Received: 12 August 2021 | Revised: 21 September 2021 | Accepted: 27 September 2021

DOI: 10.1111/pai.13674

ORIGINAL ARTICLE

WILEY

A European survey of management approaches in chronic urticaria in children: EAACI pediatric urticaria taskforce

Sophia Tsabouri[1] | Stefania Arasi[2] | Burcin Beken[3] | Martin K. Church[4] | Montserrat Alvaro-Lozano[5,6,7] | Carlo Caffarelli[8] | Carsten Flohr[9] | Sherief R. Janmohamed[10] | George N. Konstantinou[11] | Susanne Lau[12] | Sebastien Lefevre[13] | Charlotte G. Mortz[14] | Giovanni Pajno[15] | Helena Pite[16] | Krzysztof Rutkowski[17] | Petra Staubach[18,19] | Lauri-Ann Van der Poel[20] | Torsten Zuberbier[4] | Tabi A. Leslie[21]

[1]Child Health Department, Medical School, University of Ioannina, Ioannina, Greece

[2]Translational Research in Pediatric Specialities Area, Division of Allergy, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

[3]Department of Pediatric Allergy and Immunology, Acibadem Mehmet Ali Aydinlar University, School of Medicine, Istanbul, Turkey

[4]Charite—Universitatsmedizin Berlin, Corporate Member of Freie Universitat Berlin, Humboldt-Universitat zu Berlin, and Berlin Institute of Health, Department of Dermatology and Allergy, Allergy-Centre-Charite, Berlin, Germany

[5]Pediatric Allergy and Clinical Immunology Department, Hospital Sant Joan de Déu, Esplugues de Llobregat, Spain

[6]Institut de Recerca Sant Joan de Déu, Esplugues de Llobregat, Spain

[7]Universitat de Barcelona, Barcelona, Spain

[8]Clinica Pediatrica, Department of Medicine and Surgery, University of Parma, Parma, Italy

[9]Department of Pediatric Dermatology, St John's Institute of Dermatology, Guy's and St Thomas' NHS Foundation Trust and King's College London, London, UK

[10]Department of Dermatology, Universitair Ziekenhuis Brussel (UZ Brussel), Vrije Universiteit Brussel (VUB), Brussels, Belgium

[11]Department of Allergy and Clinical Immunology, 424 General Military Training Hospital, Thessaloniki, Greece

[12]Department for Pediatric Pneumology and Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany

[13]Regional Institute for Allergic Diseases, Metz Regional Hospital, Metz, France

[14]Department of Dermatology and Allergy Center, Odense Research Center for Anaphylaxis (ORCA), Odense University Hospital, Odense, Denmark

[15]Department of Pediatrics, Allergy Unit, University of Messina, Messina, Italy

[16]Allergy Center, CUF Descobertas Hospital and CUF Tejo Hospital, Lisbon, Portugal

[17]Department of Pediatric Allergy, Guy's and St Thomas' NHS Foundation Trust, London, UK

[18]Department of Dermatology, University Medical Center Mainz, Mainz, Germany

[19]CEDOC, Chronic Diseases Research Center, NOVA Medical School/Faculdade de Ciencias Medicas, Universidade Nova de Lisboa, Lisbon, Portugal

[20]Children's Allergy Service, GSTT Foundation Trust, London, UK

[21]Department of Dermatology, Royal Free Hospital, London, UK

Correspondence
Sophia Tsabouri, Department of Pediatrics, Faculty of Medicine, School of Medicine, University of Ioannina, Ioannina, Greece.
Email: stsabouri@gmail.com

Funding information
None of the authors perceived any fee for the present work. The online platform was supported by an EAACI grant

Abstract

Background: Although well described in adults, there are scarce and heterogeneous data on the diagnosis and management of chronic urticaria (CU) in children (0–18 years) throughout Europe. Our aim was to explore country differences and identify the extent to which the EAACI/GA²LEN/EDF/WAO guideline recommendations for pediatric urticaria are implemented.

Editor: Philippe Eigenmann

Methods: The EAACI Task Force for pediatric CU disseminated an online clinical survey among EAACI pediatric section members. Members were asked to answer 35 multiple choice questions on current practices in their respective centers.

