

Mobile Technology in Allergic Rhinitis: Evolution in Management or Revolution in Health and Care?



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Smart devices and Internet-based applications (apps) are largely used in allergic rhinitis and may help to address some unmet needs. However, these new tools need to first of all be tested for privacy rules, acceptability, usability, and cost-effectiveness. Second, they should be evaluated in the frame of the digital transformation of health, their impact on health care delivery, and health outcomes. This review (1) summarizes some existing mobile health apps for allergic rhinitis and reviews those in which testing has been published, (2) discusses apps that include risk factors of allergic rhinitis, (3) examines the impact of mobile health apps in phenotype discovery, (4) provides real-world evidence for care pathways, and finally (5) discusses mobile

health tools enabling the digital transformation of health and care, empowering citizens, and building a healthier society. © 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:2511-23)

Key words: Apps; Digital transformation of health; MASK; mHealth; Mobile technology; Rhinitis

INTRODUCTION

Mobile technology has spread rapidly around the globe. Today, it is estimated that more than 5 billion people have mobile devices, more than half of which are smartphones.¹

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*Abbreviations used**AR- Allergic rhinitis**CDS- Clinical decision support**CDSS- Clinical decision support system**EU- European Union**GDPR- General Data Protection Regulation**MASK- Mobile Airways Sentinel Network**RCT- Randomized controlled trial*

Mobile health (mHealth) is the use of information and communication technology for health services and information transfer.² mHealth, including applications (apps) running on consumers' smart devices (ie, smartphones and tablets), is becoming increasingly popular and has the potential to profoundly impact health care.^{3,4} The rapid advances in mobile technologies have given rise to new opportunities for the digital transformation of health and the continued growth in coverage of mobile cellular networks. The potential applications and benefits

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of mHealth are extensive and expanding.⁵ Implementing mHealth innovations may also have disruptive consequences,⁶ so it is important to test applicability in each individual situation.⁷ Appropriately identifying and representing stakeholders' interests and viewpoints in evaluations of mHealth is a critical part of ensuring continued progress and innovation.⁸ Patient, caregiver, and clinician evaluations and recommendations play an important role in the development of asthma/allergic rhinitis (AR) mHealth tools in supporting the provision of disease management.⁹

Smart devices and internet-based applications are already used in AR and may help to address some of the unmet needs.³ According to recent position papers from the European Academy of Allergy and Clinical Immunology¹⁰ and from the American College of Allergy and Immunology,¹¹ mHealth apps can support the provision of high-quality care to patients with allergy, in particular those with AR and/or asthma. This is satisfying for patients and health care professionals, and has led to a reduction in health care use and costs. However, these new tools need to first of all be tested for privacy rules, acceptability, usability, and cost-effectiveness. Second, they should be evaluated in the frame of the digital transformation of health, their impact on health care delivery, and health outcomes.

STRENGTHS AND WEAKNESSES OF mHealth

Smartphones have radically changed people's lives. However, despite the global advent of mHealth over the past 2 decades, their use and benefits in disease management are unclear.

The benefits of mHealth include paperless information, the potential increase in medication adherence, and improved monitoring (Table I). mHealth technology has great potential to increase health care quality, expand access to services, reduce costs, and improve personal wellness and public health.¹³ However, mHealth may be harmful. Technically, the development of an app is an easy task, which incurs very low initial investments and does not require in-depth knowledge of the subject itself. The low entry barrier, dramatically democratizing the app development environment, also results in a large number of ad hoc apps targeting various health concerns of the public. Most mHealth apps have been neither tested on patients nor approved by regulatory organizations such as the US Food and Drug Administration or the European Medicines Agency. However, many patients rely on these apps in their everyday lives.

A few weaknesses emerge from the use of mHealth apps that are used in observational studies to assess real-world evidence for the evaluation of allergy phenotypes or treatments. As for all studies using participatory data, potential biases include (1) the likelihood of sampling bias, (2) the difficulty to assess generalizability of the study, because app users are usually not representative of all patients with AR. In Mobile Airways Sentinel Network (MASK), it was found that most users report bothersome symptoms,¹⁴ (3) outcome misclassification that cannot be assessed, (4) very little information on patient characteristics, (5) lack of physicians' support in the diagnosis of AR, (6) potential measurement biases due to the so-called informatics illiteracy of many patients,¹⁵ and (7) poor adherence to electronic diary compilation, which makes proving poor adherence to treatment impossible.

