



ARIA digital anamorphosis: Digital transformation of health and care in airway diseases from research to practice

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Abbreviations: AIRWAYS-ICPs, integrated care pathways for airway diseases; AIT, allergen immunotherapy; AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; CARAT, Control of Allergic Rhinitis and Asthma Test; CDSS, clinical decision support system; DB-PC-RCT, double-blind, placebo-controlled, randomized trial; EFA, European Federation of Allergy and Airways Diseases Patients' Association; EIP on AHA, European Innovation Partnership on Active and Healthy Ageing; EIT, European Institute for Innovation and Technology; EQ5D, EuroQuol; EU, European Union; GA²LEN, Global Allergy and Asthma European network; GARD, Global Alliance against Chronic Respiratory Diseases; GRADE, *Grading of Recommendations Assessment, Development and Evaluation*; ICP, integrated care pathway; IT, Internet technology; JA-CHRODIS, Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle; MACVIA, fighting chronic diseases for active and healthy ageing; MASK, Mobile Airways Sentinel Network; MASK-air[®], (formerly Allergy Diary); MeDALL, Mechanisms of the Development of Allergy; POLLAR, Impact of air POLLution on Asthma and Rhinitis; QOL, quality of life; RCT, randomized controlled trials; RWD, real-world data; RWE, real-world evidence; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy; SMS, symptom-medication score; TRL, technology readiness level; TWINNING, Transfer of Innovation; WHO, World Health Organization.

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Abstract

Digital anamorphosis is used to define a distorted image of health and care that may be viewed correctly using digital tools and strategies. MASK digital anamorphosis represents the process used by MASK to develop the digital transformation of health and care in rhinitis. It strengthens the ARIA change management strategy in the prevention and management of airway disease. The MASK strategy is based on validated digital tools. Using the MASK digital tool and the CARAT online enhanced clinical framework, solutions for practical steps of digital enhancement of care are proposed.

KEYWORDS

ARIA, asthma, CARAT, digital transformation of health and care, MASK, rhinitis

1 | INTRODUCTION

Anamorphosis—from the Greek *αναμόρφωση*: *transformation*—is used in several fields to describe the transformation of a distorted object (e.g. painting, architecture, entomology, biology). Digital technology reveals the day-to-day experience of patients and provides a new type of information that—when properly collected and interpreted—will restore the real expression of the disease. In this paper, anamorphosis is used to define a distorted image of health and care that may be viewed correctly using digital tools and strategies.

The strategic overview (Table 1, Figure 1) and the vision of MASK include several considerations (Table 2). The disease burden and the healthcare costs for people with allergic and chronic respiratory diseases are increasing rapidly.¹ Transformation of the healthcare system for integrated care through leveraging developments in digital health is urgently needed.² The term “digital health” includes advanced medical technologies, disruptive innovations and digital communication tools aiming to provide best practice health care.³ Smart devices and internet-based applications are largely used in airway diseases and are likely to address certain unmet needs.⁴ However, these new tools need to be tested (a) for privacy rules, security and legislation of the Medical Device Regulation (May 2020); (b) for acceptability, usability and cost-effectiveness⁵; and (c) for validity. They should then be evaluated in the frame of the overall digital transformation of health and care, their impact on healthcare delivery as well as health outcomes. mHealth tools and strategies enabling the digital transformation of health and care, empowering citizens and building a healthier society represent a novel important step in health care. However, a practical integrated approach is required.

In 2014, on behalf of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA),⁶ AIRWAYS-ICPs (integrated care pathways for airway diseases) was initiated.^{7,8} The objective was

to launch a collaboration to develop multisectoral care pathways (ICPs) for chronic respiratory diseases in European countries and beyond as a Global Alliance against Chronic Respiratory Diseases (GARD) demonstration project (Figure 1). MASK (Mobile Airways Sentinel Network) is the mHealth strategy of AIRWAYS-ICPs and ARIA.⁹ It was based on the ARIA study group which exists in 92 countries. MASK is deployed in 26 countries and 18 languages. MASK, as a practical ICT integrated approach, was initially developed as an app (MASK-air[®]) and is now an e-platform for allergic diseases and asthma.

The Control of Allergic Rhinitis and Asthma Test (CARAT) is a patient-reported outcome that assesses the level of control of both asthma and AR using a single tool.¹⁰ It enables the implementation of the ARIA recommendations in the simultaneous assessment and management of both allergic rhinitis (AR) and asthma.¹¹

This paper proposes the ARIA change management strategy in the prevention and management of airway disease.¹² MASK digital anamorphosis represents the process used by MASK to develop the digital transformation of health and care in rhinitis. It also strengthens ARIA change management. Using the MASK digital tool and the CARAT online enhanced clinical framework, solutions for each practical step of digital enhancement of care are provided.

2 | DIGITAL TRANSFORMATION OF HEALTH AND CARE IN RHINITIS AND ASTHMA MULTIMORBIDITY

2.1 | The MASK e-platform

MASK, the Phase 3 ARIA (Allergic Rhinitis and its Impact on Asthma) initiative,^{11,13} is a Good Practice of DG Santé for digitally-enabled,

patient-centred care.¹⁴ It has been developed from the MASK-air® app and is a flexible e-platform for allergic diseases and asthma. It includes (a) a freely available app (MASK-air®, formerly the Allergy Diary, Android and iOS),¹³ (b) tools to support healthcare professionals in shared decision-making through an interoperable electronic decision support system (e-CDSS),¹⁵ (c) a web-based interoperable questionnaire for physicians,¹⁶ (d) a questionnaire on asthma and rhinitis (CARAT) for screening allergic diseases and assessing their control and (e) a sentinel network for air quality and pollen seasons. Other tools can be added when needed.

