



HAL
open science

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

Jean Bousquet, Ignacio Ansotegui, Josep M Antó, Sylvie Arnavielhe, Claus Bachert, Xavier Basagaña, Annabelle Bédard, Anna Bedbrook, Matteo Bonini, Sinthia Bosnic-Anticevich, et al.

► To cite this version:

Jean Bousquet, Ignacio Ansotegui, Josep M Antó, Sylvie Arnavielhe, Claus Bachert, et al.. Mobile Technology in Allergic Rhinitis: Evolution in Management or Revolution in Health and Care?. *Journal of Allergy and Clinical Immunology: In Practice*, 2019, 7 (8), pp.2511-2523. 10.1016/j.jaip.2019.07.044 . hal-02565239

HAL Id: hal-02565239

<https://hal.umontpellier.fr/hal-02565239v1>

Submitted on 20 Jul 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53

Mobile technology in allergic rhinitis: evolution in management or revolution in health and care?

Jean Bousquet, MD (1-3), Ignacio J Ansotegui, MD (4), Josep M Anto, PhD (5-8), Sylvie Arnavielhe, PhD (9), Claus Bachert, MD (10), Xavier Basagaña, PhD (5,7,8), Annabelle Bédard, PhD (5,7,8), Anna Bedbrook, BSc (2), Matteo Bonini, MD (11), Sinthia Bosnic-Anticevich, PhD (12), Fulvio Braido, MD (13), Vicky Cardona, MD (14), Wiencyslawa Czarlewski, MD (15), Alvaro A Cruz, MD (16), Pascal Demoly, MD (17-18), Govert De Vries, MSc (19), Stephanie Dramburg, MD (47), Eve Mathieu-Dupas, PhD (9), Marina Erhola, PhD (20), Wytske J Fokkens, MD (21), Joao A Fonseca, MD (22), Tari Haahtela, MD (23), Peter W Hellings, MD (24), Maddalena Illario, MD (25), Juan Carlos Ivancevich, MD (26), Vesa Jormanainen, MD (20), Ludger Klimek, MD (27), Piotr Kuna, MD (28), Violeta Kvedariene, MD (29), Daniel Laune, PhD (9), Désirée Larenas-Linnemann, MD (30), Olga Lourenço, PhD (31), Gabrielle L Onorato, MSc (2), Paolo M Matricardi, MD (32), Erik Melén, MD (33), Joaquim Mullol, MD (34), Nikos G Papadopoulos, MD (35), Oliver Pfaar, MD (36), Nhân Pham-Thi, MD (37), Aziz Sheikh, MD (38), Rachel Tan, PhD (12), Teresa To, PhD (39), Peter Valentin Tomazic, MD (40), Sanna Toppila-Salmi, MD (23), Salvatore Tripodi, MD (41), Dana Wallace, MD (42), Arunas Valiulis, MD (43), Michiel van Eerd, MSc (19), Maria Teresa Ventura, MD (44), Arzu Yorgancioglu, MD (45), Torsten Zuberbier, MD (46)

1. University Hospital, Montpellier, France.
2. MACVIA-France, Fondation partenariale FMC VIA-LR, Montpellier, France.
3. VIMA. INSERM U 1168, VIMA : Ageing and chronic diseases Epidemiological and public health approaches, Villejuif, Université Versailles St-Quentin-en-Yvelines, UMR-S 1168, Montigny le Bretonneux, France, Euforea, Brussels, Belgium, and Charité, Universitätsmedizin Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Comprehensive Allergy Center, Department of Dermatology and Allergy, Berlin, Germany.
4. Department of Allergy and Immunology, Hospital Quirónsalud Bizkaia, Erandio, Spain.
5. ISGlobAL, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain.
6. Hospital del Mar Research Institute, Barcelona, Spain.
7. CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain.
8. Universitat Pompeu Fabra (UPF), Barcelona, Spain.
9. KYomed INNOV, Montpellier, France.
10. Upper Airways Research Laboratory, ENT Dept, Ghent University Hospital, Ghent, Belgium.
11. UOC Pneumologia, Istituto di Medicina Interna, F Policlinico Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy, and National Heart and Lung Institute, Royal Brompton Hospital & Imperial College London, UK.
12. Woolcock Institute of Medical Research, University of Sydney and Woolcock Emphysema Centre and Sydney Local Health District, Glebe, NSW, Australia.
13. University of Genoa, Department of Internal Medicine (DiMI), and IRCCS Ospedale Policlinico San Martino, Genova, Italy.
14. Allergy Section, Department of Internal Medicine, Hospital Vall d'Hebron & ARADyAL research network, Barcelona, Spain.
15. Medical Consulting Czarlewski, Levallois, France.
16. ProAR – Nucleo de Excelencia em Asma, Federal University of Bahia, Brazil and WHO GARD Planning Group, Brazil.
17. Department of Pulmonology, Division of Allergy, Hôpital Arnaud de Villeneuve, University Hospital of Montpellier, Montpellier, France.
18. Equipe EPAR - IPLESP, Sorbonne Université, Paris, France .
19. Peercode BV, Geldermalsen, The Netherlands.
20. National Institute for Health and Welfare, Helsinki, Finland.
21. Department of Otorhinolaryngology, Amsterdam University Medical Centres, AMC, Amsterdam, the Netherlands and EUFOREA, Brussels, Belgium.

- 54 22. CINTESIS, Center for Research in Health Technology and Information Systems, Faculdade de Medicina da
55 Universidade do Porto; and Medida, Lda Porto, Portugal
- 56 23. Skin and Allergy Hospital, Helsinki University Hospital, and University of Helsinki, Helsinki, Finland.
- 57 24. Dept of Otorhinolaryngology, Univ Hospitals Leuven, Belgium, and Academic Medical Center, Univ of
58 Amsterdam, The Netherlands and Euforea, Brussels, Belgium.
- 59 25. Division for Health Innovation, Campania Region and Federico II University Hospital Naples (R&D and
60 DISMET) Naples, Italy.
- 61 26. Servicio de Alergia e Immunologia, Clinica Santa Isabel, Buenos Aires, Argentina.
- 62 27. Center for Rhinology and Allergology, Wiesbaden, Germany.
- 63 28. Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz,
64 Poland.
- 65 29. Institute of Biomedical Sciences, Department of Pathology, Faculty of Medicine, Vilnius University, and
66 Institute of Clinical Medicine, Clinic of Chest diseases and Allergology, Faculty of Medicine, Vilnius,
67 Lithuania.
- 68 30. Center of Excellence in Asthma and Allergy, Médica Sur Clinical Foundation and Hospital, México City,
69 Mexico.
- 70 31. Faculty of Health Sciences and CICS – UBI, Health Sciences Research Centre, University of Beira Interior,
71 Covilhã, Portugal.
- 72 32. AG Molecular Allergology and Immunomodulation, Department of Pediatric Pneumology and Immunology,
73 Charité Medical University, Berlin, Germany.
- 74 33. E. Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm and Institute of Environmental Medicine,
75 Karolinska Institutet, Stockholm, Sweden.
- 76 34. Rhinology Unit & Smell Clinic, ENT Department, Hospital Clínic; Clinical & Experimental Respiratory
77 Immunoallergy, IDIBAPS, CIBERES, University of Barcelona, Spain.
- 78 35. Division of Infection, Immunity & Respiratory Medicine, Royal Manchester Children's Hospital, University of
79 Manchester, Manchester, UK, and Allergy Department, 2nd Pediatric Clinic, Athens General Children's
80 Hospital "P&A Kyriakou," University of Athens, Athens, Greece.
- 81 36. Department of Otorhinolaryngology, Head and Neck Surgery, Section of Rhinology and Allergy, University
82 Hospital Marburg, Philipps-Universität Marburg, Germany.
- 83 37. Allergy department, Pasteur Institute, Paris, France.
- 84 38. The Usher Institute of Population Health Sciences and Informatics, The University of Edinburgh, Edinburgh,
85 UK.
- 86 39. Sidkkids Hospital and Institute of Health Policy, Management and Evaluation, Toronto, Canada.
- 87 40. Department of General ORL, H&NS, Medical University of Graz, Austria.
- 88 41. Allergy Unit, Policlinico Casilino, Roma, Italy.
- 89 42. Nova Southeastern University, Fort Lauderdale, Florida, USA.
- 90 43. Vilnius University Institute of Clinical Medicine, Clinic of Children's Diseases, and Institute of Health
91 Sciences, Department of Public Health, Vilnius, Lithuania. European Academy of Paediatrics (EAP/UEMS-SP),
92 Brussels, Belgium.
- 93 44. University of Bari Medical School, Unit of Geriatric Immunoallergology, Bari, Italy.
- 94 45. Department of Pulmonary Diseases, Celal Bayar University, Faculty of Medicine, Manisa, Turkey
- 95 46. Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu
96 Berlin and Berlin Institute of Health, Comprehensive Allergy-Centre, Department of Dermatology and
97 Allergy, member of GA²LEN, Berlin, Germany.
- 98 47. Department of Pediatric Pulmonology, Immunology and Intensive Care Medicine, Charité - University
99 Medicine Berlin, Berlin, Germany

100
101
102

103 **Short title: mHealth apps in allergic rhinitis**

104
105

106 **Author for correspondence**

107 Professor Jean Bousquet

108 CHU Arnaud de Villeneuve, 371 Avenue du Doyen Gaston Giraud, 34295 Montpellier Cedex 5, France
109 Tel +33 611 42 88 47, Fax :+33 467 41 67 01 jean.bousquet@orange.fr

110

111

112 **Conflict of interest**

113

114

115 Dr. Ansotegui reports personal fees from Mundipharma, personal fees from Roxall, personal fees from Sanofi,
116 personal fees from MSD, personal fees from Faes Farma, personal fees from Hikma, personal fees from UCB, personal
117 fees from Astra Zeneca, outside the submitted work; .

118 J Bousquet reports personal fees and other from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis,
119 Sanofi-Aventis, Takeda, Teva, Uriach, outside the submitted work, Kyomed within the submitted work.

120 Dr. Bosnic-Anticevich reports personal fees from Teva, GSK, AstraZeneca, MEDA, outside the submitted work.

121 Dr. Cruz reports grants and personal fees from Astrazeneca, grants from GSK, personal fees from Boehringer
122 Ingelheim, CHIESI, NOVARTIS, Eurofarma, MEDA Pharma, Boston Scientific, outside the submitted work.

123 Dr. Haahtela reports personal fees from Mundipharma and Orion Pharma, outside the submitted work.

124 Dr. Hellings reports grants and personal fees from Mylan, during the conduct of the study; personal fees from Sanofi,
125 Allergopharma, Stallergenes, outside the submitted work.

126 Dr. Ivancevich reports personal fees from Eurofarma Argentina, Faes Farma, other from Sanofi, other from
127 Laboratorios Casasco, outside the submitted work.