One of the major problems with apps is the low adherence to their use. Achieving sufficient mHealth app engagement and user

retention rates is a difficult task. In MASK-air, about half the patients use the app only once.¹²

The benefits of mHealth apps are presented in Table I.

REGULATORY FRAMEWORK

mHealth raises significant privacy and security challenges in terms of information technology privacy, data sharing and consent management, access control and authentication, confidentiality and anonymity, policies and compliance, accuracy and data provenance, and security technology.¹³

In May 2018, the European Union (EU) General Data Protection Regulation (GDPR) brought major changes in data privacy regulation in the EU. The aim of the GDPR is to protect all EU citizens from privacy and data breaches in today's data-driven world. It harmonizes data privacy laws across Europe, protects and empowers all EU citizens' data privacy, and reshapes the way organizations across the region approach data privacy. Thus, all mHealth apps used in the EU should follow the GDPR. The law applies to personal data (Art. 4 para. 1 no. 1, GDPR).¹⁶ Anonymous or anonymized data should lack identifiability. Anonymization principally enables the sharing of data in a way that preserves privacy with minimal data loss. Geolocation information is not only personal data but also has to be considered as an identifier itself.^{17,18} Thus, mHealth apps should follow a geolocation deanonymization that is rarely found in apps. The k-anonymity method is acceptable and was found to fulfill the GDPR regulations in AR.¹⁹ The GDPR fixes general rules applying to any kind of personal data processing as well as specific rules applying to the processing of special categories of personal data such as health data.²⁰ In May 2020, a new EU law will regulate mobile technology (Medical Device Regulation),²¹ making its use tightly regulated.

The US regulations were recently reviewed in detail.²² The US Food and Drug Administration and the Federal Trade Commission both guide the development and regulation of mHealth devices. Since the recently enacted amendment to the Twenty-First Century Cures Act—the Food, Drug and Cosmetic Act—certain software functions are no longer considered to be medical devices.²³ Thus, the US Food and Drug Administration is now using enforcement discretion for mHealth apps that do not present risks to patients and consumers.

mHealth APPS FOR AR

Apps informing on risk factors for AR

Risk factors for exacerbations of AR and asthma include allergen exposure,²⁴ climatic factors,^{25,26} and air pollutants.²⁷ It is therefore of great importance to identify levels of risk factors that can induce symptoms in patients with allergy. Among these, pollen exposure is the most important for patients allergic to pollen. Therefore, forecasting symptoms of pollen-related AR for the individual patient should improve disease control and plan pharmacological intervention and/or prevention of exposure. Besides pollen diaries, mHealth apps allow an easy and fast documentation of pollen allergy counts.²⁸⁻³⁰ A study that analyzed 9 mobile apps delivering pollen information and pollen forecasts found that the quality of pollen forecasts needs to be improved. It recommended quality control for pollen forecasts to avoid potential harm to patients.³¹ Patients with AR could consider the need to avoid the more polluted routes when walking, biking, or exercising. In many cities, traffic air pollution

TABLE I. Global applicability of mHealth apps in AR

Applicability	mHealth apps
Clinical practice	Physicians will be able to read the files of the patients to: • Optimize treatment for the patient and, in particular, for the current or the next pollen season • Assess and increase adherence to treatment • Help in shared decision making • Prescribe allergen immunotherapy (AIT) more rapidly when the patient is not controlled despite optimal pharmacologic treatment • Determine the efficacy of any treatment including AIT
Change management	Apps are an essential tool for providing personalized medicine in AR and asthma • Many patients are uncontrolled and nonadherent to treatment. Apps can indirectly assess and help (eg, reminders) adherence • Patients appear to use their medications as needed and not on a regular basis as prescribed • Change management is needed and may be facilitated by apps
Patient empowerment	• Better understanding of the symptoms • Sentinel network linking aerobiology data and control • Improved adherence • Self-management • Alert systems • Messages sent by the app
Clinical trials	• To assess environmental control measures • To assess pharmacotherapy For RCTs, it is essential to have clarity on definitions, and relevant tools. Apps allow • To better stratify the patients, in particular for AIT • To assess the efficacy of treatments during the trial • To assess the efficacy when the treatment is stopped • Feasibility of real-life studies • To confirm RCTs • And bring new hypotheses for the treatment of AR and asthma
Registration and reimbursement of medicines	• Controlled trials designed with a uniform approach will be more easily evaluated by the health technology assessment agencies (such as the National Institute for Health and Care Excellence) for reimbursement • Better understanding of direct and indirect costs • Controlled trials designed with a uniform approach will help to synchronize data from the real-life world regarding clinical effects and safety/tolerability of new drugs (postmarketing pharmacovigilance for some apps)
Research on mechanisms and genetics	• A uniform definition and a collaborative approach to epidemiological, genetic, and mechanistic research is important and will be enhanced by the stratification of patients using apps • Different levels of phenotype characterization (granularity) can be applied to assess phenotypic characterization in elderly subjects
Epidemiology	• In epidemiologic population studies, standardized definitions and tools are fundamental • Apps may allow novel approaches combining classical cross-sectional and longitudinal studies with real-life studies in large populations
Employers	• AR and asthma represent a major burden for the employers, and the estimated annual costs in the EU range from €30 billion to €60 billion. Better control of the disease was shown to reduce costs • Apps have the potential to improve the control of allergic diseases and to significantly improve work productivity at the EU level

