# Contribution of MASK-air® as an mHealth Tool for Digitally Enabled Person-Centered Care in Rhinitis and Asthma

Sousa-Pinto B[1,2], Fonseca JA[1,2], Bousquet J[3-5]

[1]MEDCIDS – Department of Community Medicine, Information and Health Decision Sciences, Faculty of Medicine, University of Porto, Porto, Portugal
[2]CINTESIS@RISE - Health Research Network, MEDCIDS, Faculty of Medicine, University of Porto, Porto, Portugal
[3]Institute of Allergology, Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany
[4]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Germany
[5]MASK-air, Montpellier, France

J Investig Allergol Clin Immunol 2024; Vol. 34(3): 148-156
doi: 10.18176/jiaci.0994

## Abstract

In chronic diseases, mHealth apps help to improve clinical management and provide valuable real-world scientific evidence. In allergic rhinitis, a market research study identified only 4 mHealth apps that were multilingual, resulted in scientific publications, and displayed a comprehensive list of medications. Of these 4 apps, MASK-air® generated the highest number of scientific publications. MASK-air was launched in 2015 and is currently available in 30 countries, with data collected from more than 30 000 users. It comprises a daily monitoring questionnaire, enabling patients to register their daily allergy symptoms by means of visual analog scales and their medication use. The achievements of MASK-air include the development of 2 digital biomarkers for daily monitoring of rhinitis and asthma (combined symptom-medication score and electronic daily asthma control score). MASK-air data have also made it possible to assess patients' behavior, suggesting that patients do not follow guideline recommendations, but rather treat themselves (and often use comedication) when they feel worse. Using MASK-air data, we quantified the impact of allergic diseases on quality of life and school and work productivity. Real-world MASK-air data are being used as a source of evidence for the Allergic Rhinitis and its Impact on Asthma 2024 guidelines in an innovative process of incorporation of mobile health data into guidelines. This review discusses the clinical and scientific contributions of MASK-air to person-centred care of rhinitis and asthma, providing an illustrative example on the use of mHealth data in chronic diseases.

**Key words:** Allergic rhinitis. Asthma. mHealth. Patient-reported outcome measures.

## Resumen

En el caso de las enfermedades crónicas, las aplicaciones de salud asistida por el móvil pueden ayudar a mejorar la gestión clínica y proporcionar valiosas pruebas científicas en la vida real. En el caso de la rinitis alérgica, un estudio de mercado solo ha identificado cuatro aplicaciones de salud móvil multilingües, con publicaciones científicas y una lista completa de medicamentos. De ellas, MASK-air® era la aplicación con mayor número de publicaciones científicas. MASK-air se lanzó en 2015 y actualmente está disponible en 30 países, habiendo recogido datos de más de 30.000 usuarios. Consta de un cuestionario de seguimiento diario, que permite a los pacientes registrar sus síntomas diarios de alergia mediante escalas analógicas visuales y el uso de medicación. Los logros de MASK-air incluyen el desarrollo de dos biomarcadores digitales para el seguimiento diario de la rinitis y el asma (puntuación combinada de síntomas y medicación y puntuación electrónica diaria del control del asma). Además, los datos de MASK-air han permitido evaluar los comportamientos de los pacientes, demostrando que los pacientes no siguen las recomendaciones de las guías, sino que se tratan ellos mismos (y a menudo recurren a la medicación conjunta) cada vez que se sienten peor. Con los datos de MASK-air también se ha podido cuantificar el impacto de las enfermedades alérgicas en la calidad de vida y la productividad escolar y laboral. Los datos del mundo real de MASK-air se están utilizando como fuente de pruebas para las guías de rinitis alérgica y su impacto en el asma 2024, en un proceso innovador de incorporación de datos de salud móvil en estas. Esta revisión analiza las contribuciones clínicas y científicas de MASK-air para la atención centrada en el paciente de la rinitis y el asma, proporcionando un ejemplo ilustrativo sobre el uso de la salud móvil en las enfermedades crónicas.

**Palabras clave:** Rinitis alérgica. Asma. Salud móvil. Resultado de medidas notificadas por el paciente.

## Introduction

mHealth apps may help to address unmet needs in chronic diseases, including respiratory allergic diseases such as rhinitis and asthma [1]. In fact, they have the potential to facilitate high-quality care and the satisfaction of patients and health care professionals, with reduced use of health care resources and costs. However, these tools first need to be tested for privacy rules, validity, acceptability, usability, and cost-effectiveness. In addition, they should be evaluated in terms of the digital transformation of health, their impact on health care delivery, and health outcomes.

Randomized controlled trials (RCTs) provide evidence of the highest level for the assessment of the efficacy and safety of interventions. However, RCTs are subject to important limitations. Firstly, on account of the strict eligibility criteria that are frequently adopted, enrolled patients are not usually representative of those seen in daily clinical practice (a study performed in general practice has reported that only 7% of patients would be eligible to participate in RCTs) [2,3], thus limiting the capacity of RCTs to assess the behavior of real-world patients. In addition, given that RCTs consume considerable resources, they typically have a limited geographical and temporal scope. Consequently, there is an increasing need for evidence from RCTs to be complemented from that based on real-world data [3,4]. Among the various real-world sources, mHealth stands out for its potential to generate large volumes of data, advance knowledge, and improve clinical practice [4,5]. This is particularly so considering the ubiquitous ownership of smartphones and the possibility for patients to provide data directly using apps [5].

In the case of rhinitis and asthma, mHealth has already resulted in relevant scientific findings that can be translated into more patient-centred clinical practice. These findings were mostly based on the MASK-air® mHealth app. In fact, having collected data from more than 30 000 users, MASK-air has resulted in more than 25 original scientific publications on rhinitis and/or asthma [6]. The underlying scientific evidence may then support the development of clinical recommendations, as is already occurring with the Allergic Rhinitis and its Impact on Asthma (ARIA) 2024 guidelines. Consequently, MASK-air constitutes a particularly interesting case study in the translation of digitally enabled direct patient data into clinical practice (Figure 1).

In this review, we discuss the scientific and clinical contribution of the MASK-air app in rhinitis and asthma. We present available mHealth tools for rhinitis and asthma and describe the characteristics of the MASK-air app. We then discuss the contributions of MASK-air to patient monitoring, assessment of patients' behavior, characterization of allergy phenotypes, quantification of the impact of rhinitis and asthma, and assessment of the impact of rhinitis and asthma interventions. Finally, we discuss how data from the MASK-air app are being incorporated into the ARIA 2024 guidelines and provide indications on future steps.