128 Dr. Klimek reports grants and personal fees from ALK Abelló, Denmark, Bionorica, Germany, Allergopharma, Germany,
129 Novartis, Switzerland, GSK, Great Britain, Lofarma, Italy, personal fees from MEDA, Sweden, Boehringer Ingelheim,
130 Germany, grants from Biomay, Austria, HAL, Netherlands, LETI, Spain, Roxall, Germany, Bencard, Great Britain, outside
131 the submitted work.

132 Dr. Kuna reports personal fees from Berlin Chemie Menarini, Allergopharma, ALK, HAL Allergy, outside the submitted
133 work.

134 Dr. Kvedariene reports personal fees from GSK, non-financial support from Stallergene Greer, Mylan, Astra Zeneca,
135 Mylan, Dimuna, Norameda, outside the submitted work.

136 Dr. Matricardi reports personal fees from TPS, outside the submitted work.

137 Dr. Mullol reports grants from MYLAN-MEDA Pharma, during the conduct of the study; grants and personal fees from
138 MYLAN-MEDA Pharma, UCB Pharma, URIACH Group, personal fees from SANOFI-Genzyme-Regeneron, ALK-Abelló
139 A/S, Menarini Group, MSD, GlaxoSmithKline, Novartis, GENENTECH - Roche, outside the submitted work.

140 Dr. Papadopoulos reports grants from Gerolymatos, personal fees from Hal Allergy B.V., Novartis Pharma AG,
141 Menarini, Hal Allergy B.V., Mylan, outside the submitted work.

142 Dr. Pfaar reports grants and personal fees from ALK-Abelló, Anergis S.A., Allergopharma, Stallergenes Greer, HAL
143 Allergy Holding B.V./HAL Allergie GmbH, Bencard Allergie GmbH/Allergy Therapeutics, ASIT Biotech Tools S.A.,
144 Lofarma, Laboratorios LETI/LETI Pharma , grants from Biomay, Glaxo Smith Kline , Nuvo, Circassia, personal fees from
145 MEDA Pharma/MYLAN, Mobile Chamber Experts (a GA²LEN Partner), Indoor Biotechnologies, Astellas Pharma Global,
146 outside the submitted work.

147 Dr. Toppila-Salmi reports personal fees from Mylan Laboratories Ltd, ERT Ltd, Roche Products Ltd, outside the
148 submitted work.

149 Dr. Tripodi reports personal fees and other from TPS Production srl, during the conduct of the study; In addition, Dr.
150 Tripodi has a patent PCT/IT2018/000119 WPTR issued.

151 Dr. Wallace reports and I am the co-chair of the AAAAI/ACAAI Joint Task Force on Practice Parameters.

152 Dr. Zuberbier reports personal fees from Bayer Health Care, FAES, Novartis, Henke, AstraZeneca Fee for talk, AbbVie
153 Fee for talk, ALK Fee for talk, Almirall Fee for talk, Astellas Fee for talk, Bayer Health Care Fee for talk, Bencard Fee for
154 talk, Berlin Chemie Fee for talk, HAL Fee for talk, Leti Fee for talk, Meda Fee for talk, Menarini Fee for talk, Merck Fee
155 for talk, MSD Fee for talk, Novartis Fee for talk, Pfizer Fee for talk, Sanofi Fee for talk, Stallergenes Fee for talk, Takeda
156 Fee for talk, Teva Fee for talk, UCB Fee for talk, Henkel Fee for talk, Kryolan Fee for talk, L'Oréal Fee for talk, outside
157 the submitted work.

158

159

160

161

162 **Abstract**

163 Smart devices and internet-based applications are largely used in allergic rhinitis and may help to
164 address some unmet needs. However, these new tools need to first of all be tested for privacy rules,
165 acceptability, usability and cost-effectiveness. Secondly, they should be evaluated in the frame of the
166 digital transformation of health, their impact on healthcare delivery and health outcomes. This review
167 (i) summarizes some existing mHealth apps for allergic rhinitis and reviews those in which testing has
168 been published, (ii) discusses apps that include risk factors of allergic rhinitis, (iii) examines the impact
169 of mHealth apps in phenotype discovery, (iv) provides real-world evidence for care pathways, and
170 finally (v) discusses mHealth tools enabling the digital transformation of health and care, empowering
171 citizens and building a healthier society.

172

173

174 **Key words**

175

176 Apps, digital transformation of health, MASK, mHealth, Mobile technology, rhinitis

177

178

179 **Abbreviations**

180

181 AHA: Active and healthy ageing

182 AIRWAYS ICPs: Integrated care pathways for airway diseases

183 AR: Allergic rhinitis

184 ARIA: Allergic Rhinitis and Its Impact on Asthma

185 CARAT: Control of Allergic Rhinitis and Asthma Test

186 CDS: clinical decision support

187 CDSS: Clinical decision support system

188 DG CONNECT: Directorate General for Communications Networks, Content & Technology

189 DG Santé: Directorate General for Health and Food Safety

190 DG: Directorate General

191 EIP on AHA: European Innovation Partnership on AHA

192 EU: European Union

193 EQ-5D: Euroquol

194 FDA : US Food and Drug Administration

195 GARD: WHO Global Alliance against Chronic Respiratory Diseases

196 GDPR: General Data Protection Regulation

197 GIS: Geographic Information System

198 GP: Good Practice

199 GRADE: Grading of Recommendations Assessment, Development and Evaluation

200 GT: Google Trends

201 ICP: Integrated care pathway

202 ICT: Information and Communication Technology

203 JA-CHRODIS: Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle

204 MACVIA-LR: contre les MALadies Chroniques pour un Vieillissement Actif (Fighting chronic diseases for AHA)

205 MASK: Mobile Airways Sentinel Network

206 MeDALL: Mechanisms of the Development of ALLergy (FP7)

207 mHealth: mobile health

208 POLLAR: Impact of air POLLution on Asthma and Rhinitis

209 RCT: Randomized control trial

210 RWD: Real-world data

211 RWE: Real-world evidence

212 TRL: Technology Readiness level
213 VAS: Visual analogue scale
214 WHO: World Health Organization

215

216 **Text:** 4839 words

217

218 **Abstract:** 125 words

219 Introduction

220 Mobile technology has spread rapidly around the globe. Today, it is estimated that over 5 billion people
221 have mobile devices, over half of which are smartphones
222 ([https://www.pewglobal.org/2019/02/05/smartphone-ownership-is-growing-rapidly-around-the-world-but-](https://www.pewglobal.org/2019/02/05/smartphone-ownership-is-growing-rapidly-around-the-world-but-not-always-equally/)
223 [not-always-equally/](https://www.pewglobal.org/2019/02/05/smartphone-ownership-is-growing-rapidly-around-the-world-but-not-always-equally/)).

224 mHealth (mobile health) is the use of information and communication technology (ICT) for health services
225 and information transfer (1). mHealth, including apps running on consumer smart devices (i.e.,
226 smartphones and tablets), is becoming increasingly popular and has the potential to profoundly impact
227 healthcare (2, 3). The rapid advances in mobile technologies have given rise to new opportunities for the
228 digital transformation of health and the continued growth in coverage of mobile cellular networks. The
229 potential applications and benefits of mHealth are extensive and expanding (4). Implementing mHealth
230 innovations may also have disruptive consequences (5), so it is important to test applicability in each
231 individual situation (6). Appropriately identifying and representing stakeholders' interests and viewpoints in
232 evaluations of mHealth is a critical part of ensuring continued progress and innovation (7). Patient,
233 caregiver and clinician evaluations and recommendations play an important role in the development of
234 asthma / AR mHealth tools in supporting the provision of disease management (8).

235 Smart devices and internet-based applications are already used in allergic rhinitis (AR) and may help to
236 address some of the unmet needs (2). According to recent position papers from EAACI (9) and from the
237 American College of Allergy and Immunology (10), mHealth apps can support the provision of high-
238 quality care to allergic patients, in particular those with AR and/or asthma. This is satisfying for patients
239 and health care professionals, and has led to a reduction in health care utilization and costs. However, these
240 new tools need to first of all be tested for privacy rules, acceptability, usability and cost-effectiveness.
241 Secondly, they should be evaluated in the frame of the digital transformation of health, their impact on
242 healthcare delivery and health outcomes.

243 1- Strengths and weaknesses of mHealth

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

246 The benefits of mHealth include paperless information, the potential increase in medication adherence and
247 improved monitoring (Table 1). mHealth technology has great potential to increase healthcare quality,
248 expand access to services, reduce costs, and improve personal wellness and public health (11). However,
249 mHealth may be harmful. Technically, the development of an app is an easy task, which incurs very low
250 initial investments and does not require in-depth knowledge of the subject itself. The low entry barrier,

251 dramatically democratizing the app development environment, also results in a large number of ad-hoc
252 apps targetting various health concerns of the public. The majority of mHealth apps have neither been
253 tested on patients nor approved by regulatory organizations such as the US Food and Drug Administration
254 (FDA) or the European Medicines Agency (EMA). However, many patients rely on these apps in their
255 everyday lives.

256 A few weaknesses emerge from the use of mHealth apps that are used in observational studies to assess
257 real-world evidence for the evaluation of allergy phenotypes or treatments. As for all studies using
258 participatory data, potential biases include (i) the likelihood of sampling bias, (ii) the difficulty to assess
259 generalizability of the study, as app users are usually not representative of all patients with AR. In MASK,
260 it was found that most users report bothersome symptoms (Bedard, submitted) (iii) outcome
261 misclassification that cannot be assessed, (iv) very little information on patient characteristics, (v) lack of
262 physicians' support in the diagnosis of AR, (vi) potential measurement biases due to the so-called
263 "informatics illiteracy" of many patients (12), and (vii) poor adherence to e-Diary compilation, which
264 makes proving poor adherence to treatment impossible.

265 One of the major problems with apps is the low adherence to their use. Achieving sufficient mHealth app
266 engagement and user retention rates is a difficult task. In MASK-air (Mobile Airways Sentinel NetworK),
267 around half of the patients use the app only once (13).

268 The benefits of mHealth apps are presented in Table 1.

269 **2- Regulatory framework**

270 mHealth raises significant privacy and security challenges in terms of IT privacy, data sharing and consent
271 management, access control and authentication, confidentiality and anonymity, policies and compliance,
272 accuracy and data provenance, and security technology (11).

