

PROF. ANA M GIMÉNEZ ARNAU (Orcid ID : 0000-0001-9548-5423)

DR. IVAN CHERREZ-OJEDA (Orcid ID : 0000-0002-1610-239X)

PROF. MARTIN METZ (Orcid ID : 0000-0002-4070-9976)

DR. KARSTEN WELLER (Orcid ID : 0000-0003-4437-0313)

PROF. TORSTEN ZUBERBIER (Orcid ID : 0000-0002-1466-8875)

PROF. JEAN BOUSQUET (Orcid ID : 0000-0002-4061-4766)

PROF. MARCUS MAURER (Orcid ID : 0000-0002-4121-481X)

Automatic screening of self-evaluation apps for urticaria and angioedema shows a high unmet need

Manuscript Acceptance Date: 19-Aug-2021

Aram Antó^{1,*}, Rasmus Maurer^{2,*}, Ana Gimenez-Arnau³, Ivan Cherrez-Ojeda⁴, Tomasz Hawro², Markus Magerl², Martin Metz², Karsten Weller², Torsten Zuberbier⁵, Jean Bousquet^{5, 6}, Marcus Maurer²

*Both authors contributed equally

¹ MASK-air, Montpellier, France

² Dermatological Allergology, Allergie-Centrum-Charité, Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany

³ Department of Dermatology. Hospital del Mar. Institut Mar d'Investigacions Mèdiques. Universitat Pompeu Fabra. Barcelona, Spain

⁴ Universidad Espíritu Santo, Samborondón, Ecuador

⁵ Comprehensive Allergy Centre Charité, Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/ALL.15061](#)

This article is protected by copyright. All rights reserved

20
21 **Keywords:** Wheals, itch, swelling, javascript, automatic search, Google, Apple

22
23 **Word count:** 622
24 **Table(s):** 1

25
26 **Acknowledgements:**

27 Dr. Antó has nothing to disclose.

28 Rasmus Maurer has nothing to disclose.

29 Dr. Gimenez-Arnau reports grants and personal fees from Uriach Pharma, grants, personal fees
30 and other from NOVARTIS PHARMA , personal fees from SANOFI - REGENERON , personal
31 fees from AMGEN , grants and personal fees from GSK, personal fees from THERMO FISHER ,
32 personal fees from ALMIRALL , grants from CARLOS III FEWDER , personal fees from
33 AVENE, personal fees and other from LEO, outside the submitted work.

34 Dr. Cherrez-Ojeda reports grants from Universidad Espiritu Santo, personal fees from Sanofi,
35 outside the submitted work.

36 Dr. Hawro has nothing to disclose.

37 Dr. Magerl reports personal fees and non-financial support from Shire / Takeda, personal fees and
38 non-financial support from CSL Behring, personal fees from Pharming, personal fees and non-
39 financial support from Biocryst, personal fees from Kalvista, personal fees from Octapharma,
40 personal fees from Novartis, outside the submitted work.

41 Dr. Metz reports personal fees from Novartis, personal fees from Sanofi, personal fees from
42 Celldex, personal fees from Moxie, personal fees from Pharvaris, outside the submitted work.

43 Dr. Weller reports personal fees from Biocryst, personal fees from Moxie, grants and personal fees
44 from Novartis, grants and personal fees from Takeda, outside the submitted work.

45 Dr. Zuberbier reports personal fees from Bayer Health Care, personal fees from FAES, grants and
46 personal fees from Novartis, grants and personal fees from Henkel, personal fees from
47 AstraZeneca, personal fees from AbbVie, personal fees from ALK, personal fees from Almirall,
48 personal fees from Astellas, personal fees from Bayer Health Care, personal fees from Bencard,
49 personal fees from Berlin Chemie, personal fees from FAES, personal fees from HAL, personal

fees from Leti, personal fees from Meda, personal fees from Menarini, personal fees from Merck,
personal fees from MSD, personal fees from Novartis, personal fees from Pfizer, personal fees
from Sanofi, personal fees from Stallergenes, personal fees from Takeda, personal fees from Teva,
personal fees from UCB, personal fees from Henkel, personal fees from Kryolan, personal fees
from L'Oréal, outside the submitted work; and Organizational affiliations: Committee member:
WHO-Initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA) Member of the Board:
German Society for Allergy and Clinical Immunology (DGAKI) Head: European Centre for
Allergy Research Foundation (ECARF) President: Global Allergy and Asthma European Network
(GA²LEN) Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy
Organization (WAO).