## mHealth Tools in Rhinitis and Asthma

Searching for allergic rhinitis or asthma in app stores returns a large number of results. However, not all mHealth apps addressing rhinitis and asthma are adequate for patient monitoring or are supported by published scientific evidence. In this context, market research into mobile health apps for allergic rhinitis was conducted in the Google Play and Apple app stores using both a manual and an automatic process [7]. While more than 1500 apps were identified based on rhinitis-related terms, only 21 were found to be potentially relevant for allergic rhinitis. Only 4 were multilingual, resulted in scientific publications, and displayed a list of all medications (AllergyMonitor, Galenus, MASK-air, and Pollen [Austria]). Of these apps, MASK-air was the most widely available and the one backed by the highest number of scientific publications (including publications of methodological validation and of

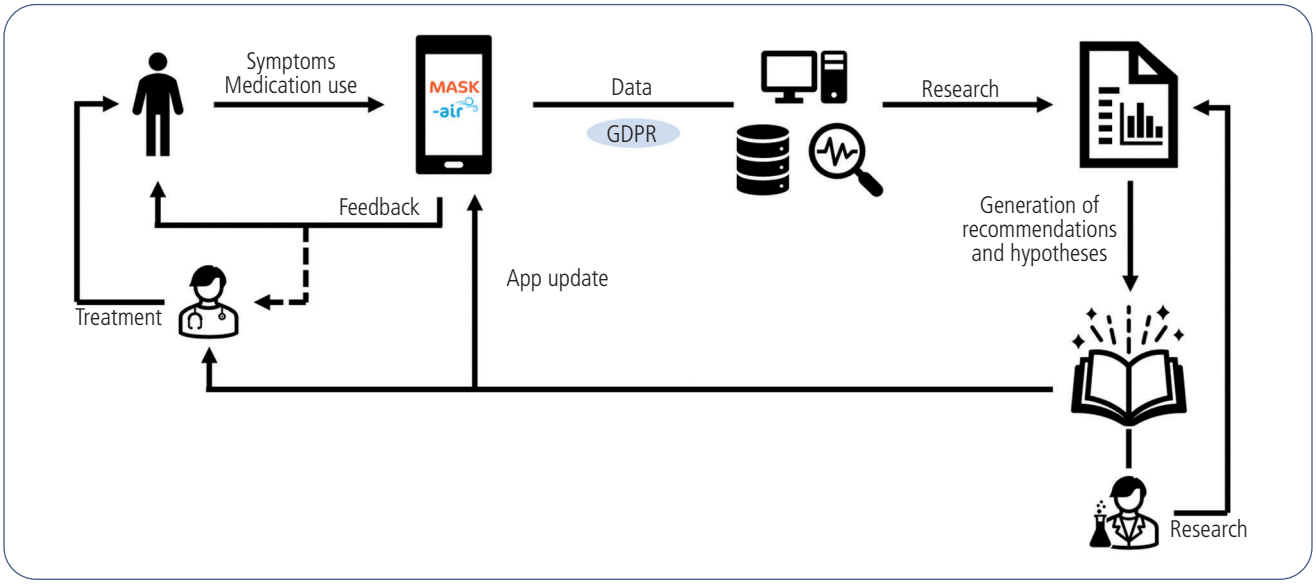


**Figure 1.** How MASK-air® can contribute to research and clinical practice. GDPR indicates General Data Protection Regulation.

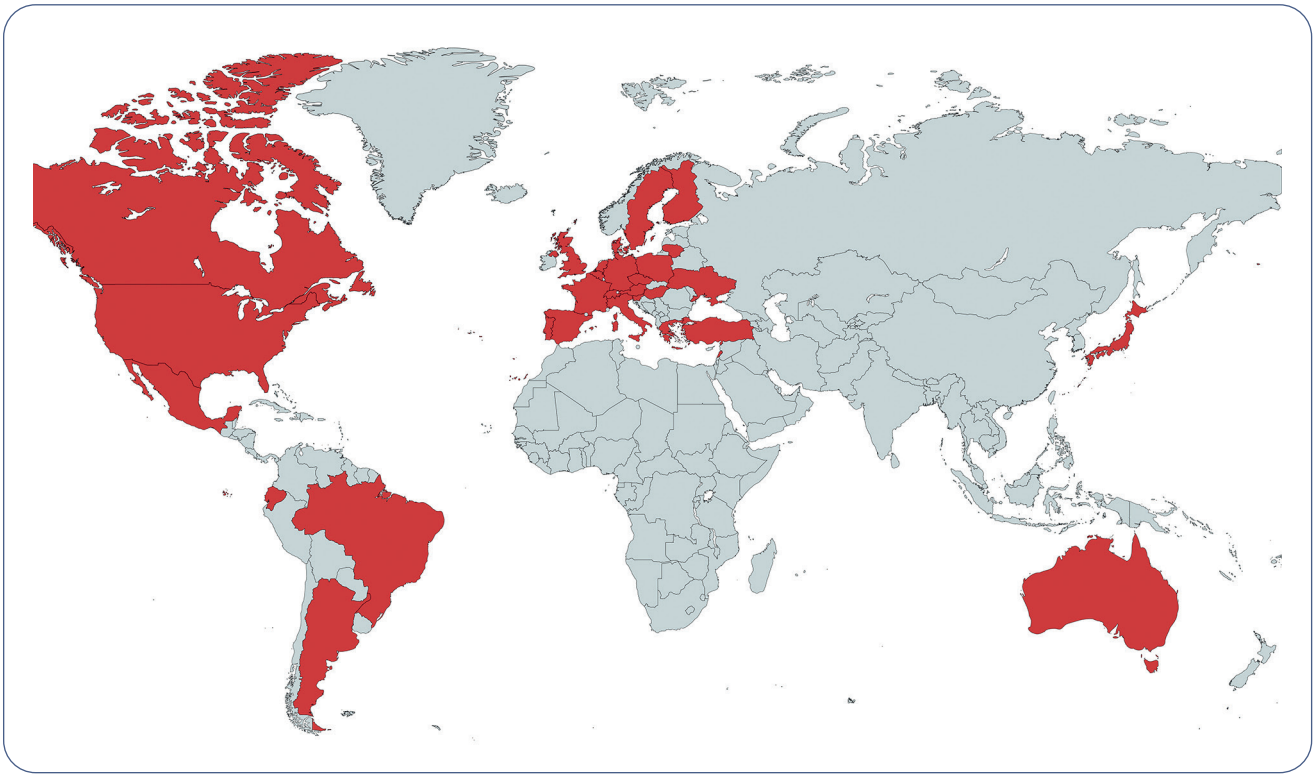

**Figure 2.** Map indicating the countries in which MASK-air® is available as of January 2024.

new scientific findings). A similar market research study is being conducted for asthma apps. However, it is expected that, as with rhinitis, only a minority of available results involve apps that are adequate for daily monitoring of patients.