Adapted with permission from Bousquet et al.¹²

concentrations decline rapidly at a few hundred meters from roadways, and web-based apps can assist individuals in finding alternative routes.³²

There are, however, drawbacks that need to be understood to provide better information: (1) The pollen season does not necessarily correspond to an individual patient's symptoms³³ and submicronic particles from pollens can induce severe symptoms such as thunderstorm-induced asthma³⁴; (2) The definition of the pollen season is still unclear³⁵ although some clarification

efforts have been made for clinical trials³⁶; (3) There is a weak correlation between pollen counts and symptoms³⁷; (4) Pollutants and weather conditions can interact with pollens to induce symptoms; (5) Only predictive models are to be used, not only for forecasting but also for near-real-time analysis (now-casting) because it takes a few days to count pollens.³⁸ However, these models may need more testing to be fully accepted; (6) Next-generation pollen monitoring is very promising but its cost prevents a large use³⁹; (7) The onset of individual symptoms

TABLE II. Examples of mHealth apps for AR

Country	Name of mHealth app	Pollen	Other risk factors	Health data
Multicountry				
	Air Matters ⁴⁴	X	X	
	Austria Pollen Information Service ⁴⁵	X		X
	BreezoMeter ⁴⁶	X	X	
	The Weather Channel ⁴⁷	X		
	POLLEN & PHD, ⁴⁸ 2 separate but interlinked apps	X		X
	MASK-air ⁴⁹			X
	Pollen alert Europe ⁵⁰	X		
Argentina	Alerta Polen Argentina ⁵¹	X		
Australia	Air Rater ⁵²			
Denmark	Dagens Pollental ⁵³	X		
France	ALK-Allergik ⁵⁴			
	Allergy Track ⁵⁵			
	i-pollen ⁵⁶			
	Plume Air Report ⁵⁷			
Germany	Pollen App ⁵⁸	X		X
Italy	Pollen App ⁵⁹	X	X	
	Allergy Control ⁶⁰	X	X	X
	Allergy Monitor ⁶¹	X		X
	MeteoAllergie ⁶²	X		
	Bollettino meteo Pollini e allergie in Italia ⁶³	X		
Spain	R-Alergo ⁶⁴	X		
	Polen Control ⁶⁵	X		
	Niveles de Polen ⁶⁶	X		
	Intolerapp ⁶⁷	X		
	ALK Polen ⁶⁸	X		
Switzerland	AllyScience ⁶⁹			
United Kingdom	My Pollen forecast UK ⁷⁰	X		
	Piri ⁷¹	X		
United States	My Pollen Forecast ⁷²	X		X
	Plume Air Report ⁷³	X		X
	Poncho: Wake Up Weather ⁷⁴	X		
	WeatherBug ⁷⁵			

(AR, asthma, conjunctivitis) may be associated with different levels of allergen exposure in patients with different intensities of sensitization and target organ reactivity.

Google Trends are interesting for complementing pollen counts,⁴⁰ but they cannot be readily used as a predictor of the pollen season. However, Google Trends, when used retrospectively, are better correlated than pollen counts with symptoms.^{37,41,42}

A large number of apps provide information to allergy sufferers regarding pollen counts and/or pollution data.⁴³ Some examples are given herein and in Table II.

BreezoMeter uses the Copernicus Atmosphere Monitoring Service pollen predictions and big data analysis to provide a continuous current condition pollen index.⁴⁶ However, its validation is not yet available.