Results: The survey was sent to 2,773 physicians of whom 358 (13.8%) responded, mainly pediatric allergists (80%) and pediatricians (49.7%), working in 69 countries. For diagnosis, Southern European countries used significantly more routine tests (eg, autoimmune testing, allergological tests, and parasitic investigation) than Northern European countries. Most respondents (60.3%) used a 2nd-generation antihistamine as first-line treatment of whom 64.8% updosed as a second line. Omalizumab was used as a second-line treatment by 1.7% and third line by 20.7% of respondents. Most clinicians (65%) follow EAACI/WAO/GA2LEN/EDF guidelines when diagnosing CU, and only 7.3% follow no specific guidelines. Some clinicians prefer to follow national guidelines (18.4%, mainly Northern European) or the AAAAI practice parameter (1.7%).

Conclusions: Even though most members of the Pediatric Section of EAACI are familiar with the EAACI/WAO/GA2LEN/EDF guidelines, a significant number do not follow them. Also, the large variation in diagnosis and treatment strengthens the need to re-evaluate, update, and standardize guidelines on the diagnosis and management of CU in children.

KEYWORDS
child, chronic urticaria, omalizumab, urticaria diagnosis, urticaria treatment

1 | INTRODUCTION

Chronic urticaria (CU), both spontaneous and inducible, although not life-threatening, is a burden on both the physical and socio-psycho-economic states of the patients.[1,2] Comorbidities, such as anxiety, depression, and sleep disorders, limit daily life, work/school, and sport activities and interfere with life within the family and in society.[3–6] Furthermore, its management can be complex and challenging. The EAACI/GA²LEN/EDF/WAO[7] guideline provides clinical recommendations for the definition, classification, diagnosis, and management of urticaria. However, because CU is less common and less studied in children than adults, treatment options in the guideline are based on adult data which have been extrapolated for children.

To investigate CU in children in more detail, an EAACI Task Force was created to investigate current clinical practice in the diagnosis and management of childhood CU, mapping activity, understanding country differences and challenges, and identifying the extent to which the EAACI/GA²LEN/EDF/WAO guideline recommendations have been implemented across Europe.

2 | METHODS

The EAACI Task Force on CU in children led by a group of expert clinicians and researchers in the field of pediatric CU, formulated a 35-question survey (Table S1). A Survey Monkey questionnaire was circulated to 2,773 members of the EAACI Pediatric Section in November and December 2019. Four weeks was allowed for responding. At the same timeframe, the survey was also disseminated via EAACI social media channels, reaching an additional audience of 8,000 followers. The survey covered the following areas. First was characterization of the participating clinicians, particularly geographical location, professional background, type of practice, and experience. Second and third were assessments of differences in diagnosis management practices including drug usage. The study protocol was approved by the Ethics Committee and Deontology of the University Hospital of Ioannina, Greece (approved number 8/7-5–2020 item 26 decision).

2.1 | Statistical analysis

Due to anticipated differences in management between different parts of Europe, Eastern and Southern European countries (South) were compared with Western and Northern European (North) countries, based on The United Nations' geoscheme.[8] Differences between Northern and Southern European countries were assessed using chi-square tests with values of $p < .05$ being considered statistically significant.

Key Message

This survey was undertaken in order to determine how pediatric urticaria patients are being managed by EAACI pediatric section members. The respondents included pediatric allergists, immunologists, dermatologists, and pediatricians. It adds background clarity as to how children all over Europe are being treated for this debilitating disease.

Responses to the questionnaire showed that the majority of patients are treated with second-generation antihistamines, which are updosed after 2–4 weeks, in keeping with the current guidelines, with cetirizine being the antihistamine of choice in children under 6 years of age. Omalizumab was used by a fifth of respondents as a third-line treatment, as recommended by the EAACI guideline, in addition to a small percentage using omalizumab as a second-line treatment.

The results of this study demonstrate that while most clinicians are now managing their patients according to EAACI guidelines, there is scope for improvement and that further re-evaluation, updating, and standardization of protocols will be helpful in this. The findings of the survey should have a positive impact on clinicians' confidence in using the EAACI algorithm in children. Clinicians are updosing antihistamines safely as per the guidelines and using omalizumab which has proved to be a safe treatment in children with no reports of anaphylaxis. The main adverse effect was local injection site reaction. The authors hope to reinforce to readers that the algorithm is not only suitable in children but provides an optimal approach to treatment of pediatric urticaria.