## The MASK-air App

The MASK-air app was developed by the ARIA group [8]. This mHealth app was launched in 2015 and is currently available in 30 countries (Figure 2) [6]. It is freely available in the GooglePlay and Apple app stores and fully complies with the General Data Protection Regulation [9].

MASK-air has been classified as a Good Practice of the Directorate General for Health and Food Safety (European Commission) for digitally enabled, patient-centered care for multimorbidity in rhinitis and asthma [10]. In addition, it is one of the 13 Organisation of Economic Cooperation and Development (OECD) Best Practices in integrated care for chronic diseases [11]. In its assessment of MASK-air, the OECD described it as "an equity enhancing digital health intervention which has improved the knowledge base on AR and asthma" [12].

The MASK-air app includes a daily monitoring questionnaire that enables patients to report their daily symptoms and medication use. Daily symptoms are reported through visual analog scales (VASs), which range between 0 and 100 (Table 1). Some VASs assess the impact of allergy symptoms on work and school productivity (they are only meant to be answered if the user reports working or attending classes on that day). The VASs for the daily monitoring questionnaire have been assessed in terms of their validity, reliability, responsiveness, and minimal important difference [13,14]; in addition, cut-offs have been defined [15].

**Table 1.** List of the Visual Analog Scales (VAS) Available in the Daily Monitoring Questionnaire of MASK-air®.

| Scale | Question |
|---|---|
| VAS Global allergy symptoms | "Overall, how much are your allergic symptoms bothering you today?" |
| VAS Nose | "How much are your nose symptoms bothering you today?" |
| VAS Eyes | "How much are your eye symptoms bothering you today?" |
| VAS Asthma | "How much are your asthma symptoms bothering you today?" |
| VAS Work | "Today, how much did allergies affect your work activities?" |
| VAS School | "Today, how much did allergies affect your productivity while in school or attending classes in an academic setting?" |

MASK-air users can report their daily medication use through a scroll list that includes all prescribed and over-the-counter medications available in the respective country. When patients report medication use, they are asked to rate their satisfaction with treatment. Daily immunotherapy can also be reported [16]. Should patients allow it, the results of

the daily monitoring questionnaire can be shared immediately with clinicians in clinical practice by scanning a QR code (enabling data to be easily pasted into the patients' electronic health records).

In addition to the daily monitoring questionnaire, MASK-air includes nonmandatory validated questionnaires, such as the Control of Allergic Rhinitis and Asthma Test (CARAT), the EQ-5D-5L, and the Work Productivity and Activity Questionnaire plus Classroom Impairment Questions: Allergy Specific (WPAI+CIQ:AS). The CARAT questionnaire assesses both allergic rhinitis and asthma control over the previous 4 weeks; its measurement properties have been systematically reviewed, and it is characterized by good consistency, reliability, construct validity, and responsiveness [17-18]. The EQ-5D-5L is a generic instrument for assessment of health-related quality-of-life [19]. It includes 5 items assessing the domains of mobility, self-care, activities, pain/discomfort, and anxiety/depression and a VAS for assessment of overall health status. The WPAI+CIQ:AS questionnaire makes it possible to quantify losses in work and academic performance due to allergies (both in terms of absenteeism and presenteeism), as well as the impact of allergies on daily activities [20-22].

## Contributions of MASK-air in Rhinitis and Asthma

### *Patient Monitoring: Patient-Reported Outcome Measures*

Patient-reported outcome measures (PROMs) are increasingly used. Validated PROMs are essential for patient monitoring. They can improve shared decision making, clinician awareness of symptoms, symptom management, patient satisfaction, and quality of life. PROMs must be carefully defined to capture important information from patients. Validated PROMs in MASK-air comprise the VASs included in the daily monitoring questionnaire [23]. In addition, MASK-air has enabled the development of 2 electronic scores that combine information on daily symptoms and medication use to monitor daily control of allergic rhinitis and asthma. These daily monitoring scores (also termed digital biomarkers) are the combined symptom-medication score (CSMS) and the electronic daily asthma control score (e-DASTHMA), which, respectively, concern allergic rhinitis and asthma [24,25].

Both the CSMS and the e-DASTHMA have been developed and validated using data-driven approaches applied to MASK-air data [24,25]. The specific data-driven approaches tested resulted in several candidate scores, among which the CSMS and e-DASTHMA displayed the best concurrent validity, test-retest reliability, responsiveness, and accuracy. The e-DASTHMA was further externally validated in a cohort of patients whose diagnosis and control of asthma were ascertained by a physician [25].

The values of the CSMS and the e-DASTHMA range between 0 and 100, with 0 indicating perfect control and 100 indicating the worst possible control. Table 2 summarizes the formulae, cut-off values, and minimal important difference for these 2 scores.

### *Patient Monitoring: Digital Biomarkers in Rhinitis and Asthma*

Noninvasive, easily applied biomarkers are particularly relevant for the diagnosis, treatment, and follow-up of asthma and rhinitis. While biologic biomarkers are widely applied in specialist care for asthma (eg, sputum eosinophils and FeNO), they are rarely used in primary care. Considering the potential of mHealth for patient monitoring, ARIA and the European Academy of Allergy and Clinical Immunology (EAACI) created a task force to propose user-friendly digital biomarkers with several objectives in rhinitis and asthma that can serve as a bridge between clinical practice, RCTs, and allergen challenges [26]. Such a task force has resulted in the development and validation—based on the MASK-air app—of the CSMS and the e-DASTHMA.