273 In May 2018, the EU General Data Protection Regulation (GDPR) brought major changes in data privacy
274 regulation in the EU. The aim of the GDPR is to protect all EU citizens from privacy and data breaches in
275 today's data-driven world. It harmonizes data privacy laws across Europe, protects and empowers all EU
276 citizens' data privacy and reshapes the way organizations across the region approach data privacy. Thus, all
277 mHealth apps used in the EU should follow the GDPR. The law applies to personal data (Art. 4 para. 1 no.
278 1, GDPR) (14). Anonymous or anonymized data should lack identifiability. Anonymization principally
279 enables the sharing of data in a way that preserves privacy with minimal data loss. Geolocation information
280 is not only personal data but also has to be considered as an identifier itself (15, 16). Thus, mHealth apps
281 should follow a geolocation de-anonymization that is rarely found in apps. The k-anonymity method is
282 acceptable and was found to fulfill the GDPR regulations in AR (17). The GDPR fixes general rules

283 applying to any kind of personal data processing as well as specific rules applying to the processing of
284 special categories of personal data such as health data (18). In May 2020, a new EU law will regulate
285 mobile technology (Medical Device Regulation, MDR) (19) making its use tightly regulated.

286 The US regulations were recently reviewed in detail (20). The FDA and the Federal Trade Commission
287 (FTC) both guide the development and regulation of mHealth devices. Since the recently enacted
288 amendment to the Twenty-First Century Cures Act - the Food, Drug and Cosmetic Act - certain software
289 functions are no longer considered to be medical devices (21). Thus, the FDA is now using enforcement
290 discretion for mHealth apps that do not present risks to patients and consumers.

291 **3- mHealth apps for allergic rhinitis**

292 **a. Apps informing on risk factors for allergic rhinitis**

293 Risk factors for exacerbations of AR and asthma include allergen exposure (22), climatic factors (23, 24)
294 and air pollutants (25). It is therefore of great importance to identify levels of risk factors that can induce
295 symptoms in allergic patients. Among these, pollen exposure is the most important for pollen allergic
296 patients. Therefore, forecasting symptoms of pollen-related AR for the individual patient should improve
297 disease control and plan pharmacological intervention and/or prevention of exposure. Besides pollen
298 diaries, mHealth apps allow an easy and fast documentation of pollen allergy counts (26-28). A study that
299 analyzed 9 mobile apps delivering pollen information and pollen forecasts found that the quality of pollen
300 forecasts needs to be improved. It recommended quality control for pollen forecasts to avoid potential harm
301 to patients (29). AR patients could consider the need to avoid the more polluted routes when walking,
302 biking, or exercising. In many cities, traffic air pollution concentrations decline rapidly at a few hundred
303 metres from roadways, and web-based applications can assist individuals in finding alternative routes
304 (30).

305 There are, however, drawbacks that need to be understood in order to provide better information: (i) The
306 pollen season does not necessarily correspond to an individual patient's symptoms (31) and sub-micronic
307 particles from pollens can induce severe symptoms such as thunderstorm-induced asthma (32); (ii) The
308 definition of the pollen season is still unclear (33) although some clarification efforts have been made for
309 clinical trials (34); (iii) There is a weak correlation between pollen counts and symptoms (35); (iv)
310 Pollutants and weather conditions can interact with pollens to induce symptoms; (v) Only predictive
311 models are to be used, not only for forecasting but also for near-real-time analysis (now-casting) since it
312 takes a few days to count pollens (36). However, these models may need more testing in order to be fully
313 accepted; (vi) Next-generation pollen monitoring is very promising but its cost prevents a large use (37);
314 (vii) The onset of individual symptoms (AR, asthma, conjunctivitis) may be associated with different levels
315 of allergen exposure in patients with different intensities of sensitization and target organ reactivity.

316 Google Trends are interesting for complementing pollen counts (38) but they cannot be readily used as a
317 predictor of the pollen season. However, Google Trends, when used retrospectively, are better correlated
318 with symptoms than pollen counts (35, 39, 40).

319 A large number of apps provide information to allergy sufferers regarding pollen counts and/or pollution
320 data (41). Some examples are given below and in Table 2.

321 BreezoMeter uses the CAMS pollen predictions and big data analysis to provide a continuous current
322 condition pollen index (<https://breezometer.com/products/pollen-api>). However, its validation is not yet available.

323 Air Matters broadcasts pollen and air quality data in most countries of the world (<https://air-matters.com>).

324 The Copernicus Atmosphere Monitoring Service (CAMS), implemented by the European Centre for
325 Medium-Range Weather Forecasts (ECMWF) on behalf of the European Union, provides forecasts for
326 birch, olive and grass pollen to allow allergy sufferers in the EU to take preventive measures days before
327 exposure. (<https://atmosphere.copernicus.eu/news-and-media/news/cams-helping-allergy-sufferers>). CAMS
328 supports a range of smartphone applications designed to limit exposure to such allergens. One of these is
329 MetéoPollen for France (<https://meteopollen.com>).

330 AccuPollen (<http://www.nynjpollen.com>) and My Pollen Forecast (<https://www.jrustonapps.com/apps/my-pollen-forecast>)
331 track pollen counts in the US using forecasts for pollen and climatic data.

332 The POLLEN app of the European Aeroallergen Network (EAN), maintained by the Medical University of
333 Vienna (<https://www.polleninfo.org>), evaluates the pollen situation in European countries using the pollen
334 counts of EAN and predictions of the SILAM pollen forecasting model (<http://silam.fmi.fi>).

335 **b. Apps including health data**

336 Many mHealth apps support patients with AR via self-monitoring through an electronic diary (e-Diary),
337 personalized feedback and/or patient education (42). They aim to improve patient education and self-
338 management on a daily basis but require an evidence-based evaluation given that the information provided
339 on the app stores is limited, in particular for the apps' validity (43-45). This can be done by evaluating the
340 effectiveness of the app with the patients' clinical outcomes (13, 28, 46). For example, children with
341 moderate-severe seasonal allergic rhinitis, treated with daily mometasone, improved their disease
342 knowledge thanks to daily informative messages sent by their e-Diary app (42). If patients are seeking an
343 approach involving the minimal interaction with health care professionals in AR management (47), it is
344 then crucial that the mHealth app is in line with evidence-based essential self-management principles. A
345 Mobile app Rating Scale (MARS) instrument (48) - available in Australia - has been used to assess the
346 mHealth apps for AR (Tan et al, in revision). A 'patient empowerment index through mobile technology'

347 was recently designed and used to evaluate AR in order to support patients choosing an mHealth app and
348 physicians recommending it (42).

349 Most but not all mHealth apps which include clinical data are available in English and some are available
350 in over 15 languages (Table 2). The majority of mHealth apps are freely available on iOS and Android.
351 However, very few have provided clinical data supporting their validity. mHealth apps for AR include:

- 352 • Self-monitoring
- 353 • Patient's feedback
- 354 • Patient's education
- 355 • Patient's empowerment
- 356 • Pollen and/or air pollution data

357 At present (May 2019), some mHealth apps are in non-English languages such as ALK-Allergik
358 (<https://maviedallergik.fr/nos-services>), Allergy Track, (<https://www.android-logiciels.fr/allergy-track/>),
359 AllyScience (<https://allyscience.ch/>), e-symptoms (<https://www.aha.ch/centre-allergie-suisse>), i-pollen
360 (<http://www.gammehumex.fr/application-i-pollen/>), Plume Air Report (<https://air.plumelabs.com/fr/>) and Pollen
361 App (<http://www.pollenstiftung.de/ak>). Others in English may be restricted to a limited geographic area such
362 as Air Rater in Australia (<https://airrater.org>) or are not available from app stores.

363 Besides those with a commercial interest (e.g. Sensio Air <https://www.wlab.io> and Zyrtec AllergyCast
364 <https://www.zyrtec.com/allergy-forecast-tools-apps>), there are few mHealth apps with health data on AR (e.g.
365 AllergyMonitor®, MASK-air®, WebMD Allergy® <https://www.webmd.com/allergy-app> and the Austrian
366 Pollen Information Service www.pollenwarndienst.at) (Table 2).

367 **c. Apps connected with sensors**

368 In asthma, many mHealth apps are connected with sensors for inhalers (20). Such devices do not yet exist
369 in AR but there are attempts to connect pollution sensors to mHealth apps. Unfortunately, those existing for
370 asthma appear to be in an exploratory phase and need validation. In addition to external sensors,
371 smartphones and tablets have embedded sensors such as camera, microphone, atmospheric pressure sensor,
372 accelerometer and GPS. These sensors can be used to provide contextual information for the collected
373 clinical data. Moreover, using signal processing, data from on board sensors, already available in off-the-
374 shelf devices and used by millions of patients, are being tested as ubiquitous technologies to provide
375 verified information on cough (49), lung function (50), adherence to inhaled treatment (51), physical
376 activity parameters and other human behaviours of clinical interest (52).

377 **d- Examples of apps**

- 378 • **AllergyMonitor®** (<http://www.tpsproduction.com/>)

379 AllergyMonitor® is an app that has been translated into 10 languages. Its target is to improve allergy
380 diagnosis by matching trajectories of symptom-medication scores and pollen counts (26, 28, 46, 53, 54).
381 Furthermore, it enhances shared decision-making by fostering the exchange of information between users
382 and their health care professionals. The latter can access and view their patients' recorded data in a back-
383 office, which allows the management of patients' clinical data and gives a structured overview on the
384 individual disease management. The data recorded by the user then complete the set of information being
385 integrated in the back-office in real-time. As users also register the intake of their prescribed medication,
386 this feature allows the monitoring of compliance which has been shown to effectively increase the
387 adherence to treatment with nasal corticosteroids and sublingual allergen-specific immunotherapy. To this
388 end, the app includes customized lists of over-the-counter and prescribed medications for many countries,
389 patient-doctor communication via SMS and e-mail, patient alerts for a better knowledge of the disease as
390 well as reminders for a better adherence to treatment. The potential of data sets generated through
391 AllergyMonitor® has also been investigated for the short-term prediction of patients' symptoms with
392 several symptom and medication scores for rhinitis and asthma.

393 • **MASK (<http://www.mask-air.com>)**

394 MASK (Mobile Airways Sentinel network), the Phase 3 ARIA initiative, was instigated to reduce the
395 global burden of AR and asthma multimorbidity, giving the patient and the health care professional simple
396 tools to better prevent and manage respiratory allergic diseases. The MASK app (MASK-air®, formerly *the*
397 *Allergy Diary*, freely available for Android and iOS) (55) is the most extensively published mHealth app
398 for AR. It is an ICT system centred around the patient (13, 55-57) and is operational in 23 countries and 17
399 languages. It uses a treatment scroll list which includes all medications customized for each country as well
400 as visual analogue scales (VASs) to assess rhinitis control and work productivity (58, 59). MASK-air® is
401 being combined with data on allergen and pollution exposure (POLLAR) (25). MASK-air® results are
402 given in Table 3.

403 MASK is scaled up using the EU European Innovation Partnership on Active and Healthy Ageing (EIP on
404 AHA) strategy (60). MASK is supported by several EU grants and is a GARD (Global Alliance against
405 Chronic Respiratory Diseases, WHO (61)) research demonstration project. It is a Good Practice of DG
406 Santé (62).