3 | RESULTS

3.1 | Participant characteristics

The survey was answered in total by 358 participants from 69 countries. The participants were mainly based on Europe (74.6%) followed by Asia (11.1%) and South America (8.4%). Less represented were clinicians from Africa (1.7%), North America (1.4%), and Australia (0.8%) (Table S2). European participants were further divided into Northern Europe ($n = 79$) and Southern Europe ($n = 179$).

Most participants had a professional background in pediatric allergy (80%) or pediatrics (50%). Less frequent were allergists (25%), pediatric immunologists (14%), immunologists (5.3%), and dermatologists (1.4%). (Table S3). Most participants work in a public (district) (41.9%) or university (teaching) hospital (27%), while others work in a private practice/clinic (19%) or private hospital (11%).

Participants see on average per month 5.6 CU patients 0–4 years old, 6.2 patients 5–11 years old, and 6.2 patients 12–18 old. Most clinicians (65%) indicated that they follow EAACI/WAO/GA2LEN/EDF guidelines when diagnosing urticaria, and only 7.3% responded that they do not follow any specific guidelines while others (20%) follow other national guidelines. When comparing Northern and Southern Europe, both regions have a preference to follow EAACI/WAO/Ga2LEN/EDF guidelines (57% and 74%). Nevertheless, there was a significant ($p = .012$) preference to use National guidelines in the Northern compared with Southern European countries (Table 1).

3.2 | Diagnosis

In the second part of the survey, clinicians were asked about patient's symptoms and diagnostic methods used in CSU and CIndU.

Reports of associated angioedema varied widely, as shown in Figure 1. In summary, 36% of clinicians reported <10%, 35% reported 10–30%, 14% reported 31–50%, and only 4% reported 51–70%.

Considering the diagnosis of CSU, a summary of the individual tests applied by the 358 responding clinicians is shown in Figure 2. The most frequent baseline investigations included the following: full blood count (FBC) 83%, thyroid profile (free triiodothyronine—fT3, thyroxine—fT4, thyroid-stimulating hormone—TSH) 62%, total IgE 59%, thyroid antibodies (antithyroglobulin, antithyroid peroxidase) 55%, and anti-nuclear antibody (ANA) or other antibodies 51%. Very rarely, clinicians use the basophil activation test (BAT, 2.5%) and basophil histamine release assay (BHRA, 2.2%).

When diagnosing CU, there is a significant trend for Southern European countries to use more routine tests than Northern countries. As shown in Figure 3, highly significant ($p < .001$) differences include full blood count, total IgE, antithyroid antibodies, parasitic

TABLE 1 Place of practice and guidelines for diagnostics

	AAAAI practice parameter	EAACI/WAO/GA2LEN/EDF guidelines	National guidelines	No guidelines followed
Northern Europe	1%	57%	35%	7%
Southern Europe	2%	74%	15%	8%

Note: Each value is the percentage of clinicians responding.

Abbreviations: AAAAI, American Academy of Allergy, Asthma & Immunology; EAACI, European Academy of Allergy and Clinical Immunology; EDF, European Dermatology Forum; GA^{2}LEN, Global Allergy and Asthma European Network; WAO, World Allergy Organization.

investigations, and hepatitis serology. Full details of the tests are shown in Table S4.

Considering the allergological work-up (ie, skin prick test for aeroallergens, specific IgE to aeroallergens, specific IgE to food allergens, and skin prick test for food allergens), 48% of the participants indicated that they use at least one of these tests when evaluating children with CU the first time.

When CIndU is suspected, 58% of clinicians use the ice cube test and 49% a dermographometer. Interestingly, 23% of clinicians do not use a formal test to assess for CIndU (Table 2). Again, there was a significant ($p = .019$) trend for Southern vs. Northern European countries to use more tests in the work-up of pediatric CIndU (Table S5).

3.3 | Patient management

When managing CU, most clinicians (60%) use a 2nd-generation antihistamine (sgAH) at a dose adjusted for age/weight and some (7.8%) clinicians updose sgAH right away. Montelukast or topical steroids were almost never used as a first-line treatment (Table 3), while some clinicians (5.3%) still use a 1st-generation antihistamine (fgAH) as their preferred first-line treatment. Most clinicians (63%) are aware that the half-life of chlorpheniramine, a fgAH, is around 24 h and may still cause morning drowsiness while only 11% were not sure and 7.5% were completely unaware. Treating children under the age of 6 years is controversial with 39% of clinicians using cetirizine, 25% desloratadine, and 7% rupatadine.

