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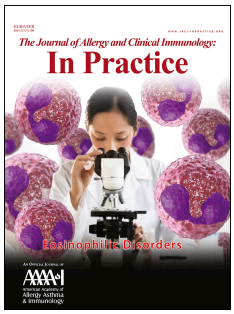

Usage prevalence of angioedema patient-reported outcome measures: results from the UCARE and ACARE PROMUSE study

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Clinical Implications Box: (32/40 words)

Despite the potential to enhance patient care, PROMs are underutilized in angioedema management. National/international medical societies should promote the widespread adoption of PROMs and assist physicians to overcome barriers to their use.

Abstract: NA

Keywords: angioedema; quality of life; patient-reported outcomes; Angioedema Activity Score; Angioedema Quality of Life Questionnaire; Angioedema Control Test

Clinical Communication

Angioedema manifests as self-limited, localized, and transient swellings of the skin or mucosal tissues due to a loss of vascular integrity. This allows fluid to move into tissues such as the face, larynx, genitals, and bowel wall(1). The global lifetime prevalence of acquired and hereditary angioedema is 7.4%(2) and 0.002%(3), respectively. Notably, angioedema is the third most common skin condition in emergency medicine.(4)

The burden of angioedema includes poor quality of life, mental issues, and reduced work and school productivity, leading to substantial direct and indirect expenses.(5) Patient-reported outcome measures (PROMs) asses disease burden, activity, and control.(6) PROMs are also used to assess the response to treatments in routine clinical practice and help to evaluate innovative therapies under development in clinical trials. Moreover, the integration of PROMs will promote cooperative decision-making among healthcare practitioners and patients, eventually improving patient satisfaction and optimizing treatment outcomes(6).

In angioedema, the three most widely used PROMs are the Angioedema Activity Score (AAS)(7), the Angioedema Quality of Life Questionnaire (AE-QoL),(8) and the Angioedema Control Test (AECT).(9) These tools are validated(7–9), recommended by current guidelines, freely available in many languages and country versions, yet the rate of their use in angioedema management is currently unknown.

To address this gap, the global networks of Urticaria Centers of Reference and Excellence (UCAREs) and Angioedema Centers of Reference and Excellence (ACAREs) performed a cross-sectional study, PROMUSE (IRB approval No. HCK-

CEISH-21-002), to assessed which and how often PROMs are used by physicians who treat patients with angioedema, and to identify what physicians perceive as barriers to the use of PROMs. In total, 370 angioedema-treating physicians from 39 countries completed the PROMUSE 53-item questionnaire.

Of 370 physicians who treat patients with angioedema, only 32 (9%) used all three PROMs, i.e. the AAS, the AE-QoL, and the AECT. Two and one of these PROMs were used by 82 and 105 of 370 physicians, i.e. 22% and 28%, respectively, and 151 physicians (41%) did not use any of them. The AAS was the most used angioedema PROM (48%; n=180), followed by the AE-QoL (43%; n=161/370) and the AECT (28%; n=102/370). Of physicians who use the AAS, the AE-QoL, and the AECT, only 19%, 19%, and 23%, respectively, reported using it always, i.e. in all of their patients (**Table 1 and Table E1**).

Allergists, compared to other specialties, used the AAS, AE-QoL, and/or the AECT more often (n=163, 44%, P=0.039), and of 163 allergists, 53% (n=86), 26% (n=42), and 12% (n=20) used one, two, and three PROMs, respectively. Multivariate regression showed that allergists use PROMS 4.3 times more often than other specialties (P<0.05; **Table 2**). Furthermore, clinicians who concurrently practiced in both public and private settings had a 3.6-fold higher use of angioedema PROMs as compared to those who worked in either a public or private setting (P<0.05). Female physicians were more likely to use angioedema PROMs as compared to male physicians, i.e. 44% vs 33%, but this difference was not statistically significant. Physicians with <20 years of specialty experience were 60% less likely to use ≥1 PROM for angioedema (OR: 0.409).

The three most common reasons for using angioedema PROMs, reported by ≥90% of PROM-using physicians, were monitoring disease control, assessing

disease activity, and guiding decision-making (**Table 1**). The most commonly perceived barriers, reported by >50% of physicians who use PROMs, were time restrictions (80%), patients' reluctance to complete questionnaires (60%), lack of PROM integration in healthcare systems (60%), that PROMs are not mandatory (54%), and unavailability for certain age groups (52%; **Table 1**). Multivariate logistic regression showed that younger specialists found “time constraints” to be a challenge more often than older ones (P<0.05) (**Table 2**). Specialists were 6.5 times more likely to perceive "time constraints" as a barrier vs non-specialists. Physicians who practice in both public and private settings were 56% less likely to cite "patients disliking questionnaires" as a barrier, compared to those who exclusively work in private or public institutions (P<0.05).