407

408 • **European Aeroallergen Network Pollen Information Service**

409 The EAN Pollen Information Service (www.polleninfo.org), developed and maintained at the Medical
410 University of Vienna, provides a pollen assessment and a three-day forecast in co-operation with local and
411 international institutions. It is available for European countries in over 10 languages. The app includes

412 symptoms and treatments. The components and functionality of the app vary between the countries
413 depending on the requests of the national pollen observing groups.

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

420 • **e-allergy**

421 The under-recognition of AR is common due to a low level of public awareness as well as limitations in
422 access to allergologists (63). AR sufferers often use OTC drugs and self-medicate. mHealth tools
423 supporting the pre-medical early diagnosis of allergic diseases are important. They use algorithms able to
424 classify respondents into certain risk groups of AR and asthma. An algorithm was created - with the use of
425 advanced statistical methods (neural networks) - on ECAP (Epidemiology of the Allergic Diseases in
426 Poland) data containing both questionnaire answers and medical diagnosis (64). This tool is constantly
427 being updated. The latest results show a sensitivity for AR in children and adolescents of 0.852 and a
428 specificity of 0.840 (65).

429 **4- Clinical decision support systems (CDSSs)**

430 A CDSS is a health information technology (IT) system designed to assist clinicians and other health care
431 professionals in clinical decision-making. In medicine, CDSSs have become a major topic in artificial
432 intelligence. According to the National Academy of Medicine (Washington DC) (66), "facilitative clinical
433 decision support (CDS) is a practical necessity for every clinician in our rapidly-evolving health and
434 healthcare landscape." A CDSS can reduce the burden that exponentially-expanding clinical knowledge
435 and care complexity places on clinicians, other health care professionals or patients. CDSs provide
436 clinicians and other health care professionals with knowledge and person-specific information -
437 intelligently filtered or presented at appropriate times - to enhance health and health care (67). CDSs can
438 enhance decision-making through the use of the following tools: (i) computerized alerts and reminders to
439 health care providers and patients, (ii) clinical guidelines, (iii) focused patient data reports and (iv)
440 diagnostic support (68). Many apps used in AR provide patients with some help for AR control. However,
441 for this, they should be labelled as CE2A in the EU. Apps that do not provide help can be registered as
442 CE1. An electronic CDSS (eCDSS) based on MASK now exists in AR and is in the process of validation
443 (69). It is not clear whether other tools have been validated as they have not been published. CDSSs may

444 also be very useful in stratification strategies and in reporting outcomes in clinical trials such as in Allergen
445 Immunotherapy (<https://www.ncbi.nlm.nih.gov/pubmed/30955224>).

446 **5- Potential of mHealth apps for allergy phenotype discovery**

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

450 A prospective analysis has compared six disease severity scores for AR against pollen counts (53). Many
451 different and incomparable symptom (medication) scores are used to assess AR control. Disease severity
452 scores for seasonal AR evaluated by an internet-based platform provide similar results at population level
453 but are heterogeneous in individual patients.

454 Multimorbidity in allergic airway diseases is well known (70), but no data has ever existed regarding how
455 multimorbidity impacts the daily dynamics of specific symptoms, including severity and work. MASK-
456 air® has enabled this investigation in a novel approach of the intra-individual variability of allergic
457 multimorbidity from day to day (71). AR and rhinoconjunctivitis did not appear to be the same disease.
458 Moreover, MASK-air® identified a previously unrecognized extreme pattern of uncontrolled
459 multimorbidity (uncontrolled rhinitis, conjunctivitis and asthma on the same day) (71). However, mHealth
460 apps are only tools generating hypotheses and need to be confirmed in classical epidemiologic studies.
461 Differences between AR alone or associated with conjunctivitis were already known (72) but new studies
462 carried out following MASK-air® data showed that (i) ocular symptoms are more common in
463 polysensitized patients whether or not they have asthma (73), (ii) ocular symptoms are associated with the
464 severity of nasal symptoms (74), (iii) ocular symptoms are important to consider in severe asthma (74) and
465 (iv) the severity of allergic diseases increases with the number of allergic multimorbidities (75). This is the
466 first time that novel allergic phenotypes have been discovered using an mHealth app and then confirmed
467 by classical epidemiologic studies.

468 **5- Real world evidence using mHealth in next-generation care** 469 **pathways**

470 mHealth apps for a better AR management are growing in number. However, their usefulness for doctors
471 and patients is still being debated. Most studies have also highlighted certain shortcomings and limitations,
472 mainly concerning security and cost-effectiveness (76).

473

474

475 **a. Adherence to treatment**

476 mHealth may help to better understand adherence to treatment and its determinants as well as how to
477 improve it. In medicine, many mHealth apps are available to support people in taking their medications and
478 thus to improve medication adherence (77, 78). However, a meta-analysis found that the majority did not
479 have many of the desirable features and/or were of low quality (77). A systematic review including 16
480 RCTs found that mobile phone text messaging approximately doubles the odds of medication adherence,
481 resulting in a net increase in adherence of 17.8% (78). A Cochrane systemic review of 7 trials in
482 cardiovascular disease found that, while the results are promising, there is insufficient evidence to draw
483 conclusions on the effectiveness of text message-based interventions for adherence to medications. The
484 authors suggested that sufficiently powered, high-quality randomised trials are needed, particularly in low-
485 and middle-income countries (79).

486 Adherence in randomized control trials (RCTs) is high but does not reflect the real-life situation (29,30)
487 and alternative measurements of adherence in a real-life setting are needed. The best studies would be
488 using electronic devices that count and record the drugs taken. However, these devices are still exploratory
489 and expensive and, as such, they are not currently a viable solution for large studies in AR patients (80) or
490 individual patients. [A potential palliative solution can be to use the smartphone's camera to register the
491 drug uptake. The photo of the drug is then processed by image recognition algorithms to provide verified
492 data on adherence to AR treatment during the patient's daily life.](#) However, there are technical challenges
493 and limitations to some types of vials and packaging. The automatic detection of progression of use of the
494 liquid in the vial using computer vision may be of special relevance for sublingual allergen immunotherapy
495 for which adherence can be a major issue (81). Other approaches already being tested for asthma but not
496 for AR are mobile direct observation of therapy (82) and multicomponent interventions based on mobile
497 technologies (83). Although there are already some mHealth apps for AR, there are few studies evaluating
498 their benefits and impact (76). One study suggested that a short message service (SMS) helps to improve
499 AR treatment (84). Internet-based telemonitoring using the AllergyMonitor[®] improved adherence to intra-
500 nasal corticosteroid treatment and disease knowledge among children and adolescents with seasonal AR as
501 well as adherence to sub-lingual immunotherapy (46). In MASK-air[®], a major lack of adherence to
502 treatment was observed for all medications (85). Auto-medication was very common (12) suggesting that
503 patients, like allergists when they are allergic (86), do not follow physicians' prescriptions or guidelines.

504 **b. mHealth in observational studies allowing novel assessment of patients'**
505 **behaviour**

506 The treatment of AR is complex as many drugs are available in oral and/or topical formulations, and
507 allergen immunotherapy and avoidance increase the complexity of the management. Many AR guidelines
508 are evidence-based and have led to a better understanding and management of AR (87-89). However,
509 guidelines are mostly based on RCTs, typically undertaken on highly-selected populations and often with
510 limited/unclear generalizability to routine care contexts. Large observational implementation studies are
511 needed to triangulate RCTs as they reflect “real world” every-day use and practice more closely than RCTs
512 in terms of the heterogeneous patient populations included and the variety of medical interventions
513 assessed. In RCTs, each subject is randomly assigned to a treatment or control group, whereas
514 observational studies examine the possible effect of a treatment on subjects where the investigator has no
515 control over the experiment and cannot randomize subject allocation (94). However, observational studies
516 provide clinically relevant information in addition to RCTs. Real-world evidence (RWE) using RCTs and
517 real-world data (RWD) is becoming increasingly important in supporting regulatory decisions using
518 mobile technology (95).

519 A pilot study in over 2,900 users allowed differentiation between treatments (12) showing that the
520 assessment of series of consecutive days was useful in understanding treatment patterns. The study showed
521 that patients did not necessarily use treatment on a daily basis and in a regular way; rather, they appeared to
522 increase treatment use when their symptom control worsened. Differences in efficacy between medications
523 were observed. This pilot study was confirmed in almost 9,000 users (96). The studies confirm the
524 usefulness of mHealth in accessing and assessing everyday use and practice in AR (12). It is hoped that
525 mHealth apps will increase patient empowerment and improve adherence.

526 **c. Next generation guidelines**

527 The selection of pharmacotherapy for patients with allergic rhinitis aims to control the disease and depends
528 on many factors. GRADE (Grading of Recommendations Assessment, Development and Evaluation)
529 guidelines have considerably improved AR management. However, there is an increasing trend to use
530 RWD to inform clinical practice, especially as RCTs are often limited with regards to the applicability of
531 results. The MACVIA algorithm proposed an AR treatment by a consensus group (97). This simple
532 algorithm can be used to step-up or step-down AR treatment. Next-generation guidelines for the
533 pharmacologic treatment of allergic rhinitis (98) were developed using existing GRADE-based guidelines
534 (87-89), RWD provided by mHealth apps (12, 85, 96) and additive studies (allergen chamber studies (99))
535 to refine the MACVIA algorithm (97).

536 **6- mHealth tools enabling the digital transformation of health and** 537 **care, empowering citizens and building a healthier society**

538 The recent report on the State of Health in the EU (State of Health in the EU "Companion Report 2017",
539 <https://ec.europa.eu/health/state>) concluded that rethinking our health and care systems can ensure its
540 sustainability aiming to continue health promotion, disease prevention and to provide patient-centred care
541 that meets citizens' needs ([https://ec.europa.eu/transparency/regdoc/rep/1/2018/FR/COM-2018-233-F1-FR-
MAIN-PART-1.PDF](https://ec.europa.eu/transparency/regdoc/rep/1/2018/FR/COM-2018-233-F1-FR-
542 MAIN-PART-1.PDF)).

543 Digital solutions for health and care can increase the well-being of millions of citizens and radically change
544 health and care services. In its mid-term review on the implementation of the digital single market strategy
545 (<https://ec.europa.eu/transparency/regdoc/rep/1/2017/EN/COM-2017-228-F1-EN-MAIN-PART-1.PDF>),
546 the EU Commission took further action in three areas:

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

559 Digital tools can also empower patients in the context of the UN sustainable development goals and in
560 particular regarding those related to sustainability and natural resources (100). Future apps in AR could
561 consider providing information to promote behavioural changes that could reduce the planetary impacts of
562 human activity.