Dr. Bousquet reports personal fees from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan,
Novartis, Sanofi-Aventis, Takeda, Teva, Uriach, other from KYomed, MASK-air, outside the
submitted work; .

Dr. Maurer reports grants and personal fees from Allakos, personal fees from Aralez, grants from
ArgenX, grants from AstraZeneca, personal fees from Celldex, grants and personal fees from CSL
Behring, grants and personal fees from FAES, grants and personal fees from Genentech, grants
from Innate Pharma, personal fees from Kalvista, grants and personal fees from Kyowa Kirin,
grants from Leo Pharma, grants from Lilly, grants and personal fees from Menarini, grants and
personal fees from Moxie, grants and personal fees from Novartis, grants from Roche, grants and
personal fees from Sanofi/Regeneron, grants and personal fees from Shire/Takeda, grants and
personal fees from UCB, grants and personal fees from Uriach, outside the submitted work.

Corresponding author:

Marcus Maurer, MD

Charité – Universitätsmedizin Berlin

Dept. of Dermatology and Allergy

Dermatological Allergology

Charitéplatz 1

10117 Berlin, Germany

79 Phone: +49-30-450-518 043
80 Fax: +49-30-450-518 972
81 Email: marcus.maurer@charite.de

82

83 To the editor

84 In chronic urticaria (CU) and recurrent angioedema (RAE), the need for effective treatment is
85 high. The goals are for patients to have no signs and symptoms, normal quality of life (QoL), and
86 complete disease control. Disease activity is assessed using scores such as the urticaria and the
87 angioedema activity scores, i.e. patient-reported outcome measures (PROMs) that rely on the daily
88 documentation, by patients, of wheals and itch and of angioedema, respectively. This is
89 complemented by the regular assessment of QoL and disease control with suitable PROMs, e.g.
90 the urticaria control test (UCT) or the angioedema control test (AECT)¹.

91 Apps are ideally suited for documentation of the patients' daily signs and symptoms and
92 regular assessments of their QoL and disease control. Apps can also help to identify relevant
93 triggers (e.g. stress, infections), consequences (e.g. sleep impairment, missing work or school),
94 and comorbidities, a major need in CU and RAE. Moreover, apps can optimize treatment by
95 individualizing therapy in order to reach goals.

96 However, the availability and functionality of apps for the self-evaluation of CU and RAE
97 are unknown. To address this knowledge gap, we developed and applied an automatic search
98 algorithm for self-evaluation apps for CU and RAE in Apple App and Google Play stores.

99 We used the methods that we had previously applied to asthma and anaphylaxis. The
100 search was performed in July 2021 (Fig. 1). Briefly, we first designed the search algorithm to
101 include seven search terms, each in three languages, i.e. English, German, and Spanish
102 (supplemental Table 1), then used the algorithm to search the app stores in 16 countries
103 (supplemental Table 2), and finally assessed the apps identified for eligibility, i.e. helping patients
104 to track their signs and symptoms and manage their disease, by integrating information on triggers,
105 consequences, comorbidities, and/or treatment. Our manual search, performed in parallel, used the
106 same search terms, app stores, languages, countries, and eligibility criteria (Table 1). The apps
107 were then assessed for their availability, functions, and features.

108 Our automatic and manual searches both identified the same nine apps for CU and/or RAE
109 self-evaluation (Table 1): (i) 4 for hereditary angioedema (HAE), i.e. Advance HAE, HAERO,
110 myHAE, and HAE & me, none of which allow for tracking of wheals or itch, and (ii) 5 for CU, i.e.
111 TARGET My Hives, UrCare, UrticariApp and SymTrac™ HIVES (Table 1). All apps can be used
112 to document signs and symptoms, an inclusion criterion of our search. Of the 9 apps, 6 allowed for
113 the documentation of triggers, 3 for PROM-based disease-driven impact, 6 for treatment, and one

114 for disease control. Only one app was available in more than two languages, and none covered
115 comorbidities or provided individualized advice (Table 1).

116 Our findings demonstrate that currently available iOS/Android apps for the self-evaluation
117 of CU and RAE are very limited in number, function, and geographical reach, and that none cover
118 comorbidities. Use of the same approach in asthma and anaphylaxis showed very similar results.
119 The results of the UCARE CURICT study demonstrated that most CU patients, especially those
120 with higher education and in rural areas, are interested in the use of digital tools for their health
121 care ^{3,4}. Clearly, better apps are needed and wanted.