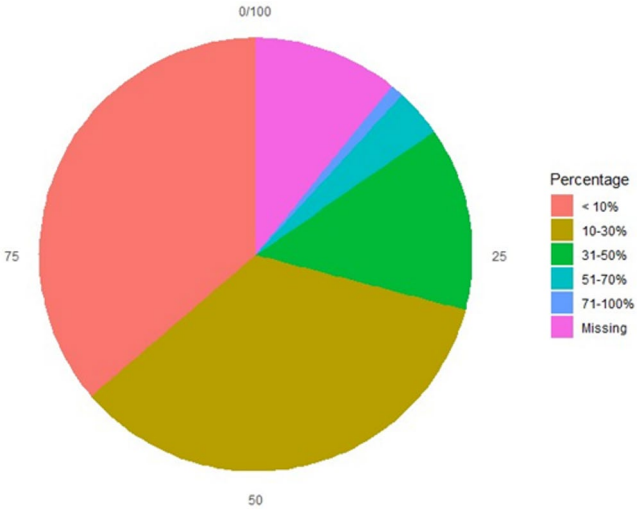

FIGURE 1 Percentage of chronic urticaria patients complain of angioedema as indicated by the respondents

Time to move second-line treatment is 1–2 weeks for 27% and 2–4 weeks for 37% of clinicians. The remainder waits for 4–6 weeks or even longer. As second-line treatment, 65% of clinicians choose to updose sgAH.

Similarly, the preferential waiting period, before moving to a third treatment step, is 1–2 weeks (21%) or 2–4 weeks (38%). As a third-line treatment, 22% of clinicians updose sgAH, 21% use omalizumab, and 11% use montelukast. Cyclosporin A is almost never used (0.8%), and no one uses methotrexate or azathioprine.

Oral steroids as a therapeutic option for children with CU were chosen by 1.1% and 5.9% of participants as second-line and third-line treatments, respectively.

When selecting the appropriate drug for patient treatment, two thirds (75%) of the clinicians do not use off-label treatment, 2.5% indicated they do not remember, and only 2% use dapsone or 0.6% danazol.

When comparing the preferential treatment lines between countries, the preference for a sgAH as 1st-line treatment and updosing a sgAH as second- and third-line treatments is consistent across all countries. However, there are significant ($p = .001$) differences in preference for third line of treatment between Southern and Northern European countries, (Table S6). Specifically, fgAH and oral corticosteroids were used by 10% and 12%, respectively, by Southern European clinicians compared with 3.5% and 2% by Northern European clinicians.

In this survey, most clinicians (36%) do not use fgAH to aid sleep, 23% use them rarely, and 1.7% use them regularly. Almost the 10% of Southern European clinicians are more likely to sometimes use