Air Matters broadcasts pollen and air quality data in most countries of the world.⁴⁴

The Copernicus Atmosphere Monitoring Service,⁷⁶ implemented by the European Centre for Medium-Range Weather Forecasts on behalf of the EU, provides forecasts for birch, olive,

and grass pollen to allow allergy sufferers in the EU to take preventive measures days before exposure. The Copernicus Atmosphere Monitoring Service supports a range of smartphone apps designed to limit exposure to such allergens. One of these is MetéoPollen for France.⁷⁷

My Pollen Forecast⁷² tracks pollen counts in the United States using forecasts for pollen and climatic data.

The POLLEN app of the European Aeroallergen Network, maintained by the Medical University of Vienna,⁴⁸ evaluates the pollen situation in European countries using the pollen counts of the European Aeroallergen Network and predictions of the SILAM pollen forecasting model.⁷⁸

Apps including health data

Many mHealth apps support patients with AR via self-monitoring through an electronic diary, personalized feedback, and/or patient education.⁷⁹ They aim to improve patient education and self-management on a daily basis but require an evidence-based evaluation given that the information provided on the app stores is limited, in particular for the apps'

validity.⁸⁰⁻⁸² This can be done by evaluating the effectiveness of the app with the patients' clinical outcomes.^{12,30,83} For example, children with moderate to severe seasonal AR, treated with daily mometasone, improved their disease knowledge thanks to daily informative messages sent by their electronic diary app.⁷⁹ If patients are seeking an approach involving the minimal interaction with health care professionals in AR management,⁸⁴ it is then crucial that the mHealth app be in line with evidence-based essential self-management principles. A Mobile app Rating Scale instrument⁸⁵—available in Australia—has been used to assess the mHealth apps for AR.⁸⁶ A “patient empowerment index through mobile technology” was recently designed and used to evaluate AR to support patients choosing an mHealth app and physicians recommending it.⁷⁹

Most but not all mHealth apps that include clinical data are available in English and some are available in more than 15 languages (Table II). Most mHealth apps are freely available on iOS and Android. However, very few have provided clinical data supporting their validity. mHealth apps for AR include the following:

- Self-monitoring
- Patient's feedback
- Patient's education
- Patient's empowerment
- Pollen and/or air pollution data

At present (May 2019), some mHealth apps such as ALK-Allergik,⁵⁴ Allergy Track,⁵⁵ AllyScience,⁶⁹ e-symptoms,⁸⁷ i-pollen,⁵⁶ Plume Air Report,⁵⁷ and Pollen App⁵⁸ are in non-English languages. Others in English may be restricted to a limited geographic area such as Air Rater in Australia⁵² or are not available from app stores.

Besides those with a commercial interest (eg, Sensio Air⁸⁸ and Zyrtec AllergyCast⁸⁹), there are few mHealth apps with health data on AR (eg, AllergyMonitor, MASK-air, WebMD Allergy,⁹⁰ and the Austrian Pollen Information Service⁴⁵) (Table II).

Apps connected with sensors

In asthma, many mHealth apps are connected with sensors for inhalers.²² Such devices do not yet exist in AR, but there are attempts to connect pollution sensors to mHealth apps. Unfortunately, those existing for asthma appear to be in an exploratory phase and need validation. In addition to external sensors, smartphones and tablets have embedded sensors such as camera, microphone, atmospheric pressure sensor, accelerometer, and global positioning system. These sensors can be used to provide contextual information for the collected clinical data. Moreover, using signal processing, data from on-board sensors, already available in off-the-shelf devices and used by millions of patients, are being tested as ubiquitous technologies to provide verified information on cough,⁹¹ lung function,⁹² adherence to inhaled treatment,⁹³ physical activity parameters, and other human behaviors of clinical interest.⁹⁴

Examples of apps

AllergyMonitor. AllergyMonitor⁹⁵ is an app that has been translated into 10 languages. Its target is to improve allergy diagnosis by matching trajectories of symptom-medication scores and pollen counts.^{28,30,83,96,97} Furthermore, it enhances shared decision making by fostering the exchange of information

between users and their health care professionals. The latter can access and view their patients' recorded data in a back-office, which allows the management of patients' clinical data and gives a structured overview on the individual disease management. The data recorded by the user then complete the set of information being integrated in the back-office in real time. As users also register the intake of their prescribed medication, this feature allows the monitoring of compliance, which has been shown to effectively increase the adherence to treatment with nasal corticosteroids and sublingual allergen-specific immunotherapy. To this end, the app includes customized lists of over-the-counter and prescribed medications for many countries, patient-doctor communication via short message service and e-mail, patient alerts for a better knowledge of the disease, as well as reminders for a better adherence to treatment. The potential of data sets generated through AllergyMonitor has also been investigated for the short-term prediction of patients' symptoms with several symptom and medication scores for rhinitis and asthma.

