ageing in France) is a reference site of the EIP on AHA.^{32,33} It initiated the project "Integrated Care Pathways for airway diseases (AIRWAYS ICPs)".^{34,35} AIRWAYS ICPs aims to develop multi-sectoral ICPs for rhinitis and its multi-morbidities in the elderly, implementing emerging technologies for individualized and predictive medicine.³⁵ A patient-centred mobile application (app for iOS and Android smartphones) has been developed.^{6,36} This app (*Allergy Diary*) uses VAS scores and enables the daily assessment of rhinitis and asthma control by patients themselves.^{37,38} It will also include a Clinical Decision Support System (CDSS).²² The *Allergy Diary* is available for free download in 21 countries and 16 languages and has already been tested by over 8,000 users of all ages. Real-time data from users' smartphones can be stored and retrieved in a functional database. This EIP on AHA Synergy project has been developed between Action Groups of the EIP on AHA to build bridges for innovation in AHA.³⁹ The *Allergy Diary* also includes CARAT.

Regional organizations engaged in the EIP on AHA were proposed to apply for a grant in order to facilitate the transfer of innovative practices (Twinning) for implementation in other regions (<http://www.scale-aha.eu/news.html>). The aim of this initiative is to facilitate the deployment of large-scale digitally-enabled innovative solutions for health and care delivery to the ageing population. It

therefore contributes to the European Scaling Up Strategy of the EIP on AHA, already initiated by MACVIA-ARIA.⁴⁰

2 | OBJECTIVES OF THE MACVIA-ARIA TWINNING

The transfer of innovative practices (Twinning) aims to transfer and implement (i) the *Allergy Diary* developed by MACVIA-LR^{37,38} and (ii) CARAT²⁵⁻²⁸ to the different EIP on AHA Reference Sites. Other tools may also be used.

The longer-term aim of the Twinning is (i) to provide care pathways for individualized and predictive medicine for rhinitis and asthma multimorbidity in the elderly,³⁶ (ii) to extend the study to sleep impairment in AR and asthma and (iii) to assess interactions of allergen exposure and air pollution. Moreover, the Twinning will allow Reference Sites from different areas of Europe to interact. This will increase knowledge, enable the transfer of know-how and support the establishment of local structured thematic networks on respiratory diseases sharing tools, indicators and knowledge that are available in the EU context (Table 1).

Although the vast majority of Reference Sites will work on the main aim of the Twinning (rhinitis and asthma multimorbidity in the elderly), some will have a different Twinning process to reinforce the project (Table 2).

As the study will last 1 year—to account for differences in allergen exposure—the starting data are not necessarily the same in all countries and new Reference Sites can join the Twinning within the next 6 months.

TABLE 1 Objectives of the twinning

General objectives

To compare phenotypic characteristics of rhinitis and asthma multimorbidity in adults and the elderly using validated ICT tools (*Allergy Diary* and CARAT) in EIP on AHA Reference Sites across Europe to better understand, diagnose and manage rhinitis and assess its burden in the elderly

Specific objectives

To assess the percentage of adults and elderly who are able to use the *Allergy Diary*:

Cross-sectional study: The study will include all users recruited by Reference Sites over a period of 1 year. All baseline characteristics will be analysed. Phenotypic characteristics and treatment of rhinitis and asthma multimorbidity in the elderly will be compared with those of adults

Longitudinal study: The study will include all users recruited by Reference Sites over a period of 1 year who have reported more than 1 day of VAS. VAS scores will be analysed. This part of the study may provide some insight into the differences between the elderly and adults in terms of response to treatment and practice

To better understand the methodological problems in this new type of observational study, and particularly age-dependent problems with ICT

TABLE 2 Complementary activities of the twinning

- Andalusia will contribute to the mHealth assessment strategy and will test the quality of the mobile health app (*Allergy Diary*) (<http://www.calidadappsalud.com/en>).
- Northern Ireland will test another aspect of rhinitis and asthma multimorbidity (Fit at work with rhinitis) as uncontrolled allergic and non-AR has a major impact on work productivity.^{2,41-45}
- Porto4Ageing will also contribute to (i) the implementation of CARAT in the *Allergy Diary* app for European countries with completed cultural adaptation processes (the Netherlands, Belgium, Germany, Greece, Ukraine, Italy, France)²⁵⁻²⁸ and (ii) the analysis of long-term longitudinal variability of CARAT scores and its associations with the MASK VAS.
- The HealthRegion CologneBonn will help with the ethical aspects of the Twinning.
- The Trentino reference site will explore the advocacy of MACVIA study results within the Trentinosalute 4.0 Competence Centre on digital health.

3 | ORIGINATOR AND ADOPTER ORGANISATIONS

There are two types of organizations involved (Table 3):

- The “Organization transferring the innovative practice” (originator organization): the organization with the experience and know-how developed in a particular field of intervention, awarded Reference Site status in the 2016 call and included in the innovative practices repository of the EIP on AHA (https://ec.europa.eu/eip/ageing/repository_en).
- The “Organization adopting the innovative practice” (receiving/adopter organization): the organization that will receive the innovative practice and deploy/implement it in its territory. This is the organization that was awarded Reference Site status in the 2016 call and that will benefit from the experience and know-how developed by the “organization transferring an innovative practice” in a particular field of intervention.