The development of CSMS and e-DASTHMA has facilitated a new approach for monitoring the control of rhinitis and asthma [26]. This new approach involves the combined assessment of allergic diseases in terms of both long-term control (using tools such as the CARAT, which has a recall period of 4 weeks) and daily control (using the CSMS and/or the e-DASTHMA). Daily control scores are particularly relevant, as they enable short-term fluctuations to be captured, thus improving disease monitoring and enabling shared management. This approach is analogous to that used in diabetes, where monitoring encompasses the combined assessment of a long-term biomarker and of a daily biomarker (respectively, glycated hemoglobin and glycemia).

**Table 2.** Formulae, Cut-offs, and MIDs for the CSMS and the e-DASTHMA.

| Score | Formula | Cut-off | MIDs |
|---|---|---|---|
| CSMS | [(0.037 × VAS Global Symptoms) + (0.033 × VAS Eyes) + (0.020 × VAS Nose) + (0.027 × VAS Asthma) + (0.450 if AzeFlu is used) + (0.424 if intranasal corticosteroids are used) + (0.243 if asthma medication is used) + (0.380 if other rhinitis relief medication is used)] × 7.577) | – Good control: <15.8<br>– Partial control: 15.8-35.3<br>– Poor control: >35.3 | 10 |
| e-DASTHMA | [(0.086 × VAS asthma) + (1.756 if ICS are used) + (0.859 if ICS-LABA except formoterol are used) + (1.238 if ICS-Formoterol are used) + (0.559 if SABA or SAMA are used) + (4.022 if biologicals or LAMA are used)] × 6.695 | – Good control: <16.4<br>– Partial control: 16.4-28.9<br>– Poor control: >28.9 | 8 |

Abbreviations: CSMS, combined symptom-medication score; e-DASTHMA, electronic daily asthma combined score; ICS, inhaled corticosteroids; LABA, long-acting ß2-agonists; LAMA, long-acting muscarinic antagonists; MID, minimally important difference; SABA, short-acting ß2-agonists; SAMA, short-acting muscarinic antagonists; VAS, visual analog scale.

Studies assessing the use of MASK-air to longitudinally monitor patients with asthma are ongoing. The concurrent daily assessment of symptoms and medication use may have implications for shared decision-making, enabling physicians and patients to determine whether adherence should be improved, further medication should be added, or biologics should be started or stopped.

### *Assessment of Patient Behavior and Adherence*

Being a source of direct patient data and having enabled the collection of over 500 000 days (reported by over 30 000 users), MASK-air can provide relevant information on patients' behavior in regard to their disease and treatments. In fact, after assessing MASK-air data on rhinitis medication patterns, we observed the following: oral antihistamines are the most commonly used medications in monotherapy; comedication is common, with almost three-quarters of the MASK-air users reporting at least 1 day of comedication [14]; and the use of various medications of the same or of different groups by the same patient throughout the year is common (observed in more than three-quarters of MASK-air patients) [27]. These findings were complemented by subsequent cross-sectional and longitudinal studies, which found that comedication tended to be more frequently reported on days when disease was more poorly controlled (by contrast, using no medication was more common on days when symptoms were well controlled) [14,28]. Overall, these results suggest that most patients do not follow guideline recommendations. In fact, instead of using rhinitis medication on a daily basis, patients tend to treat themselves when feeling worse (Figure 3) (curiously, this pattern has also been observed among allergists with allergic rhinitis [29]). These findings are particularly relevant for guideline development: person-centred guidelines may discuss whether to recommend, particularly for patients with mild rhinitis, medication on a pro re nata basis rather than on a long-term basis [30].

Complementing these assessments of patient behavior, some studies have specifically evaluated adherence to rhinitis and asthma medication. In fact, when assessing rhinitis medication, we observed that adherence was generally high, suggesting that patients who are more adherent to the app may also be more adherent to medication (future studies will assess whether adherence to MASK-air promotes adherence)

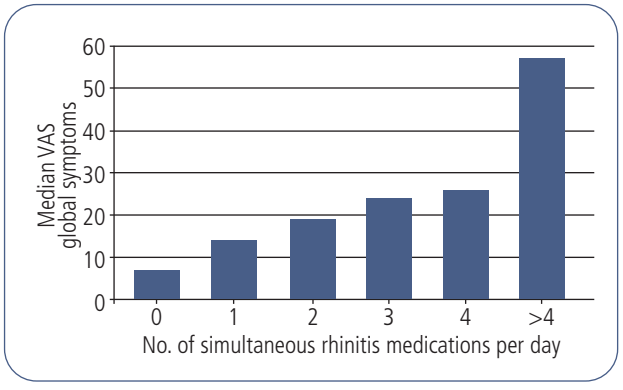


**Figure 3.** Median visual analog scale (VAS) for global allergy symptoms according to the number of medications used per day.

(Sousa-Pinto et al. Under review). The same study did not find relevant differences in adherence when comparing medication classes. On the other hand, regarding asthma medication, lower adherence was observed for inhaled corticosteroids (ICSs) + formoterol than for ICSs + other long-acting β-agonists (LABAs), despite both groups being associated with similar levels of asthma control [31]. The study reported that increased adherence to ICS-LABAs was associated with lower use of short-acting β-agonists. These studies are subject to an important limitation, namely, they were performed based on data from users who are adherent to the MASK-air app (and who are not representative of all patients).

### *Classification of Allergy Patients and Assessment of Phenotypes*

Two studies have applied clustering methods to MASK-air data in order to obtain a nonsupervised classification of allergy patients and trajectories [28,32]. One was performed in order to improve the identification of patients with asthma, as well as to assess the extent of potential underreporting and undertreatment of asthma [32]. In brief, based on whether they self-reported asthma, asthma symptoms, and use of asthma medications, MASK-air users were classified into 7 clusters and 3 major groups (no evidence of asthma, possible asthma, and probable asthma). As an example, 1 cluster consisted of patients with no self-reported asthma but with poor symptom control (suggesting underdiagnosis). Another cluster included patients with uncontrolled symptoms despite treatment. This study, therefore, presents an example of how MASK-air data can be used to identify patients who would benefit from further clinical assessment for diagnostic or therapeutic reasons (including potentially underdiagnosed or undertreated patients).

The other study used clustering methods to classify weekly trajectories for control of rhinitis symptoms over 16 177 weeks [28]. A total of 16 clusters were identified, corresponding to weeks with different levels of rhinitis control. The assessment of cluster trajectories indicated that patients who experience a week with good rhinitis control would be expected to experience another week with good rhinitis control. By contrast, for a patient who experiences a week with poor or variable control of rhinitis, more unstable trajectories are expected.