563 In the context of implementing communication on the digital transformation of health and care, DG
564 SANTE, in collaboration with the newly-established EU Commission Expert Group "Steering Group on
565 Health Promotion, Disease Prevention and Management of Non-Communicable Diseases"
566 (https://ec.europa.eu/health/non_communicable_diseases/steeringgroup_promotionprevention_en),
567 supported the scaling-up and wider implementation of good practices in the field of digitally-enabled,
568 integrated, person-centred care. MASK was one of the nine Good Practices selected along with chronic
569 disease and Parkinson's disease (62).

570 **8. Global implementation**

571 When mobile technology was initiated, it was thought that it would be used mainly in developed countries.
572 However, smartphone ownership is growing rapidly around the world. According to ITU (International
573 Telecommunication Union, Geneva), in 2015, there were more than 7 billion mobile telephone
574 subscriptions across the world, over 70% of which were in low- or middle-income countries (101).
575 However, in these countries, smartphone use is still much more among the young and educated
576 ([https://www.pewglobal.org/2019/02/05/smartphone-ownership-is-growing-rapidly-around-the-world-but-](https://www.pewglobal.org/2019/02/05/smartphone-ownership-is-growing-rapidly-around-the-world-but-not-always-equally/)
577 [not-always-equally/](https://www.pewglobal.org/2019/02/05/smartphone-ownership-is-growing-rapidly-around-the-world-but-not-always-equally/)).

578 WHO recognizes the significant role that digital technologies can play in strengthening the health systems
579 in countries to achieve universal health coverage, the health-related Sustainable Development Goals and
580 other health objectives. In 2018, 121 countries had national eHealth strategies, representing the beginning
581 of a shift from an unsustainable project-based approach towards a systematic, integrated approach designed
582 for cost-effective investment and alignment of partners (102). The joint WHO-ITU initiative “Be He@lthy,
583 Be Mobile” for the prevention and management of noncommunicable diseases, their comorbidities and
584 their risk factors, including improving disease diagnosis and tracking, is of great importance. MASK is one
585 of the examples of the “Be He@lthy, Be Mobile” handbook on how to implement mBreatheFreely for
586 asthma and COPD (103).

587 **Conclusion**

588 mHealth has the potential to profoundly impact healthcare (3). mHealth apps now represent an important
589 evolution of health and care for AR since RWE has identified patients’ behaviours and practices and this
590 will have a profound impact on current guidelines and care pathways. Rhinitis is not a severe disease but it
591 does have a major impact on social life, school and work productivity (104). Asthma-rhinitis
592 multimorbidity plays a key role in understanding asthma and can be used as a model of multimorbidity.
593 Moreover, asthma and rhinitis have a life course approach whereas most chronic diseases start early in life
594 but are only clinically evident in adulthood. The revolution is underway for AR and asthma, and the lessons
595 learnt are transposable to other chronic diseases and will design innovative health strategies and services as
596 well as change management (105).

597

598

599 **References**

600

601 1. mHealth. New horizons for health through mobile technologies. Global Observatory for eHealth
602 series- Vol 3 WHO Library Cataloguing-in-Publication Data.
603 2011;http://www.who.int/goe/publications/goe_mhealth_web.pdf.

604 2. Bousquet J, Chavannes NH, Guldemond N, Haahtela T, Hellings PW, Sheikh A. Realising the
605 potential of mHealth to improve asthma and allergy care: how to shape the future. *Eur Respir J*.
606 2017;49(5).

607 3. Ozdalga E, Ozdalga A, Ahuja N. The smartphone in medicine: a review of current and potential use
608 among physicians and students. *J Med Internet Res*. 2012;14(5):e128.

609 4. Stephani V, Opoku D, Quentin W. A systematic review of randomized controlled trials of mHealth
610 interventions against non-communicable diseases in developing countries. *BMC Public Health*.
611 2016;16:572.

612 5. Keijser W, de-Manuel-Keenoy E, d'Angelantonio M, Stafylas P, Hobson P, Apuzzo G, et al. DG
613 Connect funded projects on information and communication technologies (ICT) for old age people:
614 Beyond Silos, CareWell and SmartCare. *J Nutr Health Aging*. 2016;20(10):1024-33.

615 6. Mozaffar H, Cresswell KM, Williams R, Bates DW, Sheikh A. Exploring the roots of unintended
616 safety threats associated with the introduction of hospital ePrescribing systems and candidate
617 avoidance and/or mitigation strategies: a qualitative study. *BMJ Qual Saf*. 2017;26(9):722-33.

618 7. Lee L, Sheikh A. Understanding Stakeholder Interests and Perspectives in Evaluations of Health IT.
619 *Stud Health Technol Inform*. 2016;222:53-62.

620 8. Geryk LL, Roberts CA, Sage AJ, Coyne-Beasley T, Sleath BL, Carpenter DM. Parent and Clinician
621 Preferences for an Asthma App to Promote Adolescent Self-Management: A Formative Study. *JMIR*
622 *Res Protoc*. 2016;5(4):e229.

623 9. Matricardi PM, Dramburg S, Alvarez-Perea A, Antolin-Amerigo D, Apfelbacher C, Atanaskovic-
624 Markovic M, et al. The Role of Mobile Health Technologies in Allergy Care: an EAACI Position
625 Paper. *Allergy*. 2019.

626 10. Elliott T, Shih J, Dinakar C, Portnoy J, Fineman S. American College of Allergy, Asthma &
627 Immunology Position Paper on the Use of Telemedicine for Allergists. *Ann Allergy Asthma*
628 *Immunol*. 2017;119(6):512-7.

629 11. Kotz D, Gunter CA, Kumar S, Weiner JP. Privacy and Security in Mobile Health: A Research
630 Agenda. *Computer (Long Beach Calif)*. 2016;49(6):22-30.

631 12. Bousquet J, Devillier P, Arnavielhe S, Bedbrook A, Alexis-Alexandre G, van Eerd M, et al.
632 Treatment of allergic rhinitis using mobile technology with real-world data: The MASK
633 observational pilot study. *Allergy*. 2018;73(9):1763-74.

634 13. Bousquet J, Arnavielhe S, Bedbrook A, Bewick M, Laune D, Mathieu-Dupas E, et al. MASK 2017:
635 ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma multimorbidity using
636 real-world-evidence. *Clin Transl Allergy*. 2018;8:45.

637 14. Article 4 EU GDPR. « Definitions ». EU general data protection regulation 2016/679 (GDPR).
638 <http://www.privacy-regulation.eu/en/article-4-definitions-GDPR.htm>.

639 15. Protection of personal data. Article 29 data protection working party. Opinion 05/2014 on
640 Anonymisation Techniques. European Commission Justice Data protection. 2014;0829/14/EN
641 WP216:http://ec.europa.eu/justice/data-protection/index_en.htm.

642 16. REGULATION (EU) 2016/679 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
643 of 27 April 2016 on the protection of natural persons with regard to the processing of personal data
644 and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection
645 Regulation). Official Organ of the European Union. 2016([http://eur-lex.europa.eu/legal-](http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679&from=EN)
646 [content/EN/TXT/PDF/?uri=CELEX:32016R0679&from=EN](http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679&from=EN)).

647 17. Samreth D, Arnavielhe S, Ingenrieth F, Bedbrook A, Onorato GL, Murray R, et al. Geolocation with
648 respect to personal privacy for the Allergy Diary app - a MASK study. *World Allergy Organ J*.
649 2018;11(1):15.

650 18. Orel A, Bernik I. GDPR and Health Personal Data; Tricks and Traps of Compliance. *Stud Health*
651 *Technol Inform*. 2018;255:155-9.

- 652 19. Medical Device Regulation. Commission Implementing Regulation (EU) 2017/2185 of 23
653 November 2017 <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32017R2185>. 2017.
- 654 20. Kagen S, Garland A. Asthma and Allergy Mobile Apps in 2018. *Curr Allergy Asthma Rep*.
655 2019;19(1):6.
- 656 21. Guidance on the regulation of mobile medical applications. FDA. September 4, 2018.
657 [https://www.fda.gov/MedicalDevices/](https://www.fda.gov/MedicalDevices/DigitalHealth/MobileMedicalApplications/ucm255978.htm) DigitalHealth/MobileMedicalApplications/ucm255978.htm.
658 2018.
- 659 22. Buters JTM, Antunes C, Galveias A, Bergmann KC, Thibaudon M, Galan C, et al. Pollen and spore
660 monitoring in the world. *Clin Transl Allergy*. 2018;8:9.
- 661 23. D'Amato M, Molino A, Calabrese G, Cecchi L, Annesi-Maesano I, D'Amato G. The impact of cold
662 on the respiratory tract and its consequences to respiratory health. *Clin Transl Allergy*. 2018;8:20.
- 663 24. D'Amato G, Annesi Maesano I, Molino A, Vitale C, D'Amato M. Thunderstorm-related asthma
664 attacks. *J Allergy Clin Immunol*. 2017;139(6):1786-7.
- 665 25. Bousquet J, Anto JM, Annesi-Maesano I, Dedeu T, Dupas E, Pepin JL, et al. POLLAR: Impact of air
666 POLLution on Asthma and Rhinitis; a European Institute of Innovation and Technology Health (EIT
667 Health) project. *Clin Transl Allergy*. 2018;8:36.
- 668 26. Bianchi A, Tsilochristou O, Gabrielli F, Tripodi S, Matricardi PM. The Smartphone: A Novel
669 Diagnostic Tool in Pollen Allergy? *J Investig Allergol Clin Immunol*. 2016;26(3):204-7.
- 670 27. Bastl K, Kmenta M, Berger M, Berger U. The connection of pollen concentrations and crowd-
671 sourced symptom data: new insights from daily and seasonal symptom load index data from 2013 to
672 2017 in Vienna. *World Allergy Organ J*. 2018;11(1):24.
- 673 28. Costa C, Menesatti P, Brighetti MA, Travaglini A, Rimatori V, Di Rienzo Businco A, et al. Pilot
674 study on the short-term prediction of symptoms in children with hay fever monitored with e-Health
675 technology. *Eur Ann Allergy Clin Immunol*. 2014;46(6):216-25.
- 676 29. Bastl K, Berger U, Kmenta M. Evaluation of Pollen Apps Forecasts: The Need for Quality Control in
677 an eHealth Service. *J Med Internet Res*. 2017;19(5):e152.
- 678 30. Laumbach R, Meng Q, Kipen H. What can individuals do to reduce personal health risks from air
679 pollution? *J Thorac Dis*. 2015;7(1):96-107.
- 680 31. Prince A, Norris MR, Bielory L. Seasonal ocular allergy and pollen counts. *Curr Opin Allergy Clin*
681 *Immunol*. 2018;18(5):387-92.
- 682 32. Lee J, Kronborg C, O'Hehir RE, Hew M. Who's at risk of thunderstorm asthma? The ryegrass pollen
683 trifecta and lessons learnt from the Melbourne thunderstorm epidemic. *Respir Med*. 2017;132:146-8.
- 684 33. Bastl K, Kmenta M, Berger UE. Defining Pollen Seasons: Background and Recommendations. *Curr*
685 *Allergy Asthma Rep*. 2018;18(12):73.
- 686 34. Pfaar O, Bastl K, Berger U, Buters J, Calderon MA, Clot B, et al. Defining pollen exposure times for
687 clinical trials of allergen immunotherapy for pollen-induced rhinoconjunctivitis - an EAACI position
688 paper. *Allergy*. 2017;72(5):713-22.
- 689 35. Karatzas K, Katsifarakis N, Riga M, Werchan B, Werchan M, Berger U, et al. New European
690 Academy of Allergy and Clinical Immunology definition on pollen season mirrors symptom load for
691 grass and birch pollen-induced allergic rhinitis. *Allergy*. 2018;73(9):1851-9.
- 692 36. Cai T, Zhang Y, Ren X, Bielory L, Mi Z, Nolte CG, et al. Development of a semi-mechanistic
693 allergenic pollen emission model. *Sci Total Environ*. 2019;653:947-57.
- 694 37. Buters J, Schmidt-Weber C, Oteros J. Next-generation pollen monitoring and dissemination. *Allergy*.
695 2018;73(10):1944-5.
- 696 38. Bousquet J, Onorato GL, Oliver G, Basagana X, Annesi-Maesano I, Arnavielhe S, et al. Google
697 Trends and pollen concentrations in allergy and airway diseases in France. *Allergy*. 2019.
- 698 39. Karatzas K, Papamanolis L, Katsifarakis N, Riga M, Werchan B, Werchan M, et al. Google Trends
699 reflect allergic rhinitis symptoms related to birch and grass pollen seasons. *Aerobiologia*. 2018;in
700 press.
- 701 40. Karatzas K, Riga M, Berger U, Werchan M, Pfaar O, Bergmann KC. Computational validation of the
702 recently proposed pollen season definition criteria. *Allergy*. 2018;73(1):5-7.
- 703 41. Zhou AH, Patel VR, Baredes S, Eloy JA, Hsueh WD. Mobile Applications for Allergic Rhinitis. *Ann*
704 *Otol Rhinol Laryngol*. 2018;127(11):836-40.
- 705 42. Sleurs K, Seys S, Bousquet J, Fokkens W, Gorris S, Pugin B, et al. Mobile health tools for the
706 management of chronic respiratory diseases. *Allergy*. 2019.