There will also be Reference Sites that will help to perform the Twinning. The MACVIA-ARIA Twinning mainly includes Reference Sites but certain other sites are also included (Figure 1).

All Reference Sites wishing to join the MACVIA-ARIA Twinning at a later stage are welcome.

In France, Italy, Germany, Lithuania, Poland, Portugal and Turkey, the Twinning will be carried at a national level with the Allergy Society and national health authorities of the country.

4 | MACVIA-ARIA TWINNING METHODOLOGY

4.1 | Tools

The *Allergy Diary* will be used in all centres except for Andalusia. It is currently available on cell phones and also on tablets for health-care professionals in English (*Allergy Diary Companion*).^{37,38} Translations are pending. It includes EQ-5D,⁴⁶ the WPAI-AS questionnaire⁴⁷⁻⁴⁹ and, in some countries, CARAT^{26,28,50} (when available in electronic form).

4.1.1 | Allergy diary

App (ANDROID and IOS)

The *Allergy Diary* collects information on AR symptoms experienced (nasal and ocular), disease type (intermittent/persistent), how symptoms impact users' lives, and type(s) of AR treatment used (Table S1, Appendix S1).⁶

Geolocalized users assess their daily symptom control using the touchscreen functionality on their smart phone to click on five consecutive VAS (i.e. general, nasal and ocular symptoms, asthma and work) (Appendix S2).

Medications are also recorded daily (Appendix S3). Mobile phone messaging facilitates the management of AR, providing prompts to assess disease control, take medication, and visit a health care provider if appropriate.

The system was initially deployed in 15 European countries and in 15 languages (translated and back-translated, culturally adapted and legally compliant). It is now also available in Australia, Brazil, Canada, Mexico, Switzerland and Turkey. The system is currently being prepared for the Czech Republic.

Several observational studies have been carried out using the *Allergy Diary*.

- The *Allergy Diary* (Android and iOS) is user-friendly and has been tested for AR and conjunctivitis in over 5,000 users. The simple baseline questionnaire administered by cell phones allows the identification of phenotypic differences between *a priori* defined rhinitis and asthma multimorbidity groups and proposes novel concepts on AR.⁶
- The VAS reporting has been validated (Caimmi et al., submitted).
- Work productivity can be assessed daily (VAS) and there is a highly significant correlation between rhinitis control and work.³⁹
- A cross-sectional observational study enables the differentiation of treatment strategies in AR (Bousquet et al., in preparation).
- Over 5% of *Allergy Diary* users are ≥ 65 years of age.

4.2 | Outcomes

In this observational study, all subjects will fill in the following:

- Baseline characteristics (Table 5).
- EQ5D⁴⁶ which can be used in the elderly.
- Treatments (Appendix S3).
- Four consecutive VAS measurements (general, nasal and ocular symptoms, asthma) (Appendix S2).

In addition, adults will fill in:

- The Work Productivity and Activity Impairment Allergic Specific Questionnaire (WPAI-AS)^{47,51} (Appendix S4).
- VAS for work (Appendix S2).

TABLE 3 Originator and adopters of the Twinning

Originator
1. MACVIA-France
J Bousquet, S Arnavielhe, A Bedbrook, C Cartier, P Demoly, G Onorato, R Jaquet, D Laune, F Viart
Adopters
2. Andalucia
AM Carriazo, J Ferrero
3. Aragon
R Angles
4. Campania
M Illario, M Triggiani, C Stellato, A Vatrella, G De Feo
5. Catalonia
A Dedeu Baraldès, M Olivé Elias, JM Anto, V Cardona, J Mullol, A Valero
6. City of Helsinki
T Haahtela, T Strandberg, E Valovirta, J Salimaki, S Toppila-Salmi, J Karjalainen, T Vasankari
7. Coimbra
J Malva, A Todo Bom, C Robalo-Cordeiro, M Morais Almeida, MT Veríssimo, A Mota-Pinto
8. Heraklion
EP Prokopakis
9. HealthRegion CologneBonn
R Mösges, L Klimek, T Bieber, A Zurkuhlen, O Pfaar, T Zuberbier, KC Bergmann
10. Life Tech Valley
I Lieten, PW Hellings, C Bachert
11. Liguria
G Passalacqua, E Bacci, L Bertorello
12. Lodz
P Kuna, M Bochenska-Marciniak, M Kupczyk, P Lacwik
13. Medical Delta
NA Guldmond, NH Chavannes, R Gerth van Wijk, WJ Fokkens
14. Milan Metropolitan - Bergamo Province
M Romano, M Sorlini, AC Pozzi, D Lauri, F Corti, G Levato, M Nalin, I Baroni
15. NHS 24
A Sheikh, A Custovic
16. Northern Ireland
I Young, E Colgan
17. Olomouc
V Kolek, Z Gutter, M Sova
18. Pays de la Loire
A Magnan, J Hajjam, L Colas
19. Porto
J Fonseca, M Costa, AM Pereira
20. Puglia
MT Ventura