A growing body of evidence suggests that rhinitis alone and rhinitis + asthma may be 2 different entities [33,34]. Indeed, both conditions seem to display different genomic and sensitization patterns (polysensitization is more common in rhinitis + asthma than in rhinitis alone) [33,34]. In addition, an epidemiological study of the general population has reported that patients with rhinitis + asthma tend to display more severe rhinitis symptoms than patients with rhinitis alone [35]. This finding has also been observed using MASK-air data [36]. In fact, among MASK-air users, patients with rhinitis + asthma displayed higher CSMS values and higher VAS levels for nasal and ocular symptoms. MASK-air data have also shown that rhinitis + asthma was associated with more frequent use of rhinitis medications than rhinitis alone. This provides an elegant example of how mHealth data from MASK-air can complement other sources of evidence.

### *Assessment of the Impact of Rhinitis and Asthma*

MASK-air includes the EQ-5D-5L and the WPAI+CIQ:AS questionnaires, which assess the effect of allergy on, respectively, health-related quality of life and work and academic performance. Analysis of data from these questionnaires, alongside that of the daily monitoring questionnaire, has enabled quantification of the impact of allergic rhinitis and asthma on quality of life and on work and school productivity.

Regarding the impact of allergy on quality of life, a cross-sectional study using MASK-air data assessed the association between allergy control (assessed using VASs or the CSMS) and the levels of each EQ-5D-5L domain [37]. Using multivariable models, the authors found that poorer control of allergic rhinitis and asthma was associated with worse health-related quality of life, particularly with more severe pain/discomfort and more impairment in the performance of daily activities. In addition, poor control of rhinitis tended to be associated with worse levels of anxiety/depression, while poor control of asthma tended to be associated with greater impairment of mobility (walking around). The MASK-air EQ-5D-5L data also enabled the estimation of the utility associated with good, partial, and poor control of rhinitis and asthma in several European countries [38]. The use of multilevel regression models with poststratification has enabled computation of national estimates that account for biases in the sex and age distributions of MASK-air users.

MASK-air data have been used to compute the impact of allergic rhinitis on academic performance (measured through a VAS and using the WPAI+CIQ:AS questionnaire) [39]. In this cross-sectional study, poorer control of allergic rhinitis (especially of nasal symptoms) was associated with worse academic performance. On the other hand, immunotherapy was associated with improved academic performance. Of those users who completed the WPAI+CIQ:AS questionnaire, 35% had indicated the loss of at least some school hours due to allergies.

Studies based on MASK-air data are being performed to quantify productivity losses associated with allergic rhinitis and asthma. Productivity losses in terms of absenteeism and presenteeism are being assessed using the WPAI+CIQ:AS questionnaire. Preliminary results indicate that the impact of rhinitis and asthma on work productivity is driven mainly by presenteeism, poorer allergy control is associated with worse work productivity, and, for the same level of control, the percentage of hours with work impairment is worse for patients with rhinitis + asthma than for patients with rhinitis alone (Vieira et al. In preparation). MASK-air can also be used to assess the impact of allergic diseases on daily activities (shown to be correlated with work impairment [40]).

### *Assessment of the Impact of Allergy Interventions: The Example of Allergen Immunotherapy*

Given that MASK-air data are not collected on an experimental basis, they do not provide direct information on the effectiveness of interventions. However, they can provide some information on the levels of allergy control associated with different treatments. For instance, allergen immunotherapy has been addressed in 3 studies using MASK-air data [16,41,42]. Two of these studies have found that (*i*) users treated with immunotherapy were found to display better overall symptom control and lower impact of symptoms on work productivity and (*ii*) patients treated with sublingual immunotherapy displayed better control of rhinitis (measured using VASs and the CSMS) than those treated with subcutaneous immunotherapy or than those not receiving immunotherapy [16,41]. The third study—based on cross-sectional and longitudinal methods—assessed MASK-air users under treatment with sublingual immunotherapy [42]. Days in which sublingual immunotherapy was administered were found to be associated with better control of rhinitis than those in which such treatment was not used. These findings raise the hypothesis of a potential short-term effect of sublingual immunotherapy, which may be explored in future studies.

## Incorporation of Direct Patient Data From MASK-Air in the ARIA 2024 Guidelines

The ARIA guidelines were first published in 2001 [43] and subsequently revised in 2008 [44], 2010 [45], and 2016 [46]. The 2024 edition of the ARIA guidelines is currently being prepared and, as with previous editions, it will follow the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [47]. However, in contrast with previous editions, the ARIA 2024 guidelines will highlight the importance of contributions from MASK-air data, as follows:

- Question generation: Evidence obtained from MASK-air data has allowed for several hypotheses to be raised. Such hypotheses, as well as MASK-air–based findings, will enable the formulation of several guideline questions that may result in recommendations for clinical practice.
- Outcome identification: In the context of guideline development, a list of potentially relevant outcomes has been identified (such outcomes then undergo prioritization, so that those considered more relevant by the guideline panel members are assessed [48]). MASK-air studies will allow for the identification of some of these outcomes for allergic rhinitis.
- Formulation of recommendations: In the GRADE approach, incorporation of the best available evidence for the formulation of recommendations involves the use of the evidence-to-decision framework. This framework comprises 12 criteria, including desirable effects, undesirable effects, values and preferences, costs, equity, acceptability, and feasibility [49]. MASK-air data can provide evidence for several of these criteria (including values and preferences, costs, and acceptability), complementing more traditional sources of evidence.