Our findings demonstrate that PROMs are considerably underused in the management of patients with angioedema, even though many participating physicians practice in highly specialized allergy and dermatology facilities. Notably, there are several free access tools available, including BiblioPRO (www.bibliopro.org) and Moxie (www.moxie-gmbh.de), to access and download the angioedema PROMs discussed here. Also, for mast cell-mediated angioedema, the CRUSE app (https://cruse-control.com/)incorporates the AAS and the AECT.

Our study lays the groundwork for identifying the gaps in PROM usage in angioedema, a disorder which substantially impacts patients’ quality of life. We recommend that medical societies consider these findings to overcome barriers and enhance the provision of continuing medical education on patient-reported outcome measures (PROMs). Furthermore, they should also consider incorporating additional objective biomarkers into PROMs to optimize the monitoring and follow-up tools for this condition.

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Table 1. Demographic characteristics of participants included in the analysis (N=370)

Variables	**N (%)**
Male	134 (36.2%)
Female	236 (63.8%)
Specialist	309 (83.5%)
Age Group	
20-29	44 (11.9%)
30-39	132 (35.7%)
40-49	84 (22.7%)
50-59	69 (18.6%)
60+	41 (11.1%)
Type of consultation	
Public practice	152 (41.1%)
Private practice	67 (18.1%)
Both public and private	151 (40.8%)
Specialty	
Family_medicine	21 (5.7%)
Pediatrics	58 (15.7%)

Allergist	163 (44.1%)
Dermatologist	132 (35.7%)
Other	39 (10.5%)
Years being a specialist	
1 to 9 years	146 (39.5%)
10 to 19 years	109 (29.5%)
20 to 29 years	60 (16.2%)
30+ years	55 (14.9%)
Reasons to use PROMs	
To monitor disease control	353 (95.4%)
To monitor disease severity	347 (93.8%)
To facilitate decision-making	332 (89.7%)
To monitor performance and therapeutic approach	329 (88.9%)
To improve efficiency of consultation	296 (80.0%)
To facilitate communication with patients	275 (74.3%)
For research	244 (65.9%)
To facilitate communication across different health care sectors	225 (60.8%)
Other	38 (10.3%)
Barriers to the use PROMs	

Time constraints	295 (79.7%)
Lack of integration into clinical systems	222 (60.0%)
Patients dislike questionnaires	220 (59.5%)
Not mandated to complete	201 (54.3%)
Not available for certain age groups	192 (51.9%)
Sufficient understanding of the disease without PROMs	170 (45.9%)
Not available in the native language of my patients	149 (40.3%)
Uncertainty about reliability	141 (38.1%)
Lack of confidence in interpreting	124 (33.5%)
Too complicated to fill in	124 (33.5%)
Too complicated to evaluate/score	121 (32.7%)
Not suitable for obtaining the information I need	101 (27.3%)
Feel uncomfortable	112 (30.3%)
Perceived as additional cost	90 (24.3%)
Constrain doctor-patient relationship	70 (18.9%)

Table 2: Multivariate Logistic Regression: Correlates to Barriers of PROMs Use (n=370)

	Use of PROMs in Angioedema Odds Ratio (SE)				PROM Barriers in Angioedema Odds Ratio (SE)			
Variables	Number of PROMs used	To monitor disease control	To monitor disease severity	To facilitate decision making	Time constraints	Lack of integration into clinical systems	Patients dislike questionnaires	Sufficient understanding of the disease without PROMs
Female (Reference, Sex=Male)	1.161 (0.479)	0.829 (0.479)	0.669 (0.378)	0.691 (0.269)	1.192 (0.344)	0.814 (0.191)	0.906 (0.217)	0.907 (0.215)
Age Group (Reference=20-29 years old)								
30-39 years old	1.102 (0.585)	1.722 (1.671)	0.228 (0.255)	0.172 (0.186)	0.240** (0.161)	0.784 (0.310)	1.669 (0.687)	1.003 (0.393)
40-49 years old	0.808 (0.595)	0.589 (0.652)	0.0690** (0.0873)	0.214 (0.254)	0.169** (0.131)	0.732 (0.355)	1.625 (0.812)	0.874 (0.426)
50-59 years old	1.289 (1.322)	2.207 (3.419)	0.653 (1.157)	0.365 (0.481)	0.105** (0.0929)	0.711 (0.427)	1.053 (0.645)	1.398 (0.856)
60+ years old	0.249 (0.392)	4.610 (9.433)	0.0628 (0.125)	0.253 (0.376)	0.0395*** (0.0430)	0.232* (0.189)	1.177 (0.925)	2.235 (1.556)
Type of consultation (Reference=Public practice)								
Private practice	0.678 (0.376)	0.460 (0.318)	1.358 (0.833)	0.550 (0.272)	0.882 (0.358)	0.819 (0.257)	0.673 (0.220)	0.813 (0.261)
Both public and private	0.739 (0.306)	0.754 (0.498)	3.550** (2.257)	0.739 (0.311)	0.924 (0.295)	1.023 (0.258)	0.436*** (0.114)	0.915 (0.233)
Type of Physician (Reference=Non								