122 Taken together, we identified a major unmet need in CU and RAE: that of the lack of
123 suitable apps for patients to (i) self-evaluate their disease activity, impact, and control, (ii) improve
124 the self-management of their condition by recognizing important triggers of exacerbation,
125 comorbidities, and consequences of their disease, and (iii) optimize their therapy including allergic
126 comorbidities. Novel apps that allow patients to do this are needed globally. Such apps are
127 expected to improve the management of CU and RAE and may also serve as important tools for
128 CU and RAE research.

129

130

Table 1 Available apps for the self-evaluation of urticaria and angioedema

Name of App	For	App store(s) availability	Signs and symptoms	Triggers	Impact	Comorb -idities	Medication	Advice	Languages	Made by
Advance HAE	HAE	Apple, Google	• Angioedema (duration and location)	N = 22 ¹ Others (can be entered)	Impact of attack School/work days missed	No	N = 7 ² regular N = 16 ³ on demand Others (can be entered)	No	Eng	HAEA
HAERO	HAE	Apple, Google	• Angioedema (location) • Pain	N = 9 ⁴ Others (can be entered)	School/work days missed	No	N = 5 ⁵	No	Eng, Fre	AOHQ
myHAE	HAE	Apple, Google	• Angioedema (body part affected)	N = 6 ⁶ Others (can be entered)	No	No	On demand and regular medication can be entered	No	Eng, Ger	Takeda
HAE & Me	HAE	Apple	• Angioedema (location) • Angioedema severity	N = 8 ⁷ Others (can be entered)	No	No	N = 9 ⁸	No	Eng	Pharming
TARGET My Hives	CU	Apple	• Urticaria severity • Angioedema severity	N = 99 Others (can be entered)	Yes	No	On demand medication can be entered	No	Eng, Fre, Ger, Gre, Por, Spa, Tur	Novartis
UrCare	CU	Apple, Google	• Urticaria severity • Angioedema severity • Number of hives	No	QoL (CU-Q2oL)	No	Yes, access to online drug database	No	Eng, Spa	Novartis

Urticaria	CU	Google	• Wheals, Redness, Swellings (numbers) • Itch (duration and intensity)	Yes (can be entered)	Yes (question 3 of UCT)	No	On demand and regular medication can be entered	No	Eng, Ger	GAAPP
UrticariApp	CU	Apple, Google	• Wheals (number) • Itch (severity) • Angioedema (location)	No	Yes, can be entered	No	No	No	Eng, Spa	AAUC
SymTrac™ HIVES	CU	Google	• Urticaria (severity) • Angioedema severity • Number of hives	No	QoL (DLQI)	No	No	No	Eng	Novartis