The maturity level of the MASK Good Practice is presented in Tables 1 and 3.

MASK is scaled up using the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA) strategy.^{16,25}

2.2 | MASK-air®

2.2.1 | Characteristics

MASK-air® is an ICT (Information and Communication Technology) system centred around the patient.¹⁷ It is operational in 26 countries and 18 languages. It uses a treatment scroll list which includes all of the medications customized for each country. Furthermore, a visual analogue scale (VAS) assesses rhinitis control (global allergy impact, nose, eyes, asthma), sleep and work productivity.^{26,27} MASK-air® is combined with prediction on allergen season and air quality (POLLAR: Impact of POLLution on Asthma and Rhinitis, EIT Health-funded project).²³ MASK is available in 26 countries and

18 languages including some middle-income countries (Table 2). Patients' organizations and scientific societies are involved.

2.2.2 | Privacy, General Data Protection Regulation (GDPR) and Medical Device Regulation (MDR)

The General Data Protection Regulation (GDPR) regulates the processing of personal data in the European Union (EU).^{28,29} MASK-air® follows the five main principles of personal data protection to be respected during the development of the app: purpose, proportionality and relevance, limited retention period, security and confidentiality, as well as the rights of the users regarding management of personal data (including withdrawal and modification).³⁰ Moreover, MASK-air® uses k-anonymity for geolocation.³¹ A double encryption database has been set up.

MASK-air® is currently a Class 1 Medical Device but will be upgraded to Class 2A with the new MDR to be enforced in the EU in May 2021.³²

2.2.3 | Validation

There are absolute prerequisites for the launch of an app. They include the following:

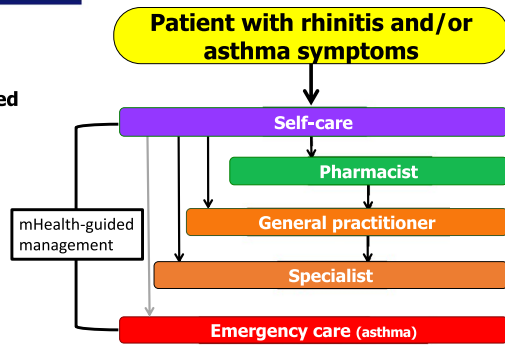
1. The MASK-air® questions have been validated by patients (studies by Madopa and STIMCO, unpublished) and are easily understood by patients in different countries.

TABLE 1 Strategic overview

Acronym	Name	Dates
WHO-associated projects		
ARIA	Allergic Rhinitis and its Impact on Asthma	1999–
	WHO Collaborating Center for Rhinitis and Asthma	2004–2014
GARD	Global Alliance against Chronic Respiratory Diseases	2003–
EU grants and projects		
GA ² LEN	Global Allergy and Asthma European Network (FP6)	2004–
MeDALL	Mechanisms of the Development of Allergy (FP7)	2009–2014
Sunfrail		
EIP on AHA	European Innovation Partnership on Active and Healthy Ageing (DG Santé & CONNECT)	2012–2020
TWINNING	Transfer of Innovation	2017–2019
DHE TWINNING	Transfer of innovation in severe asthma (H2020)	2019–2020
Vigour		2019–2021
POLLAR	Impact of Pollution on Asthma and Rhinitis (EIT health)	2018–2019
	Good Practice DG Santé on digital health (DG Santé)	2018

Abbreviations: ARIA, Allergic Rhinitis and its Impact on Asthma; CARAT, Control of Allergic Rhinitis and Asthma Test; EAACI, European Academy of Allergy and Clinical Immunology; e-CDSS, electronic clinical decision support system; GA²LEN, Global Allergy and Asthma European Network; GARD, Global Alliance against Chronic Respiratory Diseases; POLLAR, Impact of Pollution on Asthma and Rhinitis; WHO, World Health Organization.

POLICY

Transformation of Health and Care in the Digital Single Market**Chapter 5****"Digital tools for citizen empowerment and for person-centred care"**

Differences exist between countries/regions and health care systems

FIGURE 1 Care pathways proposed in the MASK strategy (adapted from Ref. [6])

2. MASK-air[®] has followed the COSMIN (CONsensus-based Standards for the selection of health Measurement INSTRUMENTS) guidelines.³³
3. The independence of data has been confirmed.²⁴
4. Translations have been validated using a back-translation.
5. MASK-air[®] has been implemented in the different situations in which it is used.^{14,15,17,18,24,30,33–41}

2.3 | CARAT

CARAT is a validated questionnaire that can summarize the clinical status of asthma and rhinitis (multimorbidity) of the previous 4 weeks. It complements the frequent/daily self-assessment in the MASK-air app and the physician's clinical assessment.