MASK. MASK,⁴⁹ the Phase 3 Allergic Rhinitis and Its Impact on Asthma initiative, was initiated to reduce the global burden of AR and asthma multimorbidity, giving the patient and the health care professional simple tools to better prevent and manage respiratory allergic diseases. The MASK app (MASK-air, formerly *the Allergy Diary*, freely available for Android and iOS)⁹⁸ is the most extensively published mHealth app for AR. It is an information and communication technology system centered around the patient^{12,98-100} and is operational in 23 countries and 17 languages. It uses a treatment scroll list that includes all medications customized for each country as well as visual analogue scales to assess rhinitis control and work productivity.^{101,102} MASK-air is being combined with data on allergen and pollution exposure (Impact of air POLLution on Asthma and Rhinitis).²⁷ MASK-air results are presented in Table III.

MASK is scaled up using the EU European Innovation Partnership on Active and Healthy Ageing strategy.¹²⁰ MASK is supported by several EU grants and is a World Health Organization¹²⁴ research demonstration project. It is a Good Practice of the Directorate General for Health and Food Safety.¹⁰⁴

European Aeroallergen Network Pollen Information Service. The European Aeroallergen Network Pollen Information Service,⁴⁸ developed and maintained at the Medical University of Vienna, provides a pollen assessment and a 3-day forecast in cooperation with local and international institutions. It is available for European countries in more than 10 languages. The app includes symptoms and treatments. The components and functionality of the app vary between the countries depending on the requests of the national pollen observing groups.

The service also takes the user's pollen diary entries into account and calculates personal burden level. Allergic symptoms can be documented and compared with the pollen count in the pollen diary. Personal load, Pollen News, Pollen-Countdown notifications, and a reminder for a doctor's visit are all available. The pollen diary was restructured in 2018 and provides information on preventing impaired performance in everyday life, the time of the highest burden, and the time(s) of being

TABLE III. The global MASK Good Practice and IT solution

App (MASK-air) deployed in 23 countries: TRL9 (Technology Readiness level), Electronic CDSS (ARIA e-CDSS): TRL7, e-physician questionnaire deployed in 16 countries: TRL9
• App: 29,000 users, 23 countries, 17 languages • Tested with patients • GDPR including geolocation¹⁹ • Good Practice of the EIP on AHA, follows CHRODIS¹⁰³ • Good Practice on digitally enabled, integrated, patient-centered care endorsed by DG Santé¹⁰⁴ • Based on 11 EU grants (MeDALL,¹⁰⁵ GA²LEN¹⁰⁶) including—in 2018—POLLAR,²⁷ VIGOUR, DigitalHealthEurope, Euriphi (Digital transformation of health) and—in 2019— Gatekeeper • From a validated “research” tool (2004-2018) to large-scale deployment (2019-) ○ Validation with COSMIN guidelines¹⁰⁷ ○ Baseline characteristics¹⁰⁸ ○ Work productivity^{109,110} ○ EQ-5D and WPAI-AS¹¹¹ ○ Novel phenotypes of allergic diseases¹¹² ○ Adherence to treatment^{15,113} ○ Novel approaches to inform the efficacy of treatment^{14,15} • Patients’ organizations and scientific societies involved • GARD (WHO alliance) • Presented during WHO and EU ministerial meetings^{114,115} • Next-generation care pathways meeting (December 3, 2018) with the EIP on AHA, POLLAR (EIT Health), and GARD • 51 MASK articles in 12 languages¹¹⁶⁻¹¹⁹ • Dissemination according to the EIP on AHA¹²⁰
Transfer of innovation (TWINNING ¹²¹)
• Interoperable platform with MASK • 25 reference sites of the European Innovation Partnership on Active and Healthy Ageing plus Argentina, Australia, Brazil, Canada, and Mexico¹¹⁶⁻¹¹⁹ • 900 patients enrolled • GDPR solutions solved
ARIA e-CDSS
• Interoperable platform with MASK • Based on an expert meeting,¹²² and validation by Delphi questionnaire¹²³ and real-world evidence using MASK-air^{14,15} • Electronic version available¹²³