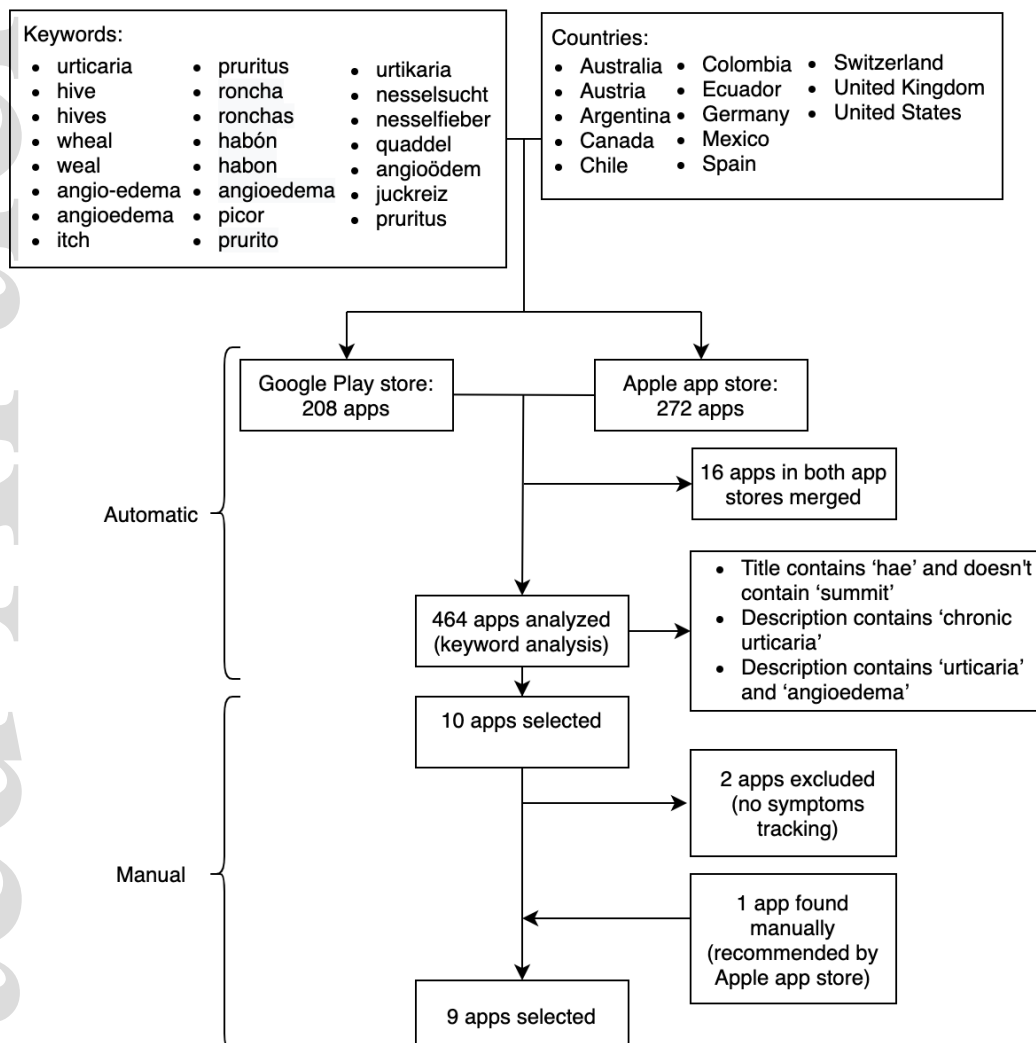
For = Disease the app was developed for, i.e. HAE = hereditary angioedema or CU = chronic spontaneous urticaria (all CU apps are only for patients chronic spontaneous urticaria, and not for patients with other forms of chronic urticaria); Advice = Does the app offer individualized advice to user, based on the user's data/documentation. Abbreviations: UAS = urticaria activity score, i.e. assessment of itch (none, mild, moderate, severe) and wheals (0, 0-19, 20-50, >50) in last 24h; AAS = angioedema activity score; i.e. yes/no = screener question, 5 follow up questions for yes; UCT = urticaria control test; DLQI = dermatologic quality of life index; CU-Q2oL = chronic urticaria quality of life questionnaire; AAUC = Asociación der Afectados de Urticaria Crónica; HAEA = US Hereditary Angioedema Association; AOHQ = Association des Patients d'Angio-Oedeme Hereditaire du Quebec; GAAPP = Global Allergy and Asthma Patient Platform ; Eng = English, Fre = French, Ger = German, Gre = Greek, Por = Portuguese, Spa = Spanish, Tur = Turkish; ¹routine dental cleaning, other dental procedure, medical procedure, minor injury or prolonged physical pressure, infection/illness, taking birth control, menstrual period, menopause, being pregnant, fatigue, being on hormone replacement therapy, food or non-alcoholic beverages, stress, anger/frustration, lack of sleep, medication, alcohol, sadness/depression, constipation, anxiety, weather; ²androgens, antifibrinolytics, C1-inhibitor intravenously; C1-Inhibitor subcutaneously, progesterone, clinical study drug (can be typed in), lanadelumab; ³berinert, cinryze, ruconest, heagarda, kalbitor, firazyf, corticosteroids, antihistamines, clinical trial study drug (can be typed in), narcotic pain medicine, non-narcotic pain medicine, intravenous fluids, additional androgens, additional anti-fibrinolytics, fresh frozen plasma, epinephrine; ⁴stress, trauma, surgical procedures, contraceptives, angiotensin converting enzyme-inhibitors, dental work, viral infections, hormone replacement therapy, unknown; ⁵berinert, cinryze, firazyf, heagarda, takhzyro; ⁶infection, stress, medical or dental procedure, trauma, flue-like symptoms, unknown; ⁷anxiety, stress, minor injury, dental/medical/surgical procedure, fatigue, certain medications, infection, hormonal changes; ⁸ruconest, firazyf, kalbitor, berinert, cinryze, heagarda, takhzyro, orladeyo, generic icatibant; ⁹scratching, cold, sun, pressure, exercise, heat, alcohol, allergies, unknown; Remind = apps reminds user to enter data and/or to refill prescription.