(Continues)

TABLE 3 (Continued)

21. Regione Piemonte
C Bucca, G Moda, G Rolla, A Romano, V Tibaldi
22. Region of Southern Denmark
C Bindslev-Jensen, E Eller, C Wanscher
23. Région Nouvelle Aquitaine
I Bosse
24. Turkey (Global Alliance against Chronic Respiratory Diseases Regional Network)
A Yorgancioglu, B Gemicioglu, C Cingi, O Kalayci, F Kalyoncu
25. ARIA Sweden
M Wickman, E Melén
26. ARIA Lithuania
A Valiulis, R Dubakiene, R Emuzyte, V Kvedariene
27. Australia
S Bosnic-Anticevich, RE O'Hehir
28. Brazil
AA Cruz
29. Mexico
D Larenas-Linnemann
30. Argentina
JC Ivancevich

4.2.1 | Printing of app data using a computer

Patients cannot give access of their electronic data to a HCP due to privacy policies. However, they can print the daily control of their disease as well as their medication details that they filled in in the *Allergy Diary*. The procedure is as follows (Figure 2):

4.2.2 | CARAT

CARAT will be implemented in the *Allergy Diary* app for European countries with completed cultural adaptation processes (the Netherlands, Belgium, Germany, Greece, Ukraine, Italy, France). Every 2-4 weeks, participants with rhinitis and asthma will be prompted to fill in the CARAT questionnaire.

4.2.3 | The physician's questionnaire

For some patients, physicians will fill in a questionnaire that includes the questions of the *Allergy Diary* and of CARAT (Table 4).

The questionnaire will be filled in directly using the ARIA website.

4.3 | Ethics

The terms of use have been translated into all languages and customized according to the country's legislation. They allow the use of the results for research purposes. The example of the UK terms of use is given in Appendix S5.³⁹ The data are anonymized except for

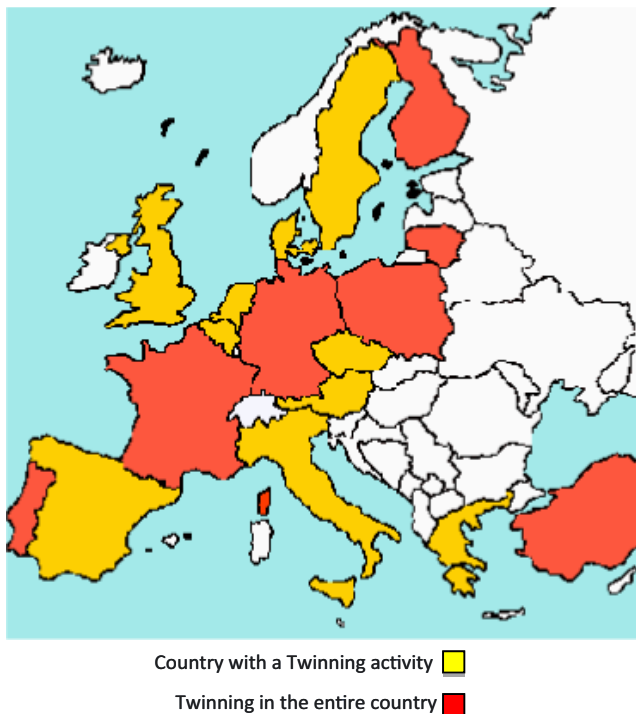


FIGURE 1 Twinning of the *Allergy Diary* in EIP on AHA Reference Sites (15-11-2016) [Colour figure can be viewed at wileyonlinelibrary.com]

the geolocalized data that are never totally anonymous. The European Commission's Article 29 Working Party stated that geolocation information is personal data (http://ec.europa.eu/newsroom/just/item-detail.cfm?item_id=50083) and that information can only be collected, shared, or stored with people's express consent. This is the case for MASK as users agree on geolocation in the terms of use of the app. Moreover, geolocation is optional and the user can allow it or not on his/her cell phone. Geolocation can be removed at any time. The problem of privacy due to geolocation was examined by the lawyers of each of the countries in which MASK has been launched and it was found to be in accordance with the existing laws. Moreover, geolocation is not used in the data mining process neither is the phone IP.

The *Allergy Diary* is a CE1 medical device and does not require ethical approval. An ethical agreement has been approved by a German ethics committee for the questionnaire. This ethical agreement will serve for all EU countries.

A participation agreement to be signed by the patient has been proposed.