- 707 43. Ramsey RR, Carmody JK, Holbein CE, Guilbert TW, Hommel KA. Examination of the uses, needs,
708 and preferences for health technology use in adolescents with asthma. *J Asthma*. 2018;1-9.
- 709 44. Braido F, Baiardini I, Puggioni F, Garuti S, Pawankar R, Walter Canonica G. Rhinitis: adherence to
710 treatment and new technologies. *Curr Opin Allergy Clin Immunol*. 2017;17(1):23-7.
- 711 45. Carpenter DM, Geryk LL, Chen AT, Nagler RH, Dieckmann NF, Han PK. Conflicting health
712 information: a critical research need. *Health Expect*. 2016;19(6):1173-82.
- 713 46. Pizzulli A, Perna S, Florack J, Pizzulli A, Giordani P, Tripodi S, et al. The impact of telemonitoring
714 on adherence to nasal corticosteroid treatment in children with seasonal allergic rhinoconjunctivitis.
715 *Clin Exp Allergy*. 2014;44(10):1246-54.
- 716 47. Tan R, Cvetkovski B, Kritikos V, Price D, Yan K, Smith P, et al. Identifying the hidden burden of
717 allergic rhinitis (AR) in community pharmacy: a global phenomenon. *Asthma Res Pract*. 2017;3:8.
- 718 48. Stoyanov SR, Hides L, Kavanagh DJ, Zelenko O, Tjondronegoro D, Mani M. Mobile app rating
719 scale: a new tool for assessing the quality of health mobile apps. *JMIR Mhealth Uhealth*.
720 2015;3(1):e27.
- 721 49. Tinschert P, Rassouli F, Barata F, Steurer-Stey C, Fleisch E, Puhan MA, et al. Prevalence of
722 nocturnal cough in asthma and its potential as a marker for asthma control (MAC) in combination
723 with sleep quality: protocol of a smartphone-based, multicentre, longitudinal observational study
724 with two stages. *BMJ Open*. 2019;9(1):e026323.
- 725 50. Jácome C, R RG, Almeida R, Teixeira JF, Pinho B, Vieira-Marques P, et al. Protocol for a
726 multicentre observational study: mINSPIRERS - Feasibility of a mobile application to measure and
727 improve adherence to inhaled controller medications among adolescents and adults with persistent
728 asthma. *Rev Port ImmunoAll*. 2018;26(1):47-61.
- 729 51. Harari GM, Lane ND, Wang R, Crosier BS, Campbell AT, Gosling SD. Using Smartphones to
730 Collect Behavioral Data in Psychological Science: Opportunities, Practical Considerations, and
731 Challenges. *Perspect Psychol Sci*. 2016;11(6):838-54.
- 732 52. Silsupadol P, Teja K, Lugade V. Reliability and validity of a smartphone-based assessment of gait
733 parameters across walking speed and smartphone locations: Body, bag, belt, hand, and pocket. *Gait
734 Posture*. 2017;58:516-22.
- 735 53. Florack J, Brighetti MA, Perna S, Pizzulli A, Pizzulli A, Tripodi S, et al. Comparison of six disease
736 severity scores for allergic rhinitis against pollen counts a prospective analysis at population and
737 individual level. *Pediatr Allergy Immunol*. 2016;27(4):382-90.
- 738 54. Tripodi S, Comberiat P, Di Rienzo Businco A. A web-based tool for improving adherence to
739 sublingual immunotherapy. *Pediatr Allergy Immunol*. 2014;25(6):611-2.
- 740 55. Bousquet J, Hellings PW, Agache I, Bedbrook A, Bachert C, Bergmann KC, et al. ARIA 2016: Care
741 pathways implementing emerging technologies for predictive medicine in rhinitis and asthma across
742 the life cycle. *Clin Transl Allergy*. 2016;6:47.
- 743 56. Bourret R, Bousquet J, J M, T C, Bedbrook A, P D, et al. MASK rhinitis, a single tool for integrated
744 care pathways in allergic rhinitis. *World Hosp Health Serv*. 2015;51(3):36-9.
- 745 57. Bousquet J, Schunemann HJ, Fonseca J, Samolinski B, Bachert C, Canonica GW, et al. MACVIA-
746 ARIA Sentinel NetworK for allergic rhinitis (MASK-rhinitis): the new generation guideline
747 implementation. *Allergy*. 2015;70(11):1372-92.
- 748 58. Hellings PW, Muraro A, Fokkens W, Mullol J, Bachert C, Canonica GW, et al. A common language
749 to assess allergic rhinitis control: results from a survey conducted during EAACI 2013 Congress.
750 *Clin Transl Allergy*. 2015;5:36.
- 751 59. Klimek L, Bergmann KC, Biedermann T, Bousquet J, Hellings P, Jung K, et al. Visual analogue
752 scales (VAS): Measuring instruments for the documentation of symptoms and therapy monitoring in
753 cases of allergic rhinitis in everyday health care: Position Paper of the German Society of
754 Allergology (AeDA) and the German Society of Allergy and Clinical Immunology (DGAKI), ENT
755 Section, in collaboration with the working group on Clinical Immunology, Allergology and
756 Environmental Medicine of the German Society of Otorhinolaryngology, Head and Neck Surgery
757 (DGHNOKHC). *Allergo J Int*. 2017;26(1):16-24.
- 758 60. Bousquet J, Farrell J, Crooks G, Hellings P, Bel EH, Bewick M, et al. Scaling up strategies of the
759 chronic respiratory disease programme of the European Innovation Partnership on Active and
760 Healthy Ageing (Action Plan B3: Area 5). *Clin Transl Allergy*. 2016;6:29.

- 761 61. Bousquet J, Mohammad Y, Bedbrook A, To T, McGihon R, Barbara C, et al. Country activities of
762 Global Alliance against Chronic Respiratory Diseases (GARD): focus presentations at the 11th
763 GARD General Meeting, Brussels. *J Thorac Dis.* 2018;10(12):7064-72.
- 764 62. Bousquet J, Bedbrook A, Czarlewski W, Onorato GL, Arnavielhe S, Laune D, et al. Guidance to
765 2018 good practice: ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma.
766 *Clin Transl Allergy.* 2019;9:16.
- 767 63. Samolinski B, Fronczak A, Kuna P, Akdis CA, Anto JM, Bialoszewski AZ, et al. Prevention and
768 control of childhood asthma and allergy in the EU from the public health point of view: Polish
769 Presidency of the European Union. *Allergy.* 2012;67(6):726-31.
- 770 64. Raciborski F, Bousquet J, Namyslowski A, Krzych-Falta E, Tomaszewska A, Piekarska B, et al.
771 Dissociating polysensitization and multimorbidity in children and adults from a Polish general
772 population cohort. *Clin Transl Allergy.* 2019;9:4.
- 773 65. Raciborski F, Samolinski B, Krzych-Falta E, Grabczewska A, Furman F, Bieszczad M, et al. The
774 nationwide program of allergic disease prevention as an implementation of GARD guidelines in
775 Poland. *J Thorac Dis.* 2018;10(9):5595-604.
- 776 66. Tchong J, Bakken S, Bates DW, Bonner-III H, Gandhi T, Josephs M, et al. Optimizing strategies for
777 clinical decision support: Summary of a meeting series. . The learning health system series. National
778 Academy of Medicine, Washington DC. 2017:[https://www.healthit.gov/topic/safety/clinical-](https://www.healthit.gov/topic/safety/clinical-decision-support)
779 [decision-support](https://www.healthit.gov/topic/safety/clinical-decision-support).
- 780 67. Bousquet J. Electronic clinical decision support system (eCDSS) in the management of asthma: from
781 theory to practice. *Eur Respir J.* 2019;53(4).
- 782 68. Clinical Decision Support. HealthITgov. 2018;[https://www.healthit.gov/topic/safety/clinical-](https://www.healthit.gov/topic/safety/clinical-decision-support)
783 [decision-support](https://www.healthit.gov/topic/safety/clinical-decision-support).
- 784 69. Courbis AL, Murray RB, Arnavielhe S, Caimmi D, Bedbrook A, Van Eerd M, et al. Electronic
785 Clinical Decision Support System for allergic rhinitis management: MASK e-CDSS. *Clin Exp*
786 *Allergy.* 2018;48(12):1640-53.
- 787 70. Cingi C, Gevaert P, Mosges R, Rondon C, Hox V, Rudenko M, et al. Multi-morbidities of allergic
788 rhinitis in adults: European Academy of Allergy and Clinical Immunology Task Force Report. *Clin*
789 *Transl Allergy.* 2017;7:17.
- 790 71. Bousquet J, Devillier P, Anto JM, Bewick M, Haahtela T, Arnavielhe S, et al. Daily allergic
791 multimorbidity in rhinitis using mobile technology: A novel concept of the MASK study. *Allergy.*
792 2018;73(8):1622-31.
- 793 72. Cibella F, Ferrante G, Cuttitta G, Bucchieri S, Melis MR, La Grutta S, et al. The burden of rhinitis
794 and rhinoconjunctivitis in adolescents. *Allergy Asthma Immunol Res.* 2015;7(1):44-50.
- 795 73. Siroux V, Boudier A, Nadif R, Lupinek C, Valenta R, Bousquet J. Association between asthma,
796 rhinitis, and conjunctivitis multimorbidities with molecular IgE sensitization in adults. *Allergy.*
797 2019;74(4):824-7.
- 798 74. Amaral R, Bousquet J, Pereira AM, Araujo LM, Sa-Sousa A, Jacinto T, et al. Disentangling the
799 heterogeneity of allergic respiratory diseases by latent class analysis reveals novel phenotypes.
800 *Allergy.* 2019;74(4):698-708.
- 801 75. Jantunen J, Haahtela T, Salimaki J, Linna M, Makela M, Pelkonen A, et al. Multimorbidity in
802 Asthma, Allergic Conditions and COPD Increase Disease Severity, Drug Use and Costs: The Finnish
803 Pharmacy Survey. *Int Arch Allergy Immunol.* 2019:1-8.
- 804 76. Huang X, Matricardi PM. Allergy and Asthma Care in the Mobile Phone Era. *Clin Rev Allergy*
805 *Immunol.* 2019;56(2):161-73.
- 806 77. Santo K, Richtering SS, Chalmers J, Thiagalingam A, Chow CK, Redfern J. Mobile Phone Apps to
807 Improve Medication Adherence: A Systematic Stepwise Process to Identify High-Quality Apps.
808 *JMIR Mhealth Uhealth.* 2016;4(4):e132.
- 809 78. Thakkar J, Kurup R, Laba TL, Santo K, Thiagalingam A, Rodgers A, et al. Mobile Telephone Text
810 Messaging for Medication Adherence in Chronic Disease: A Meta-analysis. *JAMA Intern Med.*
811 2016;176(3):340-9.
- 812 79. Adler AJ, Casas JP, Martin N, Free C, Perel P. Cochrane corner: text messaging to improve
813 adherence to drugs for secondary prevention of cardiovascular disease. *Heart.* 2018;104(22):1814-6.
- 814 80. Passalacqua G, Baiardini I, Senna G, Canonica GW. Adherence to pharmacological treatment and
815 specific immunotherapy in allergic rhinitis. *Clin Exp Allergy.* 2013;43(1):22-8.