2.3.1 | Characteristics

The CARAT questionnaire has two domains - allergic rhinitis and asthma - and 10 items regarding symptoms, sleep, activities and drug use within the past 4 weeks.²⁰ CARAT's minimal clinically important difference can detect change over time (high responsiveness).²¹ CARAT supports shared decisions between the patient and

the physician as well as within the healthcare team. CARAT has been used in 19 countries globally including developing countries.²²

CARAT can be used in a range of different aims: (a) screening of patients with rhinitis or asthma in different settings including pharmacies,⁴² (b) follow-up consultations together with lung function,⁴³ (c) patient self-management⁴⁴ and (d) identifying patients with uncontrolled asthma at pharmacies.⁴² It should increase awareness of the level of disease control and strengthen the partnership between patients and doctors in the management of asthma and rhinitis by helping to define shared treatment goals.

CARAT has been used in epidemiology and clinical research⁴⁵: it has been included in international multicentre studies, such as the technology transfer of innovative practices (TWINNING) project¹⁶ and the observational longitudinal multicentre prospective study, the "@IT2020" study.⁴⁶ CARAT has been implemented as an mHealth tool in several smartphone applications including MASK-air,¹⁷ InspirerMundi,⁴⁷ the Adolescent Adherence Patient Tool (ADAPT) app⁴⁸ and Lung Manager.⁴⁹

2.3.2 | Validation

CARAT has been thoroughly studied in cross-sectional and prospective studies conducted at all levels of MASK Care Pathways. It meets all COSMIN criteria for patient-reported outcome measures.⁵⁰

CARAT has been used in clinical studies and in clinical practice. It has enabled comparison between groups as well as evaluation of individual patients over time.^{10,20} The questionnaire has been deployed in patient care and/or research. CARAT has been implemented in different settings (pharmacies, primary care, secondary care, epidemiology and clinical research) and technologies including mHealth tools,^{17,42,45,47,48,51–53} but also in severe asthma by specialists.⁵⁴

2.3.3 | New functionalities

CARAT has the potential to evolve in order to further strengthen multimorbidity assessment and to focus on more severe patients. This

TABLE 2 Vision of MASK

1. The burden of rhinitis and asthma (multimorbidity) and unmet medical needs are unacceptable and require a novel approach to tackle them
2. Healthcare costs should be sustainable despite the increased prevalence of allergic diseases and the availability of new expensive treatments
3. mHealth should be applied to rhinitis and asthma to reduce unmet medical needs and sustain health care costs
4. A novel approach should embed medical knowledge, patients' needs and mHealth
5. The ultimate goal is change management for rhinitis and asthma

TABLE 3 Maturity level of MASK

MASK achievement	TRL	References
App for rhinitis and multimorbidity (MASK-air [®]): available in 26 countries, 18 languages, 35 000 users	9	[17–19]
CARAT questionnaire for screening and control of rhinitis and asthma, available in 20 countries	9	[20–22]
e-physician questionnaire for rhinitis (available on the Euforea website) deployed in 23 countries and 17 languages	9	[16]
Embedding air quality (outdoor air pollution) and pollen data in MASK-air [®] (POLLAR)	9	[23]
e-CDSS for shared decision-making in rhinitis	7	[15]
EAACI-ARIACARE-digital network	8	
Allergy score	7	[24]
Embedding artificial intelligence in MASK-air [®]	3	

Note: Abbreviations: CARAT, Control of Allergic Rhinitis and Asthma Test; EAACI, European Academy of Allergy and Clinical Immunology; e-CDSS, electronic clinical decision support system; POLLAR, Impact of Pollution on Asthma and Rhinitis.

change can be carried out simply by reassessing questions that were excluded during the initial developing process.¹⁰ In particular, eye symptoms should be included: within the asthma-rhinitis multimorbidity, they are associated with more severe phenotypes as demonstrated by the MASK-air app³⁷ and confirmed by an epidemiologic study with full medical observation.²²

2.4 | Electronic clinical decision support system (eCDSS) for rhinitis

The interoperable electronic decision support system (eCDSS)¹⁵ is based on an algorithm designed by the ARIA expert group and validated using real-world evidence.⁵⁶ This eCDSS is to be used on tablets by pharmacists and physicians.

2.5 | Web-based physician's questionnaire for rhinitis and asthma

An interoperable questionnaire for physicians is available online on the Euforea website (<https://www.euforea.eu>). Around 1,000 patients have been enrolled in the rhinitis-TWINNING using the questionnaire. They are then followed up using the MASK-air[®] app.¹⁶

2.6 | Sentinel network for air quality and pollen prediction

POLLAR has confirmed the interactions between air pollution, asthma and rhinitis in order to propose the prediction of these environmental factors in MASK-air[®].^{23,40} It uses the MASK-air[®] app combined with a new tool allowing queries on pollen and air quality, in geolocalized patients. Allergic symptoms of the MASK-air[®] app are integrated with the Symptom Forecasting Model developed within the PASYFO

project of Copernicus Atmospheric Monitoring Service, which also supplies the meteorological, air quality and pollen information for Europe. Additional pollen and global air quality forecasts are generated by the SILAM model of the Finnish Meteorological Institute (FMI).^{56–58} Machine learning will be used to assess the relationship between air pollution, AR and asthma to further refine the prediction.

3 | PATIENTS' VIEWS

Many patients do not understand the needs and benefits of mHealth and may worry about data privacy (Table 3). Thus, the uptake of mHealth is slow. On the other hand, too many patients rely on internet-based information and on untested mHealth solutions. This attitude may have dangerous implications since patients may receive an incorrect diagnosis or management strategy.

3.1 | Features required to satisfy patients

A qualitative study was carried out by MADOPA in 2016 for MASK to better understand the patients' needs and expectations (Table 4).