4.4 | Possible biases

As in any other observational study, the absence of randomization may be a source of relevant biases.⁵² However, observational studies reflect "real-world" use and practice more closely than randomized control trials (RCTs) in terms of the heterogeneous patient populations included and medical interventions.⁵³ They can provide

clinically relevant information not necessarily provided by RCTs. Given the limitations of an observational study approach, it is important to optimize their study design to maximize their validity. In particular, known causes of bias and confounding should be measured.⁵³

However, this initiative was not designed to compare questionnaires with apps. A bias might be introduced because app users provide self-reported information in an uncontrolled setting. However, a recent systematic review has assessed the impact that smartphone and tablet apps as a delivery mode have on the quality of survey questionnaire responses compared to any other traditional alternative delivery mode. The review showed that apps might not affect data equivalence as long as the intended clinical application of the survey questionnaire, its intended frequency of administration and the setting in which it was validated remain unchanged.⁵⁴

4.5 | Timeframe for procurement/implementation until 2018

- The adopters will use freely available existing tools including (i) the *Allergy Diary* (Apple app Store and Google Play Store) and (ii) the questionnaire filled in by physicians.
- The *Allergy Diary* is available in 21 countries (Austria, Australia, Belgium, Brazil, Canada, Denmark, Finland, France, Germany, Greece, Italy, Lithuania, Mexico, the Netherlands, Poland, Portugal, Spain, Sweden, Switzerland, Turkey and the UK) and languages (national languages plus Catalan and Finnish Swedish). It can be implemented immediately. For other countries, translation, back-translation, cultural adaptation and legal compliance all require approximately 3-6 months.
- The phenotype, EQ-5D (MAFEIP^{39,55}) and AR/asthma medication lists (IMS list customized for each country) are included in the *Allergy Diary*.

4.6 | Action/implementation plan

Three protocols can be implemented (Table 5).

4.6.1 | Deployment of the app to the different Reference Sites (RS)

Immediate and free access (Apple app Store and Google Play Store) is available for 21 countries, from 3 to 6 months for other countries.

4.6.2 | Centres participating in the Twinning

Each Reference Site will select physicians (with training in allergy) who work in out-patient clinics, in hospitals and/or in private practice. A combination of both practices would be optimal. All physicians will be volunteers for the study. There will be no compensation.

- 1- Open the Allergy Diary app and choose "Show Data on Computer" in the main menu
- 2- Go to www.macvia-aria-allergy-diary.com/data on your PC/Laptop (enter this URL in the address bar of the browser from your PC/Laptop)
- 3- Scan the QR code with the Allergy Diary app
- 4- The screen with your personal data can be seen
- 5- And you can also print these data (see figure below).



'HOW ARE YOUR ALLERGIES AFFECTING YOU TODAY?'

Allergy Diary
Diary Data Viewer

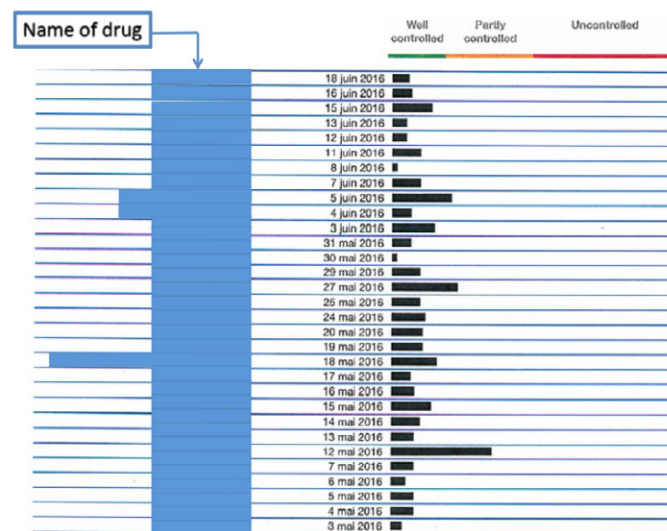


FIGURE 2 Transfer of patient information on a computer and printed information

4.6.3 | Enrolment of users (the elderly) with rhinitis

If possible, each Reference Site will enrol 50 elderly persons (≥ 65 years) able to use the *Allergy Diary* and 100 adults (< 65 years) using the longer protocol. If possible, the number of users will be increased. At the end of the year, each reference site will receive an overview of the data collected in its site. Each physician is expected to enrol at least 10 adults and 5 old age persons.

The duration of enrolment is 12 months to account for variability in allergen exposure during the year. Thus, the study can be initiated in Reference Sites from 1 January, 2017 to 1 July, 2017.

4.6.4 | Study protocol

Two different protocols can be used (and probably mixed in the same region) depending on the decision of the physician.