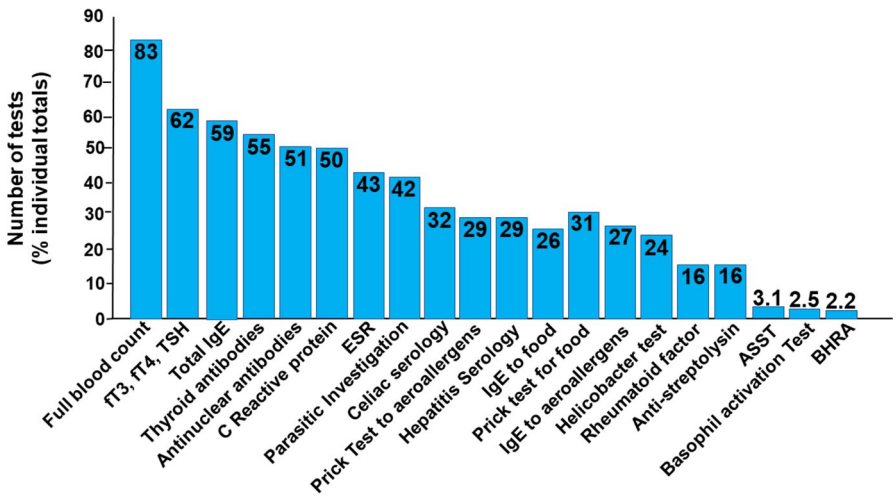

FIGURE 2 Routinely used tests in the work-up of pediatric chronic urticaria

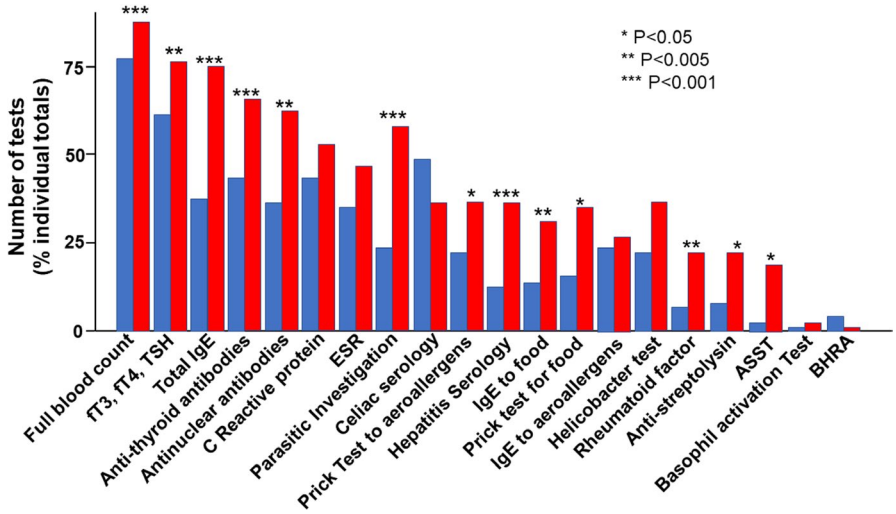

FIGURE 3 Routinely used tests in the work-up of pediatric chronic urticaria comparing Northern European Countries (Blue, $n = 79$) and Southern European Countries (Red, $n = 179$)

TABLE 2 Routinely used tests for chronic-inducible urticaria (CIndU) when suspected

Test	Number of participants	Percentage
Ice cube test (cold urticaria)	206	58%
Dermographometer (dermographism)	176	49%
No test	83	23%
Temp test (cold and heat urticaria)	58	16%
Wet compress (aquagenic urticaria)	54	15%
Treadmill/hot bath (cholinergic)	46	12%
Delayed pressure testing	26	7.3%
Vortex (vibratory reactions)	18	5.0%
Other[a]	12	3.4%

Note: Participants were allowed to select more than one test type.

[a]Other results include the following: "Dermographism without dermographometer," "depending on symptoms and suspicion," "exercise," "Fric test," "I refer them to dermatologists," "Using hand or tongue depressor to induce dermographism," "only if indicated," "stroke by sharp object".

TABLE 3 Preferred first-line treatment for chronic urticaria in children ($N = 358$)

First-line treatment	Frequency	Percentage
2nd-generation antihistamines (age/weight-adjusted)	216	60.3%
Updosed 2nd-generation antihistamines right away	28	7.8%
1st-generation antihistamines (age/weight-adjusted)	19	5.3%
Combination of these two generations	5	1.4%
Montelukast	3	0.8%
Topical steroids	1	0.3%
No answer	86	24.0%

Note: Results are ordered by frequency of the preferred treatment.

fgAH to aid sleep compared with 3.5% of Northern European clinicians ($p = .005$).

Omalizumab is not used by any clinician as first-line treatment in CU, while 1.7% use it as second-line treatment and 21% as third-line treatment. However, of these clinicians, 65% and 71% prescribed omalizumab to less than 10% of their CSU patients and CIndU patients, accordingly. Omalizumab is used by 68% of clinicians in children of 12–18 years old, by 30% in 5–11 years old, and by 1.4% in 0–4 years old. After administration, 35% of clinicians wait for 30 min and 27% 1 h, while only 6.4% let the patients leave the clinic immediately. Respondents assess the treatment outcome between 3 months (28%) and 6 months (31%) of treatment. During the omalizumab treatment, 51% of clinicians continue treatment with antihistamines until the symptoms subside while 9.5% only treat every time the symptoms appear. After administration of omalizumab, it is frequent to see local signs at the injection site (40.5%) while only a few

cases report cold or flu-like symptoms (10.9%) or body ache (5.9%). No cases of omalizumab-related anaphylaxis have been reported.

3.4 | Additional management approaches

Regarding specific dietary recommendations, 55% of clinicians do not recommend any dietary modifications, but 14% recommend a low histamine diet and 9.2% pseudo-allergen-free diet. While 47% of clinicians do not routinely recommend drug restrictions, 24% advise NSAID and 3.9% ACE (angiotensin-converting enzyme) inhibitor avoidance.