ARIA, Allergic Rhinitis and Its Impact on Asthma; COSMIN, consensus-based standards for the selection of health status measurement instruments; DG Santé, Directorate General for Health and Food Safety; e-CDSS, electronic clinical decision support system; EIP on AHA, European Innovation Partnership on Active and Healthy Ageing; EQ-5D, EuroQol 5-dimensional questionnaire; GARD, World Health Organization Global Alliance against Chronic Respiratory Diseases; MeDALL, Mechanisms of the Development of ALLergy (FP7); POLLAR, Impact of air POLLution on Asthma and Rhinitis; WHO, World Health Organization. Modified with permission from Bousquet et al.¹⁰⁴

outdoors. The encyclopedia of allergenic plants is also available to answer questions on allergy.

e-Allergy. The underrecognition of AR is common because of a low level of public awareness as well as limitations in access to allergologists.¹²⁵ AR sufferers often use over-the-counter drugs and self-medicate. mHealth tools supporting the premedical early diagnosis of allergic diseases are important. They use algorithms able to classify respondents into certain risk groups of AR and asthma. An algorithm was created—with the use of advanced statistical methods (neural networks)—on Epidemiology of the Allergic Diseases in Poland data containing both questionnaire answers and medical diagnosis.¹²⁶ This tool is constantly being updated. The latest results show a sensitivity for AR in children and adolescents of 0.852 and a specificity of 0.840.¹²⁷

CLINICAL DECISION SUPPORT SYSTEMS

A clinical decision support system (CDSS) is a health information technology system designed to assist clinicians and other health care professionals in clinical decision making. In medicine,

CDSSs have become a major topic in artificial intelligence. According to the National Academy of Medicine (Washington, DC),¹²⁸ “facilitative clinical decision support (CDS) is a practical necessity for every clinician in our rapidly-evolving health and healthcare landscape.” A CDSS can reduce the burden that exponentially expanding clinical knowledge and care complexity places on clinicians, other health care professionals, or patients. CDSs provide clinicians and other health care professionals with knowledge and person-specific information—intelligently filtered or presented at appropriate times—to enhance health and health care.¹²⁹ CDSs can enhance decision making through the use of the following tools: (1) computerized alerts and reminders to health care providers and patients, (2) clinical guidelines, (3) focused patient data reports, and (4) diagnostic support.¹³⁰ Many apps used in AR provide patients with some help for AR control. However, for this, they should be labeled as CE2A in the EU. Apps that do not provide help can be registered as CE1. An electronic CDSS based on MASK now exists in AR and is in the process of validation.¹²³ It is not clear whether other tools have been validated because they have not been published. CDSSs

may also be very useful in stratification strategies and in reporting outcomes in clinical trials such as in allergen immunotherapy.¹³¹

POTENTIAL OF mHealth APPS FOR ALLERGY PHENOTYPE DISCOVERY

Conventionally, phenotypic studies have relied on traditional observational designs. Apps provide a new source of information on daily symptoms and the opportunity to discover new phenotypes. Few studies have been published concerning allergy phenotypes assessed with an app.

A prospective analysis has compared 6 disease severity scores for AR against pollen counts.⁹⁶ Many different and incomparable symptom (medication) scores are used to assess AR control. Disease severity scores for seasonal AR evaluated by an Internet-based platform provide similar results at the population level but are heterogeneous in individual patients.

Multimorbidity in allergic airway diseases is well known,¹³² but no data have ever existed regarding how multimorbidity impacts the daily dynamics of specific symptoms, including severity and work. MASK-air has enabled this investigation in a novel approach of the intraindividual variability in allergic multimorbidity from day to day.¹¹² AR and rhinoconjunctivitis did not appear to be the same disease. Moreover, MASK-air identified a previously unrecognized extreme pattern of uncontrolled multimorbidity (uncontrolled rhinitis, conjunctivitis, and asthma on the same day).¹¹² However, mHealth apps are only tools generating hypotheses and need to be confirmed in classical epidemiologic studies. Differences between AR alone or associated with conjunctivitis were already known,¹³³ but new studies carried out following MASK-air data showed that (1) ocular symptoms are more common in polysensitized patients whether or not they have asthma,¹³⁴ (2) ocular symptoms are associated with the severity of nasal symptoms,¹³⁵ (3) ocular symptoms are important to consider in severe asthma,¹³⁵ and (4) the severity of allergic diseases increases with the number of allergic multimorbidities.¹³⁶ This is the first time that novel allergic phenotypes have been discovered using an mHealth app and then confirmed by classical epidemiologic studies.