- Protocol 1: The physician enrolling the user asks the patient to use the *Allergy Diary* and checks that this has been done and that the user has agreed to be geolocalized. This latter point is of importance as it will help to analyse differences between regions. Both specialists and physicians working in primary care can participate in the Twinning.
- Protocol 2 (allergists)
 - Only patients who have not registered to the app will be enrolled.
 - The physician enrolling the user will complete the questionnaire and will profile his/her patient in a computer by answering an online questionnaire (ARIA-EUFOREA website)
 - The physician will end the profile by adding a random alpha-numerical code to his/her patient profile (as we process during

TABLE 4 Questionnaire to be filled in by the physician

(A)

MACVIA- ARIA Physician's Questionnaire		Date : _/ _/ _		
1- Date of birth	LIST WITH YEARS _/ _/ _			
2- Sex	Male	Female		
	<input type="radio"/>	<input type="radio"/>		
3- The patient is suffering from				
Current allergic rhinitis	<input type="checkbox"/>			
Current asthma (within the past 3 months)	<input type="checkbox"/>			
Conjunctivitis	<input type="checkbox"/>			
Non-allergic rhinitis	<input type="checkbox"/>			
Asthma previously in life	<input type="checkbox"/>			
Current atopic dermatitis	<input type="checkbox"/>			
4- Impact of allergic symptoms				
	Yes	No	Don't know	
Symptoms affect sleep	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Symptoms restrict daily activities	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Symptoms restrict work or participation in school	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Symptoms are troublesome	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
5- CARAT Questionnaire Question 5- A) should be read to the patient with the patient choosing the answer. There should be no "interpretation": the physician should not fill in the questionnaire on behalf of the patient.				
A) Due to your allergic respiratory diseases (asthma, rhinitis, allergies) in the last four weeks, on average, how many times did you have:				
	Never	Up to 2 days per week	More than 2 days per week	Almost every day
Blocked nose?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sneezing?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Itchy nose?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Runny nose?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Shortness of breath/dyspnoea?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Wheezing in the chest?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Chest tightness during physical exercise?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Tiredness/limitations in doing daily tasks?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Waking up in the night?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5- CARAT Questionnaire Question 5- B) should be read to the patient with the patient choosing the answer. There should be no "interpretation": the physician should not fill in the questionnaire on behalf of the patient.				
B) Due to your allergic respiratory diseases (asthma, rhinitis, allergies) in the last four weeks, how many times did you:				
	I'm not taking any medicine	Never	Less than 7 days	7 or more days
Increase the use (dosage or frequency) of your medicine?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6- Allergic sensitization has been diagnosed (within the past 5 years) by:				
Skin test	<input type="checkbox"/>			
Specific IgE	<input type="checkbox"/>			
Skin test + Specific IgE	<input type="checkbox"/>			
Not diagnosed	<input type="checkbox"/>			
7- Positive test for:				
House dust mites	<input type="checkbox"/>			
Alder	<input type="checkbox"/>			
Hazel	<input type="checkbox"/>			
Grass pollen	<input type="checkbox"/>			

clinical study). This code will be manually registered by the patient on his/her smartphone at the downloading step of the app.

- Hence, physicians' profile data and patients' self-recorded symptoms data will be reconciled for analysis.
- The physician will ask the person to use the *Allergy Diary* and will check onsite that this has been done and that the user has agreed to be geolocalized.
- Protocol 3: Fit at work: Some enterprises (NHS Northern Ireland, Hôpital de Valenciennes, France) are participating in an analysis of work productivity.

For the three protocols, there is potential for direct benefit for the patients and the physicians.

As an example, during the patient's next visit, the physician will see a graph indicating the level of control, the compliance to the treatment and the treatments actually taken by the patient.

Moreover, the first results of the *Allergy Diary* are extremely interesting.^{3,6} Unpublished data show that the care pathways of patients with AR and asthma multimorbidity should be reconsidered as most patients self-medicate.

TABLE 4 (Continued)

(B)	
Cypress pollen	<input type="checkbox"/>
Birch pollen	<input type="checkbox"/>
Other tree pollen	<input type="checkbox"/>
Parietaria pollen	<input type="checkbox"/>
Ragweed pollen	<input type="checkbox"/>
Cat	<input type="checkbox"/>
Dog	<input type="checkbox"/>
Other inhalant allergen	<input type="checkbox"/>
Food allergen	<input type="checkbox"/>
Don't know	<input type="checkbox"/>
8- Prescribed treatment	
(Scrolling list) Add "no treatment" in the scrolling list	
9- The patient currently receives immunotherapy for :	
House dust mites	<input type="checkbox"/>
Alder	<input type="checkbox"/>
Hazel	<input type="checkbox"/>
Grass pollen	<input type="checkbox"/>
Cypress pollen	<input type="checkbox"/>
Birch pollen	<input type="checkbox"/>
Other tree pollen	<input type="checkbox"/>
Parietaria pollen	<input type="checkbox"/>
Ragweed pollen	<input type="checkbox"/>
Cat	<input type="checkbox"/>
Dog	<input type="checkbox"/>
Other inhalant allergen	<input type="checkbox"/>
None	<input type="checkbox"/>
10- Current immunotherapy is administered by:	
SCIT	<input type="checkbox"/>
SLIT drops	<input type="checkbox"/>
SLIT tablets	<input type="checkbox"/>
Oralair	<input type="checkbox"/>
Grazax	<input type="checkbox"/>
11- Date of initiation of immunotherapy	
Month/Year (Scrolling list)	
12- Education	
Secondary school or less	<input type="radio"/>
Sixth form or college	<input type="radio"/>
Bachelor degree	<input type="radio"/>
Postgraduate	<input type="radio"/>
Missing	<input type="radio"/>
13- Work Status	
Currently full time employed	<input type="radio"/>
On light duty or some restricted work assignment or part time	<input type="radio"/>
Paid leave/sick leave	<input type="radio"/>
Unemployed because of other reason	<input type="radio"/>
Student (school, college, university)	<input type="radio"/>
Keeping house/homemaker	<input type="radio"/>
Retired	<input type="radio"/>
On disability	<input type="radio"/>
Missing	<input type="radio"/>

4.6.5 | Real-time analysis of the data

The analysis will be based on the pilot study of the *Allergy Diary* (manuscript submitted and manuscript in preparation), and real-time analysis across the different Reference Sites will be available.