3.2 | Implementation and communication strategy for patients

Without a communication strategy, the app will not be largely used. However, the communication plan will only be put in place in 2020 once the POLLAR module has been added. Documents are available in 18 languages and can be downloaded from the MASK website (<https://www.mask-air.com>). They include leaflets for patients, physicians and pharmacists as well as other documents. In Mexico, this strategy was found to be effective. It will be deployed to other countries.

TABLE 4 Patients' needs and expectations of an mHealth app

A. Problems patients encounter using an app			
Fear of using an app (particularly in elderly patients)			
Customer loyalty problems (young adult patients)			
Not willing to use one app regularly			
Changing the app frequently			
Not understanding how to fill in the app			
Not understanding or caring about what must be done (e.g. seeing a physician), despite clear results/instructions provided by the app			
Not feeling ill (usually males)			
Feeling too ill and filling in the app too much (females, some males also)			
B. Patients' expectations			
Patients' expectations	Existing feature in MASK	To be added to MASK	
		Feature	Expected
Advice to modify the treatment	Simple advice exists in line with the GDPR	More sophisticated advice will be ready with Medical Device Regulation (MDR) Class 2A	06-2021 ^a
Pollen and pollution		POLLAR	06-2020
Visualization of control and medications	Existing but poorly found by patients and physicians	More user friendly and better information	06-2020
Help science to better understand the disease in order to get future benefits	Existing		

Abbreviations: GDPR, General Data Protection Regulation; MASK, Mobile Airway Sentinel Network; POLLAR, Impact of Pollution on Asthma and Rhinitis.

^aDue to new regulation not yet published.

The communication strategy must involve local patients' organizations. It will be deployed with the patients' organization EFA. The importance of patients' associations has always been recognized in ARIA. For the digital transformation of health and care, they are even more important. The following messages sent by the app need to be reinforced for the patients:

1. Better understanding the symptoms.
2. Sentinel network linking aerobiology data and control.
3. Improved adherence.
4. Self-management.
5. Patient empowerment.

4 | MASK ACHIEVEMENTS IN DIGITAL ANAMORPHOSIS

4.1 | Anamorphosis steps based on digital learning and Real-World Data

MASK-air[®] has been in use for 5 years and has evolved since its first inception. Major RWD results of the MASK strategy (MASK-air[®], POLLAR and CARAT) are presented in Table 5.

4.2 | Health outcomes

In AR and asthma, a relevant outcome providing information on the cost-effectiveness of interventions is needed. EQ-5D (EuroQol), a standardized and validated non-disease-specific instrument used to describe and value health-related quality of life, has been used in allergic rhinitis^{36,69-74} but it cannot be used for daily assessment. EQ-5D is one of the MASK-air[®] questionnaires.³⁶ In MASK, VAS work correlates with other MASK outcomes (VAS global, nose, eye and asthma)^{24,34} and should be considered as a potentially useful allergic rhinitis outcome in intervention studies.

RWD make health technology assessment possible.

4.3 | Use of real-world data to develop next-generation care pathways for chronic respiratory diseases

Care pathways are structured multi-disciplinary care plans detailing the key steps of patient care.⁷ They promote the translation of guideline recommendations into local protocols and their application to clinical practice. ICPs have been proposed with a focus on mHealth technologies that should enhance self-management and adherence to guidelines and ICPs.

TABLE 5 ARIA anamorphosis steps for the digital transformation of health and care in airway diseases towards change management

A*	Areas of innovation	Novel findings using RWD	Solutions for digital health	References
Innovation in phenotypes				
1	Allergic phenotypes (based on epidemiologic evidence)	MASK <ul style="list-style-type: none"> found novel phenotypes of rhinitis, conjunctivitis and asthma. suggested that a "severe phenotype" exists proposing a new stratification of allergic patients for optimized treatment. These findings were confirmed in classical epidemiologic studies 	A novel approach of multimorbidity is needed to select and stratify patients using artificial intelligence	[37] [59–63]
Innovation in diagnosis				
2	Diagnosis	Using the CARAT questionnaire: <ul style="list-style-type: none"> Highly motivated and experienced allergists misdiagnose asthma and conjunctivitis in patients with rhinitis. They have a different approach to assess severity. 	The CARAT questionnaire is in MASK-air® and can be used in the physician's waiting room to help in the diagnosis of allergic diseases and to initiate the stratification of patients	Submitted
Innovation in management				
3	Adherence to treatment	<ul style="list-style-type: none"> Patients often self-medicate and use OTC medications Patients do not follow the physician's prescription This attitude accords with the allergic physician's behaviour 	Poor adherence of patients to treatment indicating that RCTs carried out in adherent patients do not reflect real life and that change management is needed with a new registration of medications (prn) Need to change practice and medication registration	[37,39]
4	Novel approach for efficacy assessment	<ul style="list-style-type: none"> MASK shows that patients receiving co-medications are less well controlled than those receiving no treatment or single treatment. These observations are in contradistinction with guidelines. Patients do not follow guidelines or the physician's prescriptions. They self-medicate. Next-generation guidelines are needed. Chamber studies confirm the speed of onset of some treatments 	Guidelines assume that patients follow the doctor's orders. Adherence to medication is turned to partnership using novel models of education (IT)	[17,19,37] [63]
5	The same tool is used for RCTs, RWD, chamber studies and clinical practice	A symptom-medication score (SMS) based on MASK has been set up and can be used for all purposes	<ul style="list-style-type: none"> Assessment of SMS in RCTs, observational studies, chamber challenges and clinical practice. Direct comparison of RCTs, observational studies, chamber challenges with RWD in patients. Patient stratification for expensive treatments. 	
Health outcomes				
6	Health outcomes and impact	<ul style="list-style-type: none"> There is a significant correlation between VAS work and VAS for global symptoms, nose, eye or asthma. Daily VAS work can be used for economic studies 	<ul style="list-style-type: none"> Work productivity EQ5D Impact (sleep) 	[34–36,38,65]
Next-generation care pathways				
7	Next-generation care pathways	<ul style="list-style-type: none"> Care pathways differ from guidelines Self-care Pharmacist Physician Patients 	Next-generation care pathways are needed <ul style="list-style-type: none"> To account for real-world evidence To provide a holistic view of management and prevention of allergic symptoms and diseases 	[19,55,65–68] [41]