## Next Steps

The analysis of MASK-air data has yielded relevant scientific findings and generated new hypotheses to be explored by studies with different designs. The potential impact is

summarized in Supplementary Table 1. However, several fields have yet to be explored using MASK-air. In particular, its role in improving the management of patients with rhinitis and asthma in everyday clinical practice needs to be consolidated. In this context, a series of steps are envisioned, as follows:

- Performance of clinical studies assessing the impact of MASK-air on the monitoring of individual patients with rhinitis and asthma: While some studies in allergy clinics have already been conducted [50-52], several questions remain to be addressed, such as whether the use of MASK-air promotes adherence to rhinitis or asthma medication, better disease self-care, and reduced need for health care visits. Assessing the impact of using MASK-air to monitor patients with severe asthma may be particularly relevant both from a clinical and from a health services point of view (so that future studies are planned with this goal in mind). In fact, such an assessment may enable better identification of patients who would benefit from treatment with biologics and a better definition of stopping rules.
- Development of early warning systems for rhinitis and impact on planetary health: For users with activated geolocation, MASK-air provides information on pollen and air quality data. This information is made available from the Finnish Meteorological Institute through the System for Integrated modeLling of AtMospheric composition. Based on pollen and air quality predictions, as well as on previous symptoms reported by MASK-air users, personalized early warning systems are being developed for MASK-air [53]. Such systems are projected to generate personalized alerts to patients whenever their allergy symptoms are expected to worsen [53]. Of note, these early warning systems are being developed in the context of the Horizon Europe grant Climate Action to Advance HeaLthY Societies in Europe [53] and follow the participation of MASK-air in events on planetary health during the Finnish presidency of the European Union [54,55], in line with the Declaration of Helsinki [54,55].
- Assessment of the role of MASK-air as a tool to improve care by overcoming language barriers: Following the war in Ukraine, the UCRAID project has been developed to support provision of allergy care to Ukrainian refugees [56]. This project involved the launch of MASK-air in Ukrainian, enabling refugees to fill in the daily monitoring questionnaire in Ukrainian, but with physicians receiving the results in their native language. This model can be extended to improve care to other migrants (including refugees from other wars) and to foreign travellers, as MASK-air is available in several languages.
- Use of MASK-air as a tool in allergy RCTs: MASK-air can be used in RCTs to enable participants to introduce their data directly. This app has allowed for the development of 2 validated digital biomarkers that can potentially be used as endpoints in RCTs [24,25]. In addition, pre-enrolment adherence to the MASK-air app may help to identify the most adequate candidates for RCTs (eg, by stratifying patients according to their allergy severity and identifying those who have the highest probability of completing the RCTs). While there have been single-arm trials using MASK-air (Bousquet et al. Under review), the feasibility of using this app in RCTs has yet to be established.

In addition to the aforementioned projects, it is expected that MASK-air data will continue to bring new findings on allergy patients' behavior, on the impact of rhinitis and asthma, and on the satisfaction associated with the different medication classes.

## Conclusion

MASK-air provides an elegant example of how mHealth can advance scientific knowledge and improve clinical knowledge in chronic diseases. Its data have enabled (*i*) the development of 2 digital biomarkers for daily monitoring of rhinitis and asthma, (*ii*) a better understanding of how patients behave in relation to their diseases, (*iii*) increased knowledge of allergy phenotypes, and (*iv*) quantification of the impact on rhinitis and asthma on quality of life and productivity. Evidence obtained using the MASK-air app will support the recommendations of the ARIA 2024 guidelines, thereby contributing to more patient-centered care in respiratory allergic disease.

### *Funding*

The authors declare that no funding was received for the present study.

### *Conflicts of Interest*

MASK-air® was supported by EU grants (POLLAR, EIT Health; Structural and Development Funds, Twinning, EIP on AHA, and H2020) and educational grants from Mylan-Viatris, ALK, GSK, Novartis, and Uriach. JB reports personal fees from Cipla, Menarini, Mylan, Novartis, Purina, Sanofi-Aventis, Teva, and Uriach and is a shareholder of KYomed Innov and MASK-air-SAS. The remaining authors declare that they have no conflicts of interest.

## References

1. Bousquet J, Chavannes NH, Guldemond N, Haahtela T, Hellings PW, Sheikh A. Realising the potential of mHealth to improve asthma and allergy care: how to shape the future. Eur Respir J. 2017;49(5):1700447. doi:10.1183/13993003.00447-2017
2. Costa DJ, Amouyal M, Lambert P, Ryan D, Schunemann HJ, Daures JP, et al. How representative are clinical study patients with allergic rhinitis in primary care? J Allergy Clin Immunol. 2011;127(4):920-6 e1. doi:10.1016/j.jaci.2010.10.058
3. Kim HS, Lee S, Kim JH. Real-world Evidence versus Randomized Controlled Trial: Clinical Research Based on Electronic Medical Records. J Korean Med Sci. 2018;33(34):e213. doi:10.3346/jkms.2018.33.e213
4. Liu F, Panagiotakos D. Real-world data: a brief review of the methods, applications, challenges and opportunities. BMC