5 | EXPECTED OUTCOMES OF THE TWINNING ACTIVITIES

1. *Phenotypic characteristics*: The *Allergy Diary* collects information on AR symptoms and allergic multi-morbidities experienced (nasal

and ocular, asthma), on how symptoms impact users' lives, and on the type(s) of AR and asthma treatments used. The study provides a unique opportunity (i) to investigate the phenotype of rhinitis and asthma multimorbidity in the elderly in Europe, (ii) to study differences with other age groups using data on file and (iii) to make comparisons across countries.

2. *Treatment of rhinitis and asthma multimorbidity and disease control*: The control of rhinitis appears to differ depending on the age group. The study will show differences (i) with other age groups using data on file and (ii) between regions, allowing optimization of care pathways.
3. *Use of the EQ-5D* allows quality-of-life and utilities data to be assessed. It is a MAFEIP tool.^{39,55}

TABLE 5 Protocols of the Twinning

	Protocol 1 Short version	Protocol 2 Long version	Protocol 3 Fit at work
Allergy Diary	+	+	+
EQ5D, WP-AIAS	Optional	+	+
Physician's questionnaire		+	Optional
Ethical committee	Not needed	Obtained	Needed if physician's questionnaire
Participation agreement	Terms of use of app	Participation agreement form signed by patients	
Recruitment	Any user. Persons attending clinic visits can be included	Persons with rhinitis from clinics with a diagnosis of AR made by a specialist (with skin tests and/or specific IgE)	Users in settings participating in the "Fit at work" protocol

4. *Comparison between regions* (or countries depending on the health system)
5. Comparison between rural and urban environments.
6. *Care pathways*: the results of the study will be used to develop region-specific care pathways (AIRWAYS ICPs) using a personalized medicine approach. Self-management strategies will be of great importance.
7. *Knowledge and know-how transferred*: The epidemic wave of rhinitis in adults (over 25% of the European population) is now reaching the elderly. It is essential to better characterize, understand and manage this disease that affects social life and causes serious discomfort for sufferers. A pan-European view of the problem will allow a cost-effective and socially acceptable management of this disease. The *Allergy Diary*, developed by the MACVIA France Reference Site, is freely available for subjects in most European countries. The app will be deployed by the Reference Site Collaborative Network for transfer of knowledge.^{40,56}
8. Rhinitis and asthma multimorbidity exemplifies why a lifecourse approach to AHA is the key to effective interventions that are sustainable for the public health systems.

6 | FUTURE DEVELOPMENTS

- Sleep is impaired in rhinitis and asthma^{4,5} and the Allergy Diary has been found to accurately assess sleep impairment.⁶ More data are needed and the app is being improved to include sleep-related questions.
- To correlate Allergy Diary data with allergen exposure using classical methods such as pollen counts or Google Trends-derived methods.⁵⁷
- To better understand the links between AR and pollution in order to provide preventive and treatment strategies to reduce AR burden.