- 816 81. Incorvaia C, Mauro M, Leo G, Ridolo E. Adherence to Sublingual Immunotherapy. *Curr Allergy*
817 *Asthma Rep.* 2016;16(2):12.
- 818 82. Shields MD, F AL, Rivey MP, McElnay JC. Mobile direct observation of therapy (MDOT) - A rapid
819 systematic review and pilot study in children with asthma. *PLoS One.* 2018;13(2):e0190031.
- 820 83. Kosse RC, Bouvy ML, de Vries TW, Koster ES. Effect of a mHealth intervention on adherence in
821 adolescents with asthma: A randomized controlled trial. *Respir Med.* 2019;149:45-51.
- 822 84. Wang K, Wang C, Xi L, Zhang Y, Ouyang Y, Lou H, et al. A randomized controlled trial to assess
823 adherence to allergic rhinitis treatment following a daily short message service (SMS) via the mobile
824 phone. *Int Arch Allergy Immunol.* 2014;163(1):51-8.
- 825 85. Menditto E, Costa E, Midao L, Bosnic-Anticevich S, Novellino E, Bialek S, et al. Adherence to
826 treatment in allergic rhinitis using mobile technology. *The MASK Study. Clin Exp Allergy.*
827 2019;49(4):442-60.
- 828 86. Bousquet J, Murray R, Price D, Somekh D, Munter L, Phillips J, et al. The allergic allergist behaves
829 like a patient. *Ann Allergy Asthma Immunol.* 2018;121(6):741-2.
- 830 87. Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic
831 Rhinitis and its Impact on Asthma (ARIA) Guidelines - 2016 Revision. *J Allergy Clin Immunol.*
832 2017;140(4):950-8.
- 833 88. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, et al. Allergic
834 Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin Immunol.*
835 2010;126(3):466-76.
- 836 89. Wallace DV, Dykewicz MS, Oppenheimer J, Portnoy JM, Lang DM. Pharmacologic Treatment of
837 Seasonal Allergic Rhinitis: Synopsis of Guidance From the 2017 Joint Task Force on Practice
838 Parameters. *Ann Intern Med.* 2017;177(12):876-81.
- 839 90. Costa DJ, Amouyal M, Lambert P, Ryan D, Schunemann HJ, Daures JP, et al. How representative
840 are clinical study patients with allergic rhinitis in primary care? *J Allergy Clin Immunol.*
841 2011;127(4):920-6.e1.
- 842 91. Price D, Smith P, Hellings P, Papadopoulos N, Fokkens W, Muraro A, et al. Current controversies
843 and challenges in allergic rhinitis management. *Expert Rev Clin Immunol.* 2015:1-13.
- 844 92. Travers J, Marsh S, Williams M, Weatherall M, Caldwell B, Shirlcliffe P, et al. External validity of
845 randomised controlled trials in asthma: to whom do the results of the trials apply? *Thorax.*
846 2017;62(3):219-23.
- 847 93. Yang W, Zilov A, Soewondo P, Bech OM, Sekkal F, Home PD. Observational studies: going beyond
848 the boundaries of randomized controlled trials. *Diabetes Res Clin Pract.* 2010;88 Suppl 1:S3-9.
- 849 94. DiPietro NA. Methods in epidemiology: observational study designs. *Pharmacotherapy.*
850 2010;30(10):973-84.
- 851 95. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices.
852 Guidance for Industry and Food and Drug Administration Staff Document issued on August 31,
853 2017. Bethesda: US Food and Drug Administration, U.S. Department of Health and Human
854 Services Food and Drug Administration, Center for Devices and Radiological Health Center for
855 Biologics Evaluation and Research. CDRHClinicalEvidence@fda.hhs.gov; 2017.
- 856 96. Bedard A, Basagana X, Anto JM, Garcia-Aymerich J, Devillier P, Arnavielhe S, et al. Mobile
857 technology offers novel insights on control and treatment of allergic rhinitis. *The MASK study. J*
858 *Allergy Clin Immunol.* 2019.
- 859 97. Bousquet J, Schunemann HJ, Hellings PW, Arnavielhe S, Bachert C, Bedbrook A, et al. MACVIA
860 clinical decision algorithm in adolescents and adults with allergic rhinitis. *J Allergy Clin Immunol.*
861 2016;138(2):367-74 e2.
- 862 98. Bousquet J, Schünemann H, Togias A, Bachert C, Erhola M, Hellings P, et al. Next-generation
863 ARIA guidelines for allergic rhinitis based on GRADE and real-world evidence. *J Allergy Clin*
864 *Immunol.* 2019;in press.
- 865 99. Bousquet J, Meltzer EO, Couroux P, Koltun A, Kopietz F, Munzel U, et al. Onset of Action of the
866 Fixed Combination Intranasal Azelastine-Fluticasone Propionate in an Allergen Exposure Chamber.
867 *J Allergy Clin Immunol Pract.* 2018;6(5):1726-32.
- 868 100. Konduri N, Aboagye-Nyame F, Mibirizi D, Hoppenworth K, Kibria MG, Doumbia S, et al. Digital
869 health technologies to support access to medicines and pharmaceutical services in the achievement of
870 sustainable development goals. *Digit Health.* 2018;4:2055207618771407.