References

1. Weller K, Zuberbier T, Maurer M. Clinically relevant outcome measures for assessing disease activity, disease control and quality of life impairment in patients with chronic spontaneous urticaria and recurrent angioedema. *Curr Opin Allergy Clin Immunol*. 2015;15(3):220-226.
2. Anto A, Sousa-Pinto B, Bousquet J. Anaphylaxis and digital medicine. *Curr Opin Allergy Clin Immunol*. 2021.
3. Cherrez-Ojeda I, Vanegas E, Cherrez A, et al. How are patients with chronic urticaria interested in using information and communication technologies to guide their healthcare? A UCARE study. *World Allergy Organ J*. 2021;14(6):100542.
4. Maurer M, Weller K, Magerl M, et al. The usage, quality and relevance of information and communications technologies in patients with chronic urticaria: A UCARE study. *World Allergy Organ J*. 2020;13(11):100475.

Accepted Article

Figure 1: Search and exclusion criteria



Supplemental material

Methods

Study design and data sources

An automatic app screening tool (2) was used to identify apps for the self-management of urticaria and angioedema available on Apple App and Google Play stores. A qualitative analysis was performed on each of the apps identified as relevant. The automatic search was performed on 1st July 2021. The selected countries of app availability are listed in Supplemental Table 1.

Eligibility criteria of apps

We included all apps concerning the self-management of urticaria and angioedema. Apps were included if they allowed users to track the evolution of their signs and symptoms and aimed to help them manage their disease (i.e., integrating information on risk exposures, triggers, comorbidities, and/or treatment). We excluded apps (i) that did not belong to the “Medical” or “Health & Fitness” categories, (ii) whose description was not in English, German or Spanish, (iii) that had not been published or updated within the last three years, (iv) that had solely informative or investigative purposes, or (v) whose aim was to promote alternative treatments.

Apps search process

An automatic app search program (2), which performs web crawling on Apple and Google app stores, was used for this study. The app search program iterated over the following two input variables:

- Search terms: Supplemental Table 2
- Countries: Supplemental Table 1

The Apple App and Google Play stores were automatically searched, using the search terms listed in Supplemental Table 2. For each search term, automatic searches were performed on each of the geographic locations listed in Supplemental Table 1. Therefore, a total of 140 iterations for each store were performed (considering all the country/keyword combinations according to Supplemental Tables 1 and 2). The number of results retrieved at each iteration was limited to a maximum of 200 apps.

After retrieving the search results from all iterations, the program compared the titles of all retrieved apps, discarding the duplicates. After duplicate removal, an automatic selection algorithm based on the defined eligibility criteria was applied. According to this algorithm, apps were automatically excluded if they did not meet the following criteria:

- Apps belonging to the categories ‘Medical’ or ‘Health & Fitness’;
- Apps with an English, German or Spanish written description;
- Apps published/updated within the last three years.

In addition, the selection algorithm encompassed the application of a set of logical statements, performing text analysis within the apps’ title and description. This allowed for the automatic selection of apps for which:

- The title contained the acronym ‘hae’ and did not contain the word ‘summit’
- The description contained the text string ‘chronic urticaria’
- The description contained the words ‘urticaria’ and ‘angioedema’

The apps that did not meet any of these three conditions were automatically discarded (Figure 1).

The apps not automatically excluded by the screening algorithm were manually checked by two independent reviewers who classified them according to the predefined eligibility criteria. This manually excluded any irrelevant apps (Figure 1).

Review of relevant apps

A qualitative review was performed on each of the selected apps. The focus of the review process was on the apps' self-management features, which were classified into five different categories: signs/symptoms, triggers, impact, comorbidities, advice and medication. The apps were also classified according to the condition being addressed: CSU or HAE. Some additional information - such as the app stores on which the apps are present and the developer - were also saved.

Supplemental Table 1: Countries and corresponding languages

Countries	Languages
US	English, Spanish
Canada, UK, Australia	English
Germany, Switzerland, Austria	German, English
Spain, Ecuador, Argentina, Colombia, Chile, Mexico	Spanish

Supplemental Table 2: Search terms

English	German	Spanish
urticaria	urtikaria	urticaria
hive(s)	nesselsucht / nesselfieber	roncha(s)
wheal/weal	quaddel	habón
angio-edema	angioödem	angioedema
itch	juckreiz	picor
pruritus	pruritus	prurito