REFERENCES

1. Bousquet J, Khaltaev N, Cruz AA, 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.
2. Vandenplas O, D'Alpaos V, Van Brussel P. Rhinitis and its impact on work. *Curr Opin Allergy Clin Immunol*. 2008;8:145-149.
3. Bousquet J, Bewick M, Arnavielhe S, et al. Work productivity in rhinitis using cell phones: the MASK pilot study. *Allergy*. 2017;72:1475-1484.
4. Leger D, Annesi-Maesano I, Carat F, et al. Allergic rhinitis and its consequences on quality of sleep: an unexplored area. *Arch Intern Med*. 2006;166:1744-1748.
5. Muliol J, Maurer M, Bousquet J. Sleep and allergic rhinitis. *J Investig Allergol Clin Immunol*. 2008;18:415-419.
6. Bousquet J, Caimmi D, Bedbrook A, et al. Pilot study of mobile phone technology in allergic rhinitis in European countries. The MASK-rhinitis study. *Allergy*. 2017;72:857-865.
7. Bousquet J, Samolinski B. Allergy and active and healthy ageing. In: Akdis C, Agache I, Demoly P, Hellinbgs P, Muraro A, Papadopoulos N, et al., eds. *Global Atlas of Allergy European Academy of Allergy and Clinical Immunology*. 2014:379-381.
8. Morais-Almeida M, Pite H, Pereira AM, et al. Prevalence and classification of rhinitis in the elderly: a nationwide survey in Portugal. *Allergy*. 2013;68:1150-1157.
9. Baptist AP, Nyenhuis S. Rhinitis in the elderly. *Immunol Allergy Clin North Am*. 2016;36:343-357.
10. Ventura MT, Gelardi M, D'Amato A, et al. Clinical and cytologic characteristics of allergic rhinitis in elderly patients. *Ann Allergy Asthma Immunol*. 2012;108:141-144.
11. Ohta K, Bousquet PJ, Aizawa H, et al. Prevalence and impact of rhinitis in asthma. SACRA, a cross-sectional nation-wide study in Japan. *Allergy*. 2011;66:1287-1295.
12. Sahin-Yilmaz AA, Corey JP. Rhinitis in the elderly. *Clin Allergy Immunol*. 2007;19:209-219.
13. Song WJ, Kim MY, Jo EJ, et al. Rhinitis in a community elderly population: relationships with age, atopy, and asthma. *Ann Allergy Asthma Immunol*. 2013;111:347-351.
14. Pite H, Pereira AM, Morais-Almeida M, Nunes C, Bousquet J, Fonseca JA. Prevalence of asthma and its association with rhinitis in the elderly. *Respir Med*. 2014;108:1117-1126.
15. Hansen J, Klimek L, Hormann K. Pharmacological management of allergic rhinitis in the elderly: safety issues with oral antihistamines. *Drugs Aging*. 2005;22:289-296.
16. Bousquet PJ, Combescure C, Neukirch F, et al. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. *Allergy*. 2007;62:367-372.
17. Di Lorenzo G, Pacor ML, Amodio E, 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.
18. Lu D, Zhao Y, Zheng Y, et al. Evaluation of quality of life questionnaires for adult patients with moderate to severe allergic rhinitis. *Am J Otolaryngol*. 2011;32:494-498.
 19. del Cuvillo A, Montoro J, Bartra J, et al. Validation of ARIA duration and severity classifications in Spanish allergic rhinitis patients - The ADRIAL cohort study. *Rhinology*. 2010;48:201-205.
 20. Bousquet PJ, Bachert C, Canonica GW, 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.
 21. Demoly P, Jankowski R, Chassany O, Bessah Y, Allaert FA. Validation of a self-questionnaire for assessing the control of allergic rhinitis. *Clin Exp Allergy*. 2011;41:860-868.
 22. Bousquet J, Schunemann HJ, Hellings PW, et al. MACVIA clinical decision algorithm in adolescents and adults with allergic rhinitis. *J Allergy Clin Immunol*. 2016;138:367-374.
 23. Klimek L, Bergmann K, Biederman T, Bousquet J, Hellings P, et al. Visual analogue scales (VAS): measuring instruments for the documentation of symptoms and therapy monitoring in allergic rhinitis in everyday health care. Position Paper of the German Society of Allergology. *Allergo J Int*. 2017;26:16-24.
 24. Bousquet J, Bachert C, Canonica GW, et al. Unmet needs in severe chronic upper airway disease (SCUAD). *J Allergy Clin Immunol*. 2009;124:428-433.
 25. Azevedo P, Correia de Sousa J, Bousquet J, et al. Control of Allergic Rhinitis and Asthma Test (CARAT): dissemination and applications in primary care. *Prim Care Respir J*. 2013;22:112-116.
 26. Fonseca JA, Nogueira-Silva L, Morais-Almeida M, et al. Validation of a questionnaire (CARAT10) to assess rhinitis and asthma in patients with asthma. *Allergy*. 2010;65:1042-1048.
 27. Nogueira-Silva L, Martins SV, Cruz-Correia R, et al. Control of allergic rhinitis and asthma test—a formal approach to the development of a measuring tool. *Respir Res*. 2009;10:52.
 28. van der Leeuw S, van der Molen T, Dekhuijzen PN, 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.
 29. Mookink LB, Prinsen CA, Bouter LM, Vet HC, Terwee CB. The Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) and how to select an outcome measurement instrument. *Braz J Phys Ther*. 2016;20:105-113.
 30. Mookink LB, Terwee CB, Gibbons E, et al. Inter-rater agreement and reliability of the COSMIN (COnsensus-based Standards for the selection of health status Measurement Instruments) checklist. *BMC Med Res Methodol*. 2010;10:82.
 31. Mookink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol*. 2010;63:737-745.