specialists)								
Specialist	1.373 (1.121)	0.487 (0.565)	2.937 (2.625)	2.165 (1.691)	6.475*** (3.873)	1.148 (0.533)	0.615 (0.304)	0.676 (0.320)
Specialty (Reference=Physicians outside of the specialties below)								
Family Medicine	0.468 (0.551)	2.163 (2.715)	2.569 (3.153)	2.694 (2.972)	3.148 (3.380)	1.317 (0.697)	1.508 (0.853)	1.318 (0.682)
Pediatrics	1.081 (0.674)	1.943 (1.752)	0.490 (0.325)	3.372* (2.227)	2.462* (1.204)	0.998 (0.340)	1.396 (0.487)	2.291** (0.783)
Allergist	0.974 (0.599)	4.307* (3.729)	2.639 (1.745)	0.491 (0.267)	0.271*** (0.113)	0.882 (0.276)	0.806 (0.259)	0.405*** (0.133)
Dermatologist	0.833 (0.560)	3.141 (2.973)	1.796 (1.390)	1.036 (0.554)	0.358** (0.146)	0.719 (0.242)	0.867 (0.300)	0.635 (0.223)
Other	0.756 (0.245)	0.885 (0.811)	0.156*** (0.108)	1.147 (0.777)	0.512 (0.246)	1.227 (0.478)	2.654** (1.113)	
Years being a specialist (Reference=9 or less)								
10-19 years	0.407* (0.221)	0.569 (0.460)	0.906 (0.644)	0.729 (0.394)	0.974 (0.409)	0.862 (0.276)	0.711 (0.236)	1.078 (0.351)
20+ years	0.447 (0.396)	0.671 (0.770)	0.767 (0.809)	0.407 (0.327)	1.796 (1.131)	1.003 (0.488)	0.711 (0.354)	0.693 (0.351)

PROM=patient-reported outcome measure; SE=standard error *p<0.1, **p<0.05, ***p<0.01
The "Other" category in the medical survey includes an extensive range of specialties such as Gastroenterologists, Emergency Medicine Physicians, Hematologists, Internal Medicine Specialists, showcasing the diverse array of fields and expertise within the medical profession.

Table E1. Participating countries included in the analysis (N=370)

Participating countries	
Albania	1 (0.3%)
Argentina	21 (5.7%)
Austria	2 (0.5%)
Brazil	11 (3.0%)
Bulgaria	1 (0.3%)
Burundi	1 (0.3%)
Canada	7 (1.9%)
Chile	1 (0.3%)
China	3 (0.8%)
Colombia	3 (0.8%)
Denmark	2 (0.5%)
Ecuador	45 (12.2%)
Egypt	1 (0.3%)
Georgia	17 (4.6%)
Germany	29 (7.8%)
Greece	1 (0.3%)
India	12 (3.2%)
Iran	11 (3.0%)

Israel	1 (0.3%)
Italy	6 (1.6%)
Kuwait	13 (3.5%)
Lebanon	1 (0.3%)
Lithuania	3 (0.8%)
Malaysia	1 (0.3%)
Mexico	10 (2.7%)
North Macedonia	18 (4.9%)
Peru	3 (0.8%)
Poland	61 (16.5%)
Portugal	2 (0.5%)
Qatar	7 (1.9%)
Russia	26 (7.0%)
Slovenia	11 (3.0%)
South Sudan	1 (0.3%)
Spain	28 (7.6%)
Switzerland	1 (0.3%)
Turkey	3 (0.8%)
Ukraine	1 (0.3%)
United Kingdom	2 (0.5%)

United States of America	2 (0.5%)