Furthermore, some clinicians use patient-reported outcome measures (PROM), such as Urticaria Activity Score[9] used for 7 consecutive days (UAS7, 33%) or Urticaria Control Test[10] (UCT, 23%) to record patient outcome, but 31% do not use any PROMs. Assessment of the patients' QoL is done at every follow-up visit by 39% of respondents, although 21% of clinicians never assess QoL of their patients.

3.5 | Patient transition

In the last part of the survey, clinicians were asked about their approach to transition care practice. Despite the need to change from a pediatric clinic to an adult clinic, 21% of clinicians do not have a transition service in collaboration with adult physicians. Furthermore, 20% only provide this service occasionally while only 17% always. Approximately 19% continue treating the patients as adults.

4 | DISCUSSION

This international survey, reporting on the diagnostic approach and management of CU in children, included participants from specialized centers in Europe, Asia, and South America. Most respondents were pediatric allergists and pediatricians, and fewer were allergists and pediatric immunologists. The participants are predominantly based on Europe, and the majority work in public (district) or university (teaching) hospitals. Most clinicians (65%) follow EAACI/WAO/GA2LEN/EDF guidelines[7] when diagnosing children with urticaria. However, national guidelines are followed by some clinicians (18%), and most of whom are from Northern Europe.

The majority (70%) of the clinicians reported that less than 30% of their patients suffered from angioedema. This is in line with other studies that present a less frequent occurrence of angioedema in children with CU.[11–13]

While diagnosis is based primarily on clinical presentation, there is often a need for investigations to exclude a possible underlying cause. Regarding the work-up of CU patients, most clinicians use baseline investigations (FBC, thyroid profile and thyroid antibodies, IgE, ANA) and only 1/3 of the clinicians examined their CU patients for parasitic infections and celiac disease. This diagnostic work-up is in line with EAACI guidelines,[7] as well as the British,[14] Italian,[15] and Portuguese guidelines.[16] All these guidelines mention pediatric CU and the differences from adult CU. The list of the main guidelines in the field of chronic urticaria and the recommended diagnostic tests are summarized in Table 4. Furthermore, we noticed a significant trend of Southern European countries to use more routine diagnostic tests for CU. The BAT and BHRA were rarely used. The reasons for this are probably poor access, high cost, and lack of awareness. Nevertheless, BAT has been suggested as an *in vitro* alternative for ASST, to diagnose, examine, and predict patients with suspected CU.[17–19]

Sixty percent of clinicians, almost the same percentage who follow EAACI/WAO/GA2LEN/EDF guidelines, use a sgAH (age/weight-adjusted) which is a basic recommendation of the guidelines.[7] Five percent of participants still use a fgAH as their preferred first-line treatment even though their 24 h of half-life and their causality of drowsiness in the morning has been documented in the literature.[20,21] In this study, 18% of the physicians were little or not even aware of the sedative properties of fgAH.

A questionnaire study on the prevalence and treatment of pediatric urticaria in five European countries revealed that there was significant use of oral steroids (10–28%).[13] In a US study involving adults and children, oral corticosteroids were the most commonly prescribed medication, with 55% of patients requiring at least one course.[22] Interestingly, in our survey, oral steroids are chosen only by 1% as the second-line treatment and 6% as the third-line treatment.

When comparing the preferential first, second, and third lines of treatment between countries, we see that the preference for a sgAH as first line of treatment is consistent across all countries. Furthermore, updosing sgAH as a second line and third line of treatment is also consistent across all countries.

According to this survey, three-quarters of clinicians prefer omalizumab as a 3rd-line treatment for CSU compared with less than 10% for CIndU. These discrepancies are attributed to the current licensing indication and age cutoffs in many European countries according to national regulations and that omalizumab is not licensed for CIndU in many European countries. Omalizumab is the only approved add-on therapy for H_1-antihistamine-refractory CSU[23] for children between 12 and 18 years, but this perspective again depends on the national regulations.[24] The drug is well tolerated, apart from frequent but mild local reactions. No omalizumab-related anaphylactic episode was reported.

To record patient outcome, tools, such as UCT and UAS7, are used to measure disease control, guide treatment decisions, and help to understand the burden and impact of CU on the lives of children and their families.[9,10] However, most PROMs have been validated and can be used only by older children and adolescents,[25] which may explain that many clinicians do not use them.