(Continues)

TABLE 5 (Continued)

A*	Areas of innovation	Novel findings using RWD	Solutions for digital health	References
8	Air pollution	<ul style="list-style-type: none"> • Air pollution impacts the severity of rhinitis. • Prediction of pollution and the pollen season (POLLAR) 	<ul style="list-style-type: none"> • Embedding in MASK-air® current data and 3-day prediction for pollen season and air quality. • Alerts for peaks of pollen and pollution. 	[23,40]
Centres of excellence in digital health				
9	Centres of Excellence	ARIACARE digital is a novel network with the aim to implement the digital transformation of health and care in airway diseases	<ul style="list-style-type: none"> • ARIACARE digital 	
Transfer of innovation				
10	Rhinitis-TWINNING	Completed (but still ongoing) TWINNING in rhinitis and asthma	<ul style="list-style-type: none"> • Web-based physician's questionnaire • MASK-air® combined 	[16,68]
11	Asthma-TWINNING	DHE TWINNING in severe asthma	<ul style="list-style-type: none"> • Asthma-e-platform • MASK-air® with asthma combined • ARIACARE-Digital 	
Digital transformation of health and care to sustain planetary health				
12	POLLAR	<ul style="list-style-type: none"> • Impact of climate change, air pollution and biodiversity 	<ul style="list-style-type: none"> • Climate change 	[23,40]
13	Finland's EU Presidency meeting, December 3-4, 2019	<ul style="list-style-type: none"> • Care pathways for rhinitis and/or asthma can be used as a model for all chronic diseases. 	<ul style="list-style-type: none"> • The way to the digital transformation of health to sustain planetary health 	Bousquet et al., in preparation [104]

Note: A*: anamorphosis.

Abbreviations: CARAT: Control of Allergic Rhinitis and Asthma Test, DHE: DigitalHealthEurope, EQ5D: EuroQuol, MASK: Mobile Airway Sentinel NetworkK, RCT: randomized control trial, RWD: real-world data, TWINNING: Transfer of Innovation, VAS: visual analogue scale.

Next-generation care pathways for airway diseases follow the 2014 AIRWAYS integrated care pathways (ICPs) concept (Figures 1 and 2).⁵⁵ As a proof of concept for chronic disease care, RWD obtained from MASK provide a framework for real-life ICPs centred around the patient with rhinitis, using the mHealth monitoring of environmental exposure. This is implemented in collaboration with professional and patient organizations.

ARIA is constantly evolving and its most recent advance was determined following a meeting of experts/stakeholders in Paris in December 2018^{75,76} (Table 6). Three aspects of care pathways were developed during this meeting: (a) patient participation, health literacy and self-care through technology-assisted "patient activation", (b) implementation of care pathways by pharmacists⁶⁵ and (c) next-generation guidelines assessing the recommendations of GRADE (*Grading of Recommendations, Assessment, Development and Evaluation*) guidelines in rhinitis and asthma using RWE⁵⁵ and AIT.⁶⁶ Next-generation guidelines for the pharmacologic treatment of allergic rhinitis were developed using existing GRADE-based guidelines,⁷⁷⁻⁷⁹ RWD provided by mHealth Apps^{19,37,39} and additive studies (allergen chamber studies⁶³) to refine the MACVIA algorithm.

4.4 | Network of centres of excellence in digital health

ARIA was established 20 years ago and includes more than 600 members in over 80 countries. In ARIA Phase 4 (change

management for airways diseases), a network of centres of excellence has been organized. GA²LEN ARIACARE is one of the GA²LEN centres of excellence⁸⁴ and includes urticaria care (UCARE)⁸⁵ and atopic dermatitis care (ADCARE). Accreditation follows the UCARE proposals.

ARIACARE digital is a novel network with the aim to implement the digital transformation of health and care in airway diseases. Both members of MASK and others can join the network. ARIACARE-Digital has links with GA²LEN but is a separate entity.

4.5 | Transfer of innovation (TWINNING)

4.5.1 | Rhinitis-Asthma TWINNING

A transfer of innovative practices (TWINNING)^{16,68} was performed with the aim to transfer and implement MASK-air®. The "Organization transferring the innovative practice" (originator organization) had the experience and know-how developed in rhinitis and asthma IT solutions. The "Organization adopting the innovative practice" (receiving/adopter organization) received the innovative practice and implemented it in its territory. The rhinitis TWINNING was deployed from MASK to 22 countries. Around 1,000 patients were enrolled in the study. The phenotypic characteristics of rhinitis and asthma multimorbidity in adults and the elderly were compared using validated information and

communication technology (ICT) tools (i.e. MASK-air[®], CARAT and a physician's questionnaire developed for the TWINNING). This improved the understanding, assessment of burden, diagnosis and management of rhinitis in the elderly by comparison with an adult population. The TWINNING was selected as a success story.