 32. Bousquet J, Hajjam J, Piette F, et al. [The French reference sites of the European Innovation Partnership on active and healthy ageing]. *Presse Med*. 2013;42:1558-1561.
 33. 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.
 34. Bousquet J, Addis A, Adcock I, et al. Integrated care pathways for airway diseases (AIRWAYS-ICPs). *Eur Respir J*. 2014;44:304-323.
 35. Bousquet J, Addis A, Agache I, et al. Integrated care pathways for airway diseases (AIRWAYS ICPs). *Eur Respir J*. 2014;44:304-323.
 36. Bousquet J, Hellings PW, Agache I, et al. ARIA 2016: care pathways implementing emerging technologies for predictive medicine in rhinitis and asthma across the life cycle. *Clin Transl Allergy*. 2016;6:47.
 37. Bourret R, Bousquet J, Mercier J, et al. MASK rhinitis, a single tool for integrated care pathways in allergic rhinitis. *World Hosp Health Serv*. 2015;51:36-39.
 38. Bousquet J, Schunemann HJ, Fonseca J, et al. MACVIA-ARIA Sentinel Network for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation. *Allergy*. 2015;70:1372-1392.
 39. Bousquet J, Bewick M, Cano A, et al. Building bridges for innovation in ageing: synergies between action groups of the EIP on AHA. *J Nutr Health Aging*. 2017;21:92-104.
 40. Bousquet J, Farrell J, Crooks G, et al. Scaling up strategies of the chronic respiratory disease programme of the European Innovation Partnership on Active and Healthy Ageing (Action Plan B3: Area 5). *Clin Transl Allergy*. 2016;6:29.
 41. Vandenplas O, Van Brussel P, D'Alpaos V, Wattiez M, Jamart J, Thimpont J. Rhinitis in subjects with work-exacerbated asthma. *Respir Med*. 2010;104:497-503.
 42. Hellgren J, Cervin A, Nordling S, Bergman A, Cardell LO. Allergic rhinitis and the common cold—high cost to society. *Allergy*. 2010;65:776-783.
 43. Kakutani C, Ogino S, Ikeda H, Enomoto T. [Impact of allergic rhinitis on work productivity: a pilot study]. *Alerugi*. 2005;54:627-635.
 44. Kim SY, Yoon SJ, Jo MW, Kim EJ, Kim HJ, Oh IH. Economic burden of allergic rhinitis in Korea. *Am J Rhinol Allergy*. 2010;24:e110-e113.
 45. Marcellusi A, Viti R, Incorvaia C, Mennini FS. [Direct and indirect costs associated with respiratory allergic diseases in Italy. A probabilistic cost of illness study]. *Recenti Prog Med*. 2015;106:517-527.
 46. König HH, Bernert S, Angermeyer MC, et al. Comparison of population health status in six European countries: results of a representative survey using the EQ-5D questionnaire. *Med Care*. 2009;47:255-261.
 47. Bousquet J, Neukirch F, Bousquet PJ, et al. Severity and impairment of allergic rhinitis in patients consulting in primary care. *J Allergy Clin Immunol*. 2006;117:158-162.
 48. Devillier P, Bousquet J, Salvator H, Naline E, Grassin-Delye S, de Beaumont O. In allergic rhinitis, work, classroom and activity impairments are weakly related to other outcome measures. *Clin Exp Allergy*. 2016;46:1456-1464.
 49. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993;4:353-365.
 50. Linhares DV, da Fonseca JA, Borrego LM, 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.
 51. Virchow JC, Kay S, Demoly P, Mullol J, Canonica W, Higgins V. Impact of ocular symptoms on quality of life (QoL), work productivity and resource utilisation in allergic rhinitis patients—an observational, cross sectional study in four countries in Europe. *J Med Econ*. 2011;14:305-314.
 52. DiPietro NA. Methods in epidemiology: observational study designs. *Pharmacotherapy*. 2010;30:973-984.
 53. Yang W, Zilov A, Soewondo P, Bech OM, Sekkal F, Home PD. Observational studies: going beyond the boundaries of randomized controlled trials. *Diabetes Res Clin Pract*. 2010;88(Suppl. 1):S3-S9.
 54. Marcano Belisario JS, Jamsek J, Huckvale K, O'Donoghue J, Morrison CP, Car J. Comparison of self-administered survey questionnaire responses collected using mobile apps versus other methods. *Cochrane Database Syst Rev*. 2015;27:MR000042.

55. Boehler CE, de Graaf G, Steuten L, Yang Y, Abadie F. Development of a web-based tool for the assessment of health and economic outcomes of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA). *BMC Med Inform Decis Mak*. 2015;15 (Suppl 3):S4.
56. Calderon MA, Demoly P, Casale T, et al. Allergy immunotherapy across the life cycle to promote active and healthy ageing: from research to policies: an AIRWAYS Integrated Care Pathways (ICPs) programme item (Action Plan B3 of the European Innovation Partnership on active and healthy ageing) and the Global Alliance against Chronic Respiratory Diseases (GARD), a World Health Organization GARD research demonstration project. *Clin Transl Allergy*. 2016;6:41.
57. Bousquet J, Agache I, Anto J, et al. Google trends terms reporting rhinitis and related topics differ in European countries. *Allergy*. 2017;72:1261-1266.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Bousquet J, Agache I, Aliberti MR, et al. Transfer of innovation on allergic rhinitis and asthma multimorbidity in the elderly (MACVIA-ARIA) EIP on AHA Twinning Reference Site (GARD research demonstration project). *Allergy*. 2018;73:77-92. <https://doi.org/10.1111/all.13218>