- 871 101. Mobile-cellular telephone subscriptions. In: Key ICT indicators for developed and developing
872 countries and the world (totals and penetration rates). Geneva: International Telecommunication
873 Union ([http://www.itu.int/en/ITU-](http://www.itu.int/en/ITU-D/Statistics/Documents/statistics/2017/ITU_Key_2005-2017_ICT_data.xls)
874 [D/Statistics/Documents/statistics/2017/ITU_Key_2005-](http://www.itu.int/en/ITU-D/Statistics/Documents/statistics/2017/ITU_Key_2005-2017_ICT_data.xls)
875 [2017_ICT_data.xls](http://www.itu.int/en/ITU-D/Statistics/Documents/statistics/2017/ITU_Key_2005-2017_ICT_data.xls). 2015.
- 875 102. mHealth. Use of appropriate digital technologies for public health Report by the Director-General.
876 SEVENTY-FIRST WORLD HEALTH ASSEMBLY, WHO.
877 2018;http://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_20-en.pdf.
- 878 103. Handbook m. BE HE@LTHY BE MOBILE. A handbook on how to implement mBreatheFreely for
879 asthma and COPD. WHO Publication. 2018;<https://apps.who.int/iris/handle/10665/274575>.
- 880 104. Vandenplas O, Vinnikov D, Blanc PD, Agache I, Bachert C, Bewick M, et al. Impact of Rhinitis on
881 Work Productivity: A Systematic Review. *J Allergy Clin Immunol Pract*. 2018;6(4):1274-86 e9.
- 882 105. Bousquet J, Hellings PW, Agache I, Amat F, Annesi-Maesano I, Ansotegui IJ, et al. Allergic Rhinitis
883 and its Impact on Asthma (ARIA) Phase 4 (2018): Change management in allergic rhinitis and
884 asthma multimorbidity using mobile technology. *J Allergy Clin Immunol*. 2019;143(3):864-79.
- 885 106. Bousquet J, Onorato GL, Bachert C, Barbolini M, Bedbrook A, Bjermer L, et al. CHRODIS criteria
886 applied to the MASK (MACVIA-ARIA Sentinel Network) Good Practice in allergic rhinitis: a
887 SUNFRAIL report. *Clin Transl Allergy*. 2017;7:37.
- 888 107. Bousquet J, Anto JM, Akdis M, Auffray C, Keil T, Momas I, et al. Paving the way of systems
889 biology and precision medicine in allergic diseases: The MeDALL success story. *Allergy*.
890 2016;71(11):1513-25.
- 891 108. Bousquet J, Burney PG, Zuberbier T, Cauwenberge PV, Akdis CA, Bindslev-Jensen C, et al.
892 GA2LEN (Global Allergy and Asthma European Network) addresses the allergy and asthma
893 'epidemic'. *Allergy*. 2009;64(7):969-77.
- 894 109. Caimmi D, Baiz N, Tanno LK, Demoly P, Arnavielhe S, Murray R, et al. Validation of the MASK-
895 rhinitis visual analogue scale on smartphone screens to assess allergic rhinitis control. *Clin Exp*
896 *Allergy*. 2017;47(12):1526-33.
- 897 110. Bousquet J, Caimmi DP, Bedbrook A, Bewick M, Hellings PW, Devillier P, et al. Pilot study of
898 mobile phone technology in allergic rhinitis in European countries: the MASK-rhinitis study.
899 *Allergy*. 2017;72(6):857-65.
- 900 111. Bousquet J, Bewick M, Arnavielhe S, Mathieu-Dupas E, Murray R, Bedbrook A, et al. Work
901 productivity in rhinitis using cell phones: The MASK pilot study. *Allergy*. 2017;72(10):1475-84.
- 902 112. Bousquet J, VandenPlas O, Bewick M, Arnavielhe S, Bedbrook A, Murray R, et al. The Work
903 Productivity and Activity Impairment Allergic Specific (WPAI-AS) Questionnaire Using Mobile
904 Technology: The MASK Study. *J Investig Allergol Clin Immunol*. 2018;28(1):42-4.
- 905 113. Bousquet J, Arnavielhe S, Bedbrook A, Fonseca J, Morais Almeida M, Todo Bom A, et al. The
906 Allergic Rhinitis and its Impact on Asthma (ARIA) score of allergic rhinitis using mobile technology
907 correlates with quality of life: The MASK study. *Allergy*. 2018;73(2):505-10.
- 908 114. Hellings PW, Borrelli D, Pietikainen S, Agache I, Akdis C, Bachert C, et al. European Summit on
909 the Prevention and Self-Management of Chronic Respiratory Diseases: report of the European Union
910 Parliament Summit (29 March 2017). *Clin Transl Allergy*. 2017;7:49.
- 911 115. Valiulis A, Bousquet J, Veryga A, Suprun U, Sergeenko D, Cebotari S, et al. Vilnius Declaration on
912 chronic respiratory diseases: multisectoral care pathways embedding guided self-management,
913 mHealth and air pollution in chronic respiratory diseases. *Clin Transl Allergy*. 2019;9:7.
- 914 116. Yorgancioglu AA, Gemicioglu B, Kalayci O, Kalyoncu AF, Cingi C, Murray R, et al. [MASK
915 (Mobile Airways Sentinel network) in Turkey-the ARIA integrated mobile solution for allergic
916 rhinitis and asthma multimorbidity]. *Tuberk Toraks*. 2018;66(2):176-81.
- 917 117. Gomez RM, Gonzalez-Diaz SN, Urrutia-Pereira M, Valentin-Rostan M, Yanez A, Jares E, et al.
918 [2017 Brussels Agreement for Latin America: an initiative of the GARD and Slaai]. *Rev Alerg Mex*.
919 2018;65(3):137-41.
- 920 118. Ivancevich JC, Neffen H, Zernotti ME, Asayag E, Blua A, Ciceran A, et al. [ARIA 2016 executive
921 summary: Integrated care pathways for predictive medicine throughout the life cycle in Argentina].
922 *Rev Alerg Mex*. 2017;64(3):298-308.
- 923 119. Larenas-Linnemann D, Mullol J, Ivancevich JC, Anto JM, Cardona V, Dedeu T, et al. [MASK
924 (Mobile Airways Sentinel Network). ARIA's comprehensive solution for mobile app for the
925 multimorbidity of allergic rhinitis and asthma]. *Rev Alerg Mex*. 2019;66(1):140-6.

926 120. Bousquet J, Agache I, Aliberti MR, Angles R, Annesi-Maesano I, Anto JM, et al. Transfer of
927 innovation on allergic rhinitis and asthma multimorbidity in the elderly (MACVIA-ARIA) - EIP on
928 AHA Twinning Reference Site (GARD research demonstration project). *Allergy*. 2018;73(1):77-92.

Table 1: Global applicability of mHealth Apps in allergic rhinitis (adapted from (13))

Applicability	mHealth Apps
Clinical practice	<p>Physicians will be able to read the files of the patients in order to:</p> <ul style="list-style-type: none"> • 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 . • Apps are an essential tool for providing personalized medicine in AR and asthma.
Change management	<ul style="list-style-type: none"> • Many patients are uncontrolled and non-adherent to treatment. Apps can indirectly assess and help (e.g., 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • To assess environmental control measures • To assess pharmacotherapy • For RCTs, it is essential to have clarity on definitions, and relevant tools. Apps allow <ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> • To confirm RCTs • And bring new hypotheses for the treatment of AR and asthma
Registration and reimbursement of medicines	<ul style="list-style-type: none"> • Controlled trials designed with a uniform approach will be more easily evaluated by the Health Technology Assessment agencies (such as NICE) for reimbursement. • Better understanding of direct and indirect costs • Controlled trials designed with a uniform approach will help to synchronize the data from real-life world regarding clinical effects and safety/tolerability of new drugs (post-marketing pharmacovigilance for some apps)
Research on mechanisms and genetics	<ul style="list-style-type: none"> • A uniform definition and a collaborative approach to epidemiological, genetic and mechanistic research are 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 old age subjects.
Epidemiology	<ul style="list-style-type: none"> • 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 to 60 B€. 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.

Table 2: Examples of mHealth apps for allergic rhinitis

		Pollen	Other risk factors	Health data	
Multicountry					
	Air Matters	X	X		https://air-matters.com
	AllergyMonitor	X		X	
	Austria Pollen Information Service	X		X	www.pollenwarndienst.at
	Breezometer	X	X		https://breezometer.com/products/pollen-api
	The Weather Channel	X			https://play.google.com/store/apps/details?id=com.weather.Weather
	POLLEN & PHD	X		X	https://www.polleninfo.org , two separate but interlinked apps
	MASK-air			X	https://www.mask-air.com
	Pollen alert Europe	X			https://play.google.com/store/apps/details?id=com.bluesula.allergyalarmeuropa&hl=en
Argentina	Alerta Polen Argentina	X			https://play.google.com/store/apps/details?id=com.mobillers.alertapolen&hl=es
Australia	Air Rater				https://airrater.org
Denmark	Dagens Pollental	X			https://www.astma-allergi.dk/dagenspollental
France	ALK-Allergik				https://maviedallergik.fr/nos-services
	Allergy Track				https://www.android-logiciels.fr/allergy-track/
	i-pollen				http://www.gammehumex.fr/application-i-pollen/
	Plume Air Report				https://air.plumelabs.com/fr/
Germany	Pollen App	X		X	http://www.pollenstiftung.de/ak
Italy	Pollen App	X	X		https://itunes.apple.com/it/app/polliniitalia/id621302844?mt=8
		X	X		https://www.ilpolline.it/i-calendari-pollinici
	Allergy Control	X	X	X	https://itunes.apple.com/it/app/allergy-control/id973452501?mt=8
	Allergy Monitor	X		X	https://play.google.com/store/apps/details?id=com.tpsproduction.allergymonitor&hl=it
	MeteoAllergie	X			https://play.google.com/store/apps/details?id=com.dlsolutions.meteoallergie&hl=it

MASK-air			X	https://www.mask-air.com
----------	--	--	---	---

	Bollettino meteo Pollini e allergie in Italia	X			https://www.3bmeteo.com/meteo/italia/pollini
	RAPP (Rhinitis and Asthma Patient Perspective)			X	https://play.google.com/store/apps/details?id=com.wellnessandwireless.rapp
NL		X			https://pollennieuws.nl/
		X			https://hooikoortsradar.nl/
Poland	e-allergy			X	
Portugal	INSPIRERSMUNDI			X	https://www.facebook.com/Projeto-Inspirers-218849795347948
Spain	INSPIRERSMUNDI			X	https://www.facebook.com/Projeto-Inspirers-218849795347948
	R-Alergo	X			http://alergialafe.org/noticias/172-r-alerigo
	Polen Control	X			https://www.seaic.org/inicio/polen-control
	Niveles de Polen	X			https://play.google.com/store/apps/details?id=es.diox.android.alergia&hl=es
	Intolerapp	X			https://socialmediatica.com/intolerapp-la-aplicacion-ideal-para-alergicos-e-intolerantes-alimentarios/
	ALK Polen	X			http://www.ticsalut.cat/observatori/es_apps/265/al-k-polen
	Planttes	X			http://www.planttes.com/
Switzerland	AllyScience				https://allyscience.ch/
UK	My Pollen forecast UK	X			https://itunes.apple.com/gb/app/my-pollen-forecast-uk/id1244428929?mt=8
	Piri	X			http://www.piri allergy.com/pollen-count.html
USA	AcuPollen				http://www.nynjpollen.com
	My Pollen Forecast	X		X	https://www.jrustonapps.com/apps/my-pollen-forecast
	Plume Air Report	X		X	https://plumelabs.com/en/air/
	Poncho: wake up wheather	X			https://www.crunchbase.com/apptopia_app/39a4271c-7286-4523-bed3-7cecdf55e0bf
	WeathterBug				https://www.weatherbug.com

Table 3: The global MASK Good Practice and IT solution (modified from (62))

App (MASK-air) deployed in 23 countries: TRL9 (Technology Readiness level), Electronic clinical decision support system (ARIA e-CDSS): TRL 7, e-physician questionnaire deployed in 16 countries: TRL9.

- App: 29,000 users, 23 countries, 17 languages
- Tested with patients
- GDPR including geolocation (17)
- Good Practice of the EIP on AHA, follows CHRODIS (106)
- Good Practice on digitally-enabled, integrated, patient-centred care endorsed by DG Santé (62)
- Based on 11 EU grants (MeDALL (107), GA²LEN (108)) including - in 2018 - POLLAR (25), 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 guidelines (109).
 - Baseline characteristics (110)
 - Work productivity (111, 112)
 - EQ-5D and WPAI-AS (113)
 - Novel phenotypes of allergic diseases (71)
 - Adherence to treatment (12, 85)
 - Novel approaches to inform the efficacy of treatment (12, 96)
- Patient’s organizations and scientific societies involved
- GARD (WHO alliance)
- Presented during WHO and EU ministerial meetings (114, 115)
- Next-generation care pathways meeting (Dec 3, 2018) with the EIP on AHA, POLLAR (EIT Health) and GARD
- 51 MASK papers in 12 languages (116-119)
- Dissemination according to the EIP on AHA (60)

Transfer of innovation (TWINNING (120))

- Interoperable platform with MASK
- 25 Reference Sites of the European Innovation Partnership on Active and Healthy Ageing plus Argentina, Australia, Brazil, Canada, Mexico (116-119)
- 900 patients enrolled
- GDPR solutions solved

ARIA e-CDSS

- Interoperable platform with MASK
- Based on an expert meeting (97), and validation by Delphi questionnaire (69) and real-world evidence using MASK-air (12, 96)
- Electronic version available (69)