4.5.2 | DigitalHealthEurope (DHE) Severe Asthma TWINNING

In order to reduce the burden of severe asthma with a focus on old age people, the objectives of the transfer of innovation (DHE Severe Asthma TWINNING) are as follows:

1. To form a European network for severe asthma in old age people globally (this does not currently exist);
2. To better understand the phenotype and treatment of severe asthma with possible differences between countries, age and gender;
3. To include the results into the MASK Good Practice for disease stratification and personalized health care with a vision to optimizing the prescription of expensive treatments (biologics) and following up the patients using RWD;
4. To be the basis for a further deployment beyond the funding, including a network of centres of excellence on severe asthma (ARIACARE and ARIACARE digital).

The DHE TWINNING on SA (Project acronym: H2020, DigitalHealthEurope Grant Agreement Number: 826 353, Project full title: *Support to a Digital Health and Care Innovation initiative*

in the context of Digital Single Market strategy, Call identifier: SC1-HCC-05-2018) was accepted on 16 September 2019.

5 | ONGOING AND FUTURE MASK ACTIONS

5.1 | Advance capabilities: The same IT tool from epidemiologic studies to clinical trials and clinical practice

Symptom-medication scores (SMSs) are needed to investigate the effect of AR treatments, in particular allergen immunotherapy.⁸⁶ Several scores have been proposed and the European Academy of Allergy and Clinical Immunology has designed one.⁸⁷ However, a recent MASK analysis²⁴ has found that this commonly used SMS is not very well correlated with VAS work used as an end point. When considering MASK data,¹⁹ it is possible that some patients with very high levels of VAS global (and work) may not be able to be controlled with current pharmacologic treatments, and a new SMS has been proposed. This SMS for rhinitis has been validated with MASK-air[®] data. Other artificial intelligence analyses are being carried out to obtain an optimal score.

Real-world evidence (RWE) combines results of double-blind, placebo-controlled, randomized trials (DB-PC-RCT) and RWD. However, observational studies provide clinically relevant information in addition to DB-PC-RCT.^{19,37,39} RWD can provide new insights into disease patterns and help improve the safety and effectiveness of health interventions. The same SMS will allow the comparison of the results of DB-PC-RCTs and RWD in population

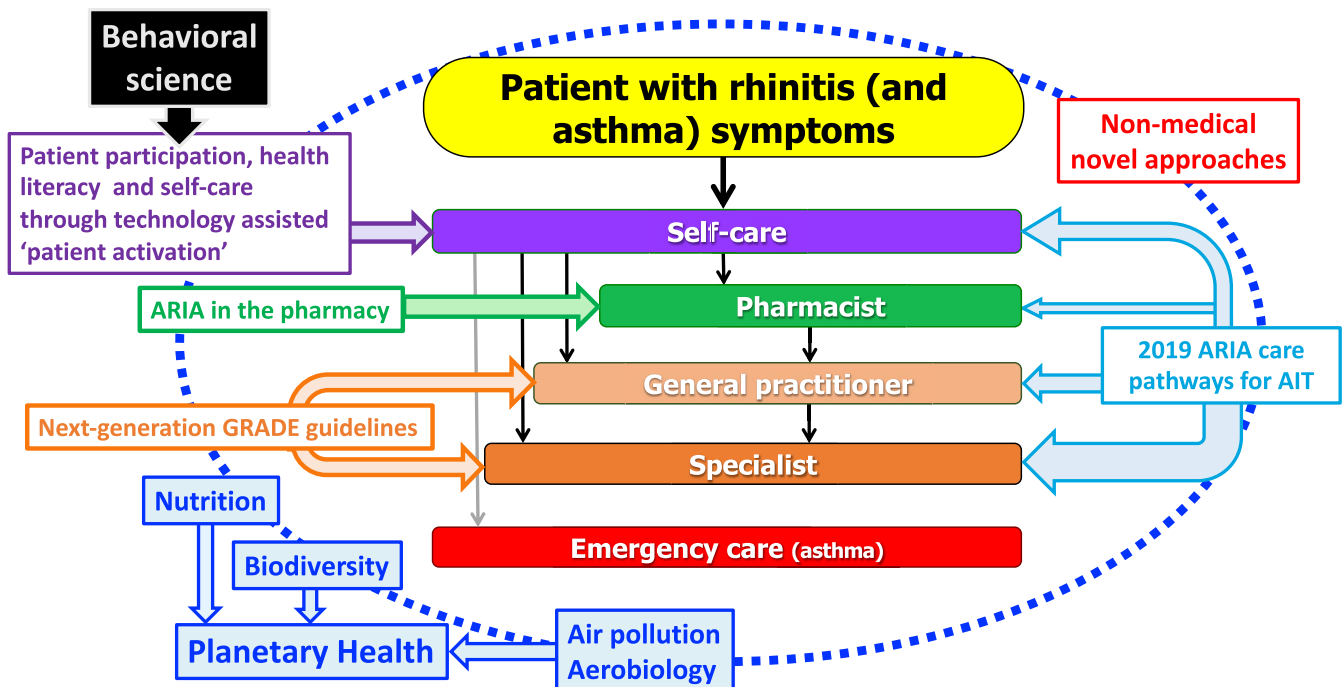


FIGURE 2 Next-generation ARIA care pathways. AIT: allergen immunotherapy (adapted from ref.14)