REAL-WORLD EVIDENCE USING mHealth IN NEXT-GENERATION CARE PATHWAYS

mHealth apps for a better AR management are growing in number. However, their usefulness for doctors and patients is still being debated. Most studies have also highlighted certain shortcomings and limitations, mainly concerning security and cost-effectiveness.¹³⁷

Adherence to treatment

mHealth may help to better understand adherence to treatment and its determinants as well as how to improve it. In medicine, many mHealth apps are available to support people in taking their medications and thus to improve medication adherence.^{138,139} However, a meta-analysis found that most did not have many of the desirable features and/or were of low quality.¹³⁸ A systematic review including 16 randomized controlled trials (RCTs) found that mobile phone text messaging approximately doubles the odds of medication adherence, resulting in a net increase in adherence of 17.8%.¹³⁹ A Cochrane systemic review of 7 trials in cardiovascular disease found that although the results are promising, there is insufficient evidence

to draw conclusions on the effectiveness of text message-based interventions for adherence to medications. The authors suggested that sufficiently powered, high-quality randomized trials are needed, particularly in low- and middle-income countries.¹⁴⁰

Adherence in RCTs is high but does not reflect the real-life situation,^{31,32} and alternative measurements of adherence in a real-life setting are needed. The best studies would be using electronic devices that count and record the drugs taken. However, these devices are still exploratory and expensive and, as such, they are not currently a viable solution for large studies in patients with AR¹⁴¹ or individual patients. A potential palliative solution can be to use the smartphone's camera to register the drug uptake. The photo of the drug is then processed by image recognition algorithms to provide verified data on adherence to AR treatment during the patient's daily life. However, there are technical challenges and limitations to some types of vials and packaging. The automatic detection of progression of use of the liquid in the vial using computer vision may be of special relevance for sublingual allergen immunotherapy for which adherence can be a major issue.¹⁴² Other approaches already being tested for asthma but not for AR are mobile direct observation of therapy¹⁴³ and multicomponent interventions based on mobile technologies.¹⁴⁴ Although there are already some mHealth apps for AR, there are few studies evaluating their benefits and impact.¹³⁷ One study suggested that a short message service helps to improve AR treatment.¹⁴⁵ Internet-based telemonitoring using the AllergyMonitor improved adherence to intranasal corticosteroid treatment and disease knowledge among children and adolescents with seasonal AR as well as adherence to sublingual immunotherapy.⁸³ In MASK-air, a major lack of adherence to treatment was observed for all medications.¹¹³ Automedication was very common,¹⁵ suggesting that patients, like allergists when they are allergic,¹⁴⁶ do not follow physicians' prescriptions or guidelines.

mHealth in observational studies allowing novel assessment of patients' behavior

The treatment of AR is complex because many drugs are available in oral and/or topical formulations, and allergen immunotherapy and avoidance increase the complexity of the management. Many AR guidelines are evidence-based and have led to a better understanding and management of AR.¹⁴⁷⁻¹⁴⁹ However, guidelines are mostly based on RCTs, typically undertaken on highly selected populations, and often with limited/unclear generalizability to routine care contexts. Large observational implementation studies are needed to triangulate RCTs because they reflect "real-world" everyday use and practice more closely than do RCTs in terms of the heterogeneous patient populations included and the various medical interventions assessed. In RCTs, each subject is randomly assigned to a treatment or control group, whereas observational studies examine the possible effect of a treatment on subjects where the investigator has no control over the experiment and cannot randomize subject allocation.¹⁵⁰ However, observational studies provide clinically relevant information in addition to RCTs. Real-world evidence using RCTs and real-world data is becoming increasingly important in supporting regulatory decisions using mobile technology.¹⁵¹ A pilot study in more than 2900 users allowed differentiation between treatments,¹⁵ showing that the assessment of series of consecutive days was useful in understanding treatment patterns. The study showed that patients did

not necessarily use treatment on a daily basis and in a regular way; rather, they appeared to increase treatment use when their symptom control worsened. Differences in efficacy between medications were observed. This pilot study was confirmed in almost 9000 users.¹⁴ The studies confirm the usefulness of mHealth in accessing and assessing everyday use and practice in AR.¹⁵ It is hoped that mHealth apps will increase patient empowerment and improve adherence.