Med Res Methodol. 2022;22(1):287. doi:10.1186/s12874-022-01768-6
5. Sim I. Mobile Devices and Health. N Engl J Med. 2019;381(10):956-68. doi:10.1056/NEJMra1806949
6. Bousquet J, Anto JM, Sousa-Pinto B, Czarlewski W, Bedbrook A, Haahtela T, et al. Digitally-enabled, patient-centred care in rhinitis and asthma multimorbidity: The ARIA-MASK-air((R)) approach. Clin Transl Allergy. 2023;13(1):e12215. doi:10.1002/clt2.12215
7. Anto A, Sousa-Pinto B, Czarlewski W, Pfaar O, Bosnic-Anticevich S, Klimek L, et al. Automatic market research of mobile health apps for the self-management of allergic rhinitis. Clin Exp Allergy. 2022;52(10):1195-207. doi:10.1111/cea.14135
8. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008;63 Suppl 86:8-160. doi:ALL1620 [pii] 10.1111/j.1398-9995.2007.01620.x
9. Laune D, Arnavielhe S, Viart F, Bedbrook A, Mercier J, Lun San Luk G, et al. [Adaptation of the General Data Protection Regulation (GDPR) to a smartphone app for rhinitis and asthma (MASK-air(R))]. Rev Mal Respir. 2019;36(9):1019-31. doi:10.1016/j.rmr.2019.08.003
10. Bousquet J, Bedbrook A, Czarlewski W, Onorato GL, Arnavielhe S, Laune D, et al. Guidance to 2018 good practice: ARIA digitally enabled, integrated, person-centred care for rhinitis and asthma. Clin Transl Allergy. 2019;9:16. doi:10.1186/s13601-019-0252-0
11. Integrating Care to Prevent and Manage Chronic Diseases: Best Practices in Public Health, OECD. Éditions OCDE, Paris, https://doiorg/101787/9acc1b1d-en. 2023;
12. OECD. Integrating Care to Prevent and Manage Chronic Diseases. 2023.
13. Sousa-Pinto B, Eklund P, Pfaar O, Klimek L, Zuberbier T, Czarlewski, W, et al. Validity, reliability, and responsiveness of daily monitoring visual analog scales in MASK-air(R). Clin Transl Allergy. 2021;11(7):e12062. doi:10.1002/clt2.12062
14. Sousa-Pinto B, Schunemann HJ, Sa-Sousa A, Vieira RJ, Amaral R, Anto JM, et al. Comparison of rhinitis treatments using MASK-air(R) data and considering the minimal important difference. Allergy. 2022;77(10):3002-14. doi:10.1111/all.15371
15. Sousa-Pinto B, Sa-Sousa A, Vieira RJ, Amaral R, Pereira AM, Anto JM, et al. Cutoff Values of MASK-air Patient-Reported Outcome Measures. J Allergy Clin Immunol Pract. 2023;11(4):1281-9 e5. doi:10.1016/j.jaip.2022.12.005
16. Pfaar O, Sousa-Pinto B, Devillier P, Canonica GW, Klimek L, Zuberbier T, et al. Effects of allergen immunotherapy in the MASK-air study: a proof-of-concept analysis. Allergy. 2021;76(10):3212-4. doi:10.1111/all.14955
17. Vieira RJ, Sousa-Pinto B, Cardoso-Fernandes A, Jacome C, Portela D, Amaral R, et al. Control of Allergic Rhinitis and Asthma Test: A systematic review of measurement properties and COSMIN analysis. Clin Transl Allergy. 2022;12(9):e12194. doi:10.1002/clt2.12194
18. Jacome C, Pereira R, Almeida R, Amaral R, Correia MA, Mendes S, et al. Validation of App and Phone Versions of the Control of Allergic Rhinitis and Asthma Test (CARAT). J Investig Allergol Clin Immunol. 2021;31(3):270-3. doi:10.18176/jiaci.0640
19. Devlin NJ, Brooks R. EQ-5D and the EuroQol Group: Past, Present and Future. Appl Health Econ Health Policy. 2017;15(2):127-37. doi:10.1007/s40258-017-0310-5
20. Reilly MC, Tanner A, Meltzer EO. Work, classroom and activity impairment instruments: validation studies in allergic rhinitis. Clinical Drug Invest. 1996;11:278-88.
21. Reilly MC, Tanner A, Meltzer EO. Allergy impairment questionnaires: validation studies. J Allergy Clin Immunol. 1996;97:989.
22. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993;4:353-65.
23. Sousa-Pinto B, Fonseca JA, Gemicioglu B, Regateiro FS, Scichilone N, Ventura MT, et al. Patient-reported outcome measures (PROMs) using the MASK-air(R) app in severe asthma. Allergy. 2022;77(5):1600-2. doi:10.1111/all.15248
24. Sousa-Pinto B, Azevedo LF, Jutel M, Agache I, Canonica GW, Czarlewski W, et al. Development and validation of combined symptom-medication scores for allergic rhinitis. Allergy. 2022;77(7):2147-62. doi:10.1111/all.15199
25. Sousa-Pinto B, Jacome C, Pereira AM, Regateiro FS, Almeida R, Czarlewski W, et al. Development and validation of an electronic daily control score for asthma (e-DASTHMA): a real-world direct patient data study. Lancet Digit Health. 2023;5(4):e227-e38. doi:10.1016/S2589-7500(23)00020-1
26. Bousquet J, Shamji MH, Anto JM, Schunemann HJ, Canonica GW, Jutel M, et al. Patient-centred digital biomarkers for allergic respiratory diseases and asthma: the ARIA-EAACI approach - ARIA-EAACI Task Force Report. Allergy. 2023;78(7):1758-76. doi:10.1111/all.15740
27. Sousa-Pinto B, Sa-Sousa A, Vieira RJ, Amaral R, Klimek L, Czarlewski W, et al. Behavioural patterns in allergic rhinitis medication in Europe: A study using MASK-air((R)) real-world data. Allergy. 2022;77(9):2699-711. doi:10.1111/all.15275
28. Sousa-Pinto B, Schunemann HJ, Sa-Sousa A, Vieira RJ, Amaral R, Anto JM, et al. Consistent trajectories of rhinitis control and treatment in 16,177 weeks: The MASK-air(R) longitudinal study. Allergy. 2023;78(4):968-83. doi:10.1111/all.15574
29. Bousquet J, Murray R, Price D, Somekh D, Munter L, Phillips, et al. The allergic allergist behaves like a patient. Ann Allergy Asthma Immunol. 2018;121(6):741-2. doi:10.1016/j.anai.2018.07.034
30. Bousquet J, Toumi M, Sousa-Pinto B, Anto JM, Bedbrook A, Czarlewski W, et al. The Allergic Rhinitis and Its Impact on Asthma (ARIA) Approach of Value-Added Medicines: As-Needed Treatment in Allergic Rhinitis. J Allergy Clin Immunol Pract. 2022;10(11):2878-88. doi:10.1016/j.jaip.2022.07.020
31. Sousa-Pinto B, Louis R, Anto JM, Amaral R, Sa-Sousa A, Czarlewski W, et al. Adherence to inhaled corticosteroids and long-acting beta2-agonists in asthma: A MASK-air study. Pulmonology. 2023;doi:10.1016/j.pulmoe.2023.07.004
32. Bousquet J, Sousa-Pinto B, Anto JM, Amaral R, Brussino L, Canonica GW, et al. Identification by cluster analysis of patients with asthma and nasal symptoms using the MASK-air(R) mHealth app. Pulmonology. 2023;29(4):292-305. doi:10.1016/j.pulmoe. 2022.10.005
33. Bousquet J, Melen E, Haahtela T, Koppelman GH, Togias A, Valenta R, et al. Rhinitis associated with asthma is distinct from rhinitis alone: The ARIA-MeDALL hypothesis. Allergy. 2023;78(5):1169-203. doi:10.1111/all.15679