TABLE 6 Papers of next-generation care pathways in the digital transformation of health and care

	Title	Journal	Publication
1	From ARIA guidelines to the digital transformation of health in rhinitis and asthma multimorbidity	Eur Respir J	[9]
2	Mobile technology in allergic rhinitis: evolution in management or revolution in health and care?	JACI Practice	[5]
3	Next-generation ARIA care pathways for rhinitis and asthma: a model for multimorbid chronic diseases	CTA	[80]
4	2018 Good Practice: ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma <i>Practice presented during the Steering Group on Promotion and Prevention marketplace workshop on "digitally-enabled, integrated, person-centred care" best practices on 12-13 December 2018 in the premises of the Joint Research Centre in Ispra, Italy</i>	CTA	[14]
5	Next-generation care pathways for allergic rhinitis and asthma multimorbidity: a model for multimorbid non-communicable diseases (Meeting Report. Part 1)	J Thorac Dis	[75]
6	Next-generation care pathways for allergic rhinitis and asthma multimorbidity: a model for multimorbid non-communicable diseases (Meeting Report. Part 2)	J Thorac Dis	[76]
7	ARIA pharmacy 2018: "Allergic rhinitis care pathways for community pharmacy"	Allergy	[65]
9	ARIA Care pathways for allergen-specific immunotherapy following the ARIA recommendations to fill gaps in knowledge ⁸¹	Allergy	[66]
10	ARIA-EAACI Care pathways for allergen-specific immunotherapy Pocket Guide		
11	Next-generation ARIA guidelines for allergic rhinitis based on GRADE and real-world evidence, validating the management algorithm, following GRADE recommendations ^{77,78,82} and chamber studies ^{63,83}	JACI	[80]
12	Digital transformation of health and care in asthma	Allergy	
13	2020 DHE TWINNING on severe asthma		
14	Uniform stratification of severe chronic diseases in adults using mobile technology: App-MM		
15	ARIA Phase 4 (2018): Change management in allergic rhinitis and asthma multimorbidity using mobile technology	JACI	[12]

Note: App-MM: App for multimorbidity, ARIA: Allergic Rhinitis and its Impact on Asthma, CARAT: Control of Allergic Rhinitis and Asthma Test, CTA: Clinical and Translational Allergy, DHE: DigitalHealthEurope, EAACI: European Academy of Allergy and Clinical Immunology, JACI: Journal of Allergy and Clinical Immunology, TWINNING: Transfer of Innovation

studies or for the individual patient.⁸⁰ This will provide complementary information to DB-PC-RCTs and a real-life approach. Since patients are using the app and the same system, it will be possible—using machine learning—to target the efficacy of AIT at the individual level and to propose automatic advice to the physician for the indication of AIT as well as an early stopping rule in clinical practice.⁶⁶

Patient stratification is an important step for expensive treatments such as allergen immunotherapy in allergic diseases or biologics in severe asthma. There are currently no validated genetic or blood biomarkers for predicting or monitoring the efficacy of treatments at an individual patient level in allergic diseases.⁸⁸ mHealth biomarkers (SMS)⁶⁶ and eCDSS¹⁵ may change the scope of AIT in allergic diseases or biologics in asthma or chronic rhinosinusitis.

5.2 | Towards severe asthma

The lessons learnt by MASK will be used to build MASK-asthma which will include (a) a standardized assessment of severity and control, (b) the development of an upgraded e-platform for severe asthma including screening, assessment by physicians and follow-up, (c) the analysis of MASK-air[®] data on file for asthma, (d) a pan-European

IT-based alert system for exacerbations, (e) MASK-asthma IT tools for registries and databases, (f) transfer of innovation, (g) a digital network of centres of excellence (ARIACARE-Digital) and (h) the development of next-generation care pathways for severe asthma.

5.3 | United perspective for chronic diseases to sustain planetary health

Planetary health refers to “the health of human civilization and the state of the natural systems on which it depends”.⁸⁹ Most risk factors for noncommunicable diseases (NCDs) are associated with planetary health.

Digital tools can also empower patients in the context of the UN sustainable development goals and in particular regarding those related to sustainability and natural resources.⁹⁰ Future apps in AR could consider providing information to promote behavioural changes that could reduce the planetary impacts of human activity.

During a conference entitled “Europe That Protects: Safeguarding Our Planet, Safeguarding Our Health” - co-organized by the Finnish Institute for Health and Welfare, the Finnish Environment Institute and the European Commission under the auspices of Finland's Presidency of the EU in 2019 - a symposium was held to better understand the digital transformation of health

and care to sustain planetary health in airway diseases. The Finnish Allergy Programme is a proof of concept of planetary health, and MASK (Mobile Airways Sentinel Network), a Good Practice of DG Santé on digitally-enabled, patient-centred care pathways, is in line with the objectives of this programme.

Lessons learnt in rhinitis and asthma multimorbidity¹⁷ can be deployed to other NCDs for change management in health care. A uniform approach can be used¹² for the development of next-generation care pathways in chronic diseases embedding the risk factors involved in planetary health.