Next-generation guidelines

The selection of pharmacotherapy for patients with AR aims to control the disease and depends on many factors. Grading of Recommendations Assessment, Development and Evaluation guidelines have considerably improved AR management. However, there is an increasing trend to use real-world data to inform clinical practice, especially because RCTs are often limited with regard to the applicability of results. The Contre les Maladies Chroniques pour un Vieillessement Actif (MACVIA) algorithm proposed an AR treatment by a consensus group.¹²² This simple algorithm can be used to step up or step down AR treatment. Next-generation guidelines for the pharmacologic treatment of AR¹⁵² were developed using existing Grading of Recommendations Assessment, Development and Evaluation–based guidelines,¹⁴⁷⁻¹⁴⁹ real-world data provided by mHealth apps,^{14,15,113} and additive studies (allergen chamber studies¹⁵³) to refine the MACVIA algorithm.¹²²

mHealth TOOLS ENABLING THE DIGITAL TRANSFORMATION OF HEALTH AND CARE, EMPOWERING CITIZENS, AND BUILDING A HEALTHIER SOCIETY

The recent report on the state of health in the EU¹⁵⁴ concluded that rethinking our health and care systems can ensure its sustainability, aiming to continue health promotion, prevent diseases, and provide patient-centered care that meets citizens' needs.¹⁵⁵

Digital solutions for health and care can increase the well-being of millions of citizens and radically change health and care services. In its midterm review on the implementation of the digital single market strategy,¹⁵⁶ the EU Commission took further action in 3 areas:

- Citizens' secure access to and sharing of health data across borders.
- Better data to advance research, disease prevention, and personalized health and care.
- Digital tools for citizen empowerment and person-centered care to allow citizens to assume responsibility for their health, improve their well-being and quality of care, and contribute to sustainable health systems. By using digital solutions, such as wearables and mHealth apps, citizens can actively engage in the health promotion and self-management of chronic diseases. Digital tools can potentially disseminate scientific knowledge in an easily accessible form, so as to help people stay in good health, thus preventing them from turning into patients. Building on scientific information on risk factors, digital solutions can be used across all sectors, including education, transport, and urban policies, to promote information and awareness campaigns on healthy lifestyles. Digital tools also enable citizens to provide feedback and data about

their health to their doctors. This can improve the quality of health services and ultimately people's health and well-being.

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.¹⁵⁷ Future apps in AR could consider providing information to promote behavioral changes that could reduce the planetary impacts of human activity.

In the context of implementing communication on the digital transformation of health and care, the Directorate General for Health and Food Safety, in collaboration with the newly established EU Commission Expert Group "Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases",¹⁵⁸ supported the scaling-up and wider implementation of good practices in the field of digitally enabled, integrated, person-centered care. MASK was one of the 9 Good Practices selected along with chronic disease and Parkinson's disease.¹⁰⁴

GLOBAL IMPLEMENTATION

When mobile technology was initiated, it was thought that it would be used mainly in developed countries. However, smartphone ownership is growing rapidly around the world. According to the International Telecommunication Union, Geneva, in 2015, there were more than 7 billion mobile telephone subscriptions across the world, more than 70% of which were in low- or middle-income countries.¹⁵⁹ However, in these countries, smartphone use is still much more among the young and educated.¹

The World Health Organization recognizes the significant role that digital technologies can play in strengthening the health systems in countries to achieve universal health coverage, the health-related Sustainable Development Goals, and other health objectives. In 2018, 121 countries had national eHealth strategies, representing the beginning of a shift from an unsustainable project-based approach toward a systematic, integrated approach designed for cost-effective investment and alignment of partners.¹⁶⁰ The joint World Health Organization-International Telecommunication Union initiative "Be He@lthy, Be Mobile" for the prevention and management of noncommunicable diseases, their comorbidities, and their risk factors, including improving disease diagnosis and tracking, is of great importance. MASK is one of the examples of the "Be He@lthy, Be Mobile" handbook on how to implement mBreatheFreely for asthma and chronic obstructive pulmonary disease.¹⁶¹

CONCLUSIONS

mHealth has the potential to profoundly impact health care.⁴ mHealth apps now represent an important evolution of health and care for AR since real-world evidence has identified patients' behaviors and practices and this will have a profound impact on current guidelines and care pathways. Rhinitis is not a severe disease but it does have a major impact on social life, school, and work productivity.¹⁶² Asthma-rhinitis multimorbidity plays a key role in understanding asthma and can be used as a model of multimorbidity. Moreover, asthma and rhinitis have a life course approach, whereas most chronic diseases start early in life but are clinically evident only in adulthood. The revolution is underway for AR and asthma, and the lessons learned are transposable to

other chronic diseases and will design innovative health strategies and services as well as change management.¹⁶³

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