34. Aguilar D, Lemonnier N, Melen E, Bustamante M, Gruzieva O, Guerra S, et al. Distinction between rhinitis alone and rhinitis with asthma using interactomics. Sci Rep. 2023;13(1):13125. doi:10.1038/s41598-023-39987-6
35. Savoure M, Bousquet J, Leynaert B, Renuy A, Siroux V, Goldberg M, et al. Rhinitis phenotypes and multimorbidities in the general population: the CONSTANCES cohort. Eur Respir J. 2023;61(2):2200943. doi:10.1183/13993003.00943-2022
36. Bousquet J, Sousa-Pinto B, Regateiro FS, Pereira AM, Brussino L, Kvedariene V, et al. MASK-air(R) direct patient data support the ARIA-MeDALL hypothesis on allergic phenotypes. Allergy. 2023;78(10):2790-4. doi:10.1111/all.15842
37. Sousa-Pinto B, Louis G, Rodrigues J, Giuliano AFM, Baiardini I, Braido F, et al. Impairment of EQ-5D-5L Domains According to Allergic Rhinitis and Asthma Control: A MASK-air Real-World Study. J Allergy Clin Immunol Pract. 2023;11(12):3742-51 e9. doi:10.1016/j.jaip.2023.08.006
38. Vieira RJ, Leemann L, Briggs A, Pereira AM, Savouré M, Kuna P, et al. Poor rhinitis and asthma control is associated with decreased health-related quality-of-life and utilities: A MASK-air study. J Allergy Clin Immunol Pract. 2024. doi.org/10.1016/j.jaip.2024.03.036
39. Vieira RJ, Pham-Thi N, Anto JM, Czarlewski W, Sa-Sousa A, Amaral R, et al. Academic Productivity of Young People With Allergic Rhinitis: A MASK-air Study. J Allergy Clin Immunol Pract. 2022;10(11):3008-17 e4. doi:10.1016/j.jaip.2022.08.015
40. Bousquet J, VandenPlas O, Bewick M, Arnavielhe S, Bedbrook A, Murray R, et al. The Work Productivity and Activity Impairment Allergic Specific (WPAI-AS) Questionnaire Using Mobile Technology: The MASK Study. J Investig Allergol Clin Immunol. 2018;28(1):42-4. doi:10.18176/jiaci.0197
41. Sousa-Pinto B, Azevedo LF, Sa-Sousa A, Vieira RJ, Amaral R, Klimek L, et al. Allergen immunotherapy in MASK-air users in real-life: Results of a Bayesian mixed-effects model. Clin Transl Allergy. 2022;12(3):e12128. doi:10.1002/clt2.12128
42. Bousquet J, Sousa-Pinto B, Shamji MH, Anto JM, Klimek L, Canonica GW, et al. Improvement of daily allergy control by sublingual immunotherapy: A MASK-air(R) study. Clin Exp Allergy. 2023;53(8):854-861. doi:10.1111/cea.14318
43. Bousquet J, Van Cauwenberge P, Khaltaev N, Aria Workshop G, World Health O. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol. 2001;108(5 Suppl):S147-334. doi:10.1067/mai.2001.118891
44. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008;63 Suppl 86:8-160. doi:10.1111/j.1398-9995.2007.01620.x
45. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol. 2010;126(3):466-76. doi:10.1016/j.jaci.2010.06.047
46. Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. J Allergy Clin Immunol. 2017;140(4):950-8. doi:10.1016/j.jaci.2017.03.050
47. Brozek JL, Akl EA, Alonso-Coello P, Lang D, Jaeschke R, Williams JW, et al. Grading quality of evidence and strength of recommendations in clinical practice guidelines. Part 1 of 3. An overview of the GRADE approach and grading quality of evidence about interventions. Allergy. 2009;64(5):669-77. doi:10.1111/j.13989995.2009.01973.x
48. Baldeh T, Saz-Parkinson Z, Muti P, Santesso N, Morgano GP, Wiercioch W, et al. Development and use of health outcome descriptors: a guideline development case study. Health Qual Life Outcomes. 2020;18(1):167. doi:10.1186/s12955-020-01338-8
49. Alonso-Coello P, Oxman AD, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. BMJ. 2016;353:i2089. doi:10.1136/bmj.i2089
50. Kvedariene V, Biliute G, Didziokaite G, Kavaliukaite L, Savonyte A, Rudzikaite-Fergize G, et al. Mobile health app for monitoring allergic rhinitis and asthma in real life in Lithuanian MASK-air users. Clin Transl Allergy. 2022;12(9):e12192. doi:10.1002/clt2.12192
51. Vardaloglu I, Sousa-Pinto B, Bousquet J, Dodek P, Bedbrook A, Karatas M, et al. In symptomatic patients on as-needed inhaled corticosteroids-formoterol, VAS asthma is associated with small airways resistance. J Asthma. 2024;61(2):132-9. doi:10.1080/02770903.2023.2248485
52. Ventura MT, Giuliano AFM, Buquicchio R, Bedbrook A, Czarlewski W, Laune D, et al. Implementation of the MASK-Air(R) App for Rhinitis and Asthma in Older Adults: MASK@Puglia Pilot Study. Int Arch Allergy Immunol. 2022;183(1):45-50. doi:10.1159/000518032
53. Sousa-Pinto B, Palamarchuk Y, Leemann L, Jankin S, Basagana X, Ballester J, et al. From MASK-air(R) and SILAM to CATALYSE (Climate Action to Advance HeaLthY Societies in Europe). J Investig Allergol Clin Immunol. 2024;34(1):12-9. doi:10.18176/jiaci.0923
54. Halonen JI, Erhola M, Furman E, Haahtela T, Jousilahti P, Barouki R, et al. A call for urgent action to safeguard our planet and our health in line with the helsinki declaration. Environ Res. 2021;193:110600. doi:10.1016/j.envres.2020.110600
55. Halonen JI, Erhola M, Furman E, Haahtela T, Jousilahti P, Barouki R, et al. The Helsinki Declaration 2020: Europe that protects. Lancet Planet Health. 2020;4(11):e503-e505. doi:10.1016/S2542-5196(20)30242-4
56. Bousquet J, Samolinski B, Kaidashev I, Maurer M, Roche N, Sousa-Pinto B, et al. UCRAID (Ukrainian Citizen and refugee electronic support in Respiratory diseases, Allergy, Immunology and Dermatology) action plan. Allergy. 2023;78(10):2581-95. doi:10.1111/all.15855

*Manuscript received January 12, 2024; accepted for publication January 23, 2024.*

**Bernardo Sousa-Pinto**

MEDCIDS - Department of Community Medicine,
Information and Health Decision Sciences
Faculty of Medicine
University of Porto
Porto, Portugal
E-mail: bernardo@med.up.pt