This perspective is global since planetary health needs to be tackled in all countries. The World Health Organization and the International Telecommunication Union recognize the importance of mHealth globally, and particularly in developing countries.⁵

5.4 | Value-added medicines: The example of the combination of intra-nasal antihistamine and corticosteroid used as needed

Value-added medicines represent the concept of drug repurposing.⁹¹ They are medicines based on known molecules that address healthcare needs and deliver relevant improvement for patients, healthcare professionals and/or payers. MASK is a proof of concept of drug repurposing as it suggests the importance of as-needed treatment for AR. Value-added medicines are medicines based on known molecules that address healthcare needs,^{8,13,17} and deliver relevant improvement for patients,^{18,37,63,92} healthcare professionals^{18,37} and payers.^{34–36,38} They contribute to addressing unmet patient needs, moving from a tailored and patient's specific approach. By answering patients' unmet needs, they represent a new horizon for those who are currently looking forward to a better quality of life with their treatment.

6 | CONTRIBUTION OF MASK TO THE EU DIGITAL SINGLE MARKET

The Digital Single Market (<https://ec.europa.eu/digital-single-market/en>), part of the Digital Agenda for Europe 2020 programme of the EU, includes three "pillars": (a) access to online products and services, (b) conditions for digital networks and services and (c) growth of the European digital economy. MASK is involved in this strategy by (a) the management of care process, (b) digital networks (ARIACARE-digital network), (c) innovation to market (I2M) to foster the cross-border adoption of digitally-driven marketable solutions, (d) the political, organizational, technological and financial readiness, (e) the contribution to European co-operation and transferability, (f) and the contribution to the European Digital Transformation of Health and Care (Bousquet et al., submitted).

The digital transformation of health and care can improve the quality of health services and ultimately people's health and well-being as well as the economy, in line with EIT Health. In the context of implementing communication on the digital transformation of health and care, DG SANTE, in collaboration with the EU Commission Expert Group "Steering

Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases" (<https://ec.europa.eu/transparency/regexpert/index.cfm?do=groupDetail.groupDetail&groupID=3622>), scaled up good practices in the field of digitally-enabled, integrated, patient-centred care. MASK was one of the nine Good Practices selected, along with chronic disease and Parkinson's disease.¹⁴

7 | POLITICAL AGENDA

In the severe Asthma TWINNING, the engagement through the Salerno local health agency of ProMIS@Campania network⁶⁸ will ensure that adoption is progressively achieved through a multicentric scale-up pilot. The good practice will then be scaled up to other Italian regions through the National ProMIS network.⁹³

The EU political agenda is of great importance in supporting the digital transformation of health and care for chronic respiratory diseases. The Polish Presidency of the EU Council (2011) prioritized the early diagnosis, prevention and control of chronic respiratory diseases in children.⁹⁴ AIRWAYS-ICPs (integrated care pathways for airway diseases),⁷ initiated in 2014 by the EIP on AHA,^{6,8} launched a collaboration to develop multisectoral ICPs. It was a GARD⁹⁵ demonstration project.⁹⁶

Euforea (European Forum for Research and Education in Allergy and Airway Diseases) proposed a yearly stepwise strategy at the EU or ministerial levels.^{97–99} Euforea organized an EU Summit in Vilnius, Lithuania (March 2018) to propose multisectoral ICPs embedding guided self-management, mHealth and air pollution in chronic respiratory diseases.¹⁰⁰

POLLAR (Impact of air POLLution on Asthma and Rhinitis, EIT Health) is focussing on the impact of allergens and air pollution on airway diseases to propose novel ICPs integrating pollution, sleep and patient literacy.²³ AQuAS, the Catalonia Health Agency, is involved in POLLAR.

8 | CHANGE MANAGEMENT

ARIA phase 4 focusses on change management with the aim of providing an active and healthy life to rhinitis sufferers and to those with asthma multimorbidity across the life cycle—whatever their gender or socio-economic status—in order to reduce health and social inequities incurred by the disease. ARIA has followed the 8-step model of Kotter¹⁰¹ to assess and implement the impact of rhinitis on asthma multimorbidity and to propose multimorbid guidelines.¹² A second change management strategy is proposed by ARIA Phase 4 on the digital transformation of health and care.

9 | CONCLUSION: TOWARDS A REVOLUTION IN RHINITIS AND ASTHMA MANAGEMENT

The MASK strategy represents a proof of concept for other chronic diseases, as asthma-rhinitis multimorbidity plays a key role

in understanding asthma and can be used as a general model of multimorbidity. Moreover, asthma and rhinitis have a life-course approach, whereas most chronic diseases start early in life but are only clinically evident in adulthood. The lessons learnt by the MASK strategy are therefore transposable to other chronic diseases.

Anamorphosis is a metaphor for reimagining and expanding on appearances and overcoming otherness. MASK digital anamorphosis makes it possible to look at data from a different angle. The data then appear to be different to their familiar, expected and/or generally accepted form. Anamorphosis may be associated with fear as phenomenological otherness often accompanies new technology. Education for a better appraisal of mHealth by all stakeholders is therefore essential. Metaphorical language can facilitate communication and shape of thought, thus providing key challenges and opportunities for future research.

mHealth has the potential to profoundly impact health care.¹⁰² mHealth apps now represent an important evolution of health and care for allergic rhinitis and asthma multimorbidity. The digital revolution is underway for rhinitis and asthma.⁵ Innovative health strategies and services will change management⁶ and create a new kind of partnership between the patients, the healthcare providers and the health system.

CONFLICT OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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