A different, yet important, part of pediatric patient treatment is transition into adult services. For most European countries, the transition age is 16 years of age. Only one third of clinicians provide transition services to their patients. This needs to be improved in line with guidelines.[26,27]

TABLE 4 Main guidelines in the field of chronic urticaria improve table in PDF by reducing space for the first columns whereas increasing the space for the last column "Recommended tests and procedures for chronic urticaria"

List of the main guidelines in the field of chronic urticaria					
				Recommended tests and procedures for chronic urticaria	
Guidelines	**Country**	**First author**	**Year**	**Routine diagnostic tests**	
German guidelines[28]	Germany	Baurer A	2021	FBC, ESR and/or CRP	Laboratory test should be performed when history and clinical data suggest an eliciting factor or a systemic disease such as autoinflammatory diseases, IgE-mediated food allergy, thyroid gland pathologies
French guidelines[29]	France	Hacard F	2021	No recommendation for diagnostic tests	
Korean guidelines[30]	Korea	Song WJ	2020	No recommendation for diagnostic tests	
ASCIA guidelines[31]	Australia	Katelaris C	2020	Not recommended	Laboratory test should be performed when history and clinical data suggest a systemic disease such as urticarial vasculitis, urticaria pigmentosa, or autoinflammatory disorders/CAPS
Italian guidelines[15]	Italy	Caffarelli C	2019	Not recommended	
EAACI/GA²LEN/EDF/WAO guidelines[7]	Europe	Zuberbier T	2018	FBC. ESR and/or CRP	• Test for infectious diseases (eg, *H. pylori*) • Functional autoantibodies (eg, ASST) • Thyroid hormones and autoantibodies • Allergy skin tests and/or allergen avoidance test/avoidance diet • Tests for severe systemic diseases (eg, tryptase) • Other (eg, skin lesion biopsy)
International guidelines[32]	America Europe	Beck LA	2017	Not given any specific recommendation, the authors summarize and compare EAACI/GA²LEN/EDF/WAO guidelines and American guidelines	
Asian guidelines[33]	Thailand	Kulthanan K	2016	FBC, ESR	• ASST • Test for *H. Pylori* • ANA, D-dimer • Stool examination for parasites • Specific IgE • Thyroid hormones and autoantibodies
Turkish guidelines[34]	Turkey	Kocaturk Goncu E	2016	FBC, ESR, CRP	Based on history; • Infectious diseases (H. pylori, etc.) • Thyroid hormones and autoantibodies • Pseudo-allergen-free diet for 3 weeks • Autologous serum skin test • Skin lesion biopsy

(Continues)

TABLE 4 (Continued)

List of the main guidelines in the field of chronic urticaria					
				Recommended tests and procedures for chronic urticaria	
Guidelines	Country	First author	Year	Routine diagnostic tests	
BSACI guidelines[14]	UK	Powell RJ	2015	Not recommended	Additional investigations if clinically indicated • Urinalysis • FBC • ESR • Liver function tests (add viral hepatitis screen if transaminases are abnormal) • Coeliac screen: Tissue transglutaminase IgA antibodies and/or endomysial IgA antibodies • Thyroid function and antithyroid antibodies • Cold, dermographism, and pressure provocation tests • Elimination rechallenge diets • Antinuclear antibodies • Skin biopsy • C4 and C1 inhibitor quantitation • (indicated for children, presenting with angioedema without urticaria) • Tests for current or postviral, bacterial, or parasitic infections
American guidelines[35]	America	Bernstein JA	2014	FBC, ESR and/or CRP, liver enzymes, TSH	Based on patient circumstances, history, and physical examination: • Skin biopsy • Physical challenge tests • Complement activity tests • Stool analysis (ova and parasites) • Urinalysis • Hepatitis B and C serologies • Chest radiography and/or imaging studies • ANA, RF, and/or anti-CCP • Cryoglobulin levels • Serologic and/or skin testing for immediate hypersensitivity • Thyroid autoantibodies to: TSH receptor, thyroglobulin, thyroid peroxidase, and sodium/iodine symporter • Serum protein electrophoresis
Japanese guidelines[36]	Japan	Hide M	2012	Not recommended if no apparent symptom except for urticaria was identified. ASST may prove the involvement of autoimmune mechanisms in a population of chronic urticaria.	Specific tests are recommended based on subtypes such as allergic urticaria, FDEIA, aspirin urticaria, physical urticarias, angioedema, urticaria vasculitis, urticaria pigmentosa, Schnitzler's syndrome, and CAPS

Abbreviations: ANA, antinuclear antibody; ASST, autologous serum skin test; CAPS, cryopirin-associated periodic fever; CCP, citrullinated protein; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FBC, full blood count; FDEIA, food-dependent exercise-induced anaphylaxis; H. Pylori, Helicobacter pylori; IgA, immunoglobulin A; IgE, immunoglobulin E; RF, rheumatoid factor; TSH, thyroid-stimulating hormone.

A limitation in this study is that data only indicates the location of the clinicians who chose to respond and disproportionately were more from Southern Europe, compared to Northern Europe. In addition, the questionnaire was only sent to pediatric section members while in some countries, dermatologists treat children with CU. Dermatologists have experience with tests for CIndU in adults as well as using PROMS and systemic treatments in adults. Also, not all allergists who follow both adults and pediatric patients are members of the pediatric section. The results may, therefore, have been different if the survey had been applied more broadly, including members from the EAACI's Dermatology Section. Furthermore, the study is biased by the retrospective nature of the survey, which hampers the reliability of some estimations. However, the lack of previous real-life data at European level and the international multicenter nature of the information are relevant strengths.

5 | CONCLUSION

This study investigated the diagnostic approach and management of CU in children, mainly by European pediatricians and pediatric allergists working in public hospitals or universities. Clinicians frequently use baseline investigations for diagnosis and largely implement current guidelines. Even though a sgAH is preferred as first-line treatment and its updosing is also consistent across all countries as a second- and third-line treatments, a few clinicians still use a fgAH as their preferred first-line treatment, despite their side effects. The results of this survey strengthen the need to re-evaluate, update, and standardize protocols on the diagnosis and management of CU in children.

ACKNOWLEDGEMENTS

The authors acknowledge the financial support of EAACI. The EAACI Task Force on Chronic Urticaria in children would like to thank the Executive Committee of the EAACI for their constructive, expert review and Ana Antunes for her help with proofreading this paper.

CONFLICT OF INTEREST

MAL reports honoraria from advisory boards for Novartis and talks for Novartis, Uriach, and FAES Pharma (relevant to urticaria). GNK and SRJ report honoraria from advisory boards for Novartis (relevant to urticarial). Nonrelevant honoraria from Pierre Fabre Benelux. MKC has been a speaker or consultant for Almirall, FAES Pharma, Menarini, Moxie, MSD, Novartis, UCB Pharma, Sanofi-Aventis, and Uriach. TL reports honoraria from advisory boards for Menlo and Novartis. GNK and KR are giving lectures for Novartis. ST,SA, BB, CC, CF, CGM, GP, HP, LVDP, PS, SL, and TZ have nothing to disclose.

AUTHOR CONTRIBUTION

Sophia Tsabouri: Conceptualization (lead); Data curation (lead); Investigation (lead); Supervision (lead); Visualization (lead); Writing-original draft (lead); Writing-review & editing (lead). **Stefania Arasi:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Writing-original draft (equal); Writing-review & editing (equal). **Burcin Beken:** Conceptualization (supporting); Data curation (equal); Methodology (equal). **Martin K Church:** Conceptualization (lead); Data curation (equal); Investigation (equal); Methodology (equal); Visualization (lead); Writing-original draft (equal); Writing-review & editing (lead). **Montserrat Alvaro:** Conceptualization (equal); Data curation (equal); Investigation (equal); Writing-original draft (supporting). **Carlo Caffarelli:** Conceptualization (supporting); Data curation (equal); Writing-original draft (supporting); Writing-review & editing (supporting). **Carsten Flohr:** Conceptualization (supporting); Data curation (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Sherief R. Janmohamed:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Visualization (equal); Writing-original draft (supporting); Writing-review & editing (supporting). **George N Konstantinou:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Susanne Lau:** Conceptualization (equal); Data curation (equal); Investigation (equal); Visualization (supporting); Writing-original draft (supporting). **Sebastian Lefevre:** Data curation (supporting). **Charlotte Gotthard Mørtz:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Visualization (equal); Writing-original draft (supporting); Writing-review & editing (supporting). **Giovanni B Pajno:** Conceptualization (equal); Data curation (equal); Investigation (equal); Visualization (equal); Writing-original draft (supporting); Writing-review & editing (supporting). **Helena Pite:** Conceptualization (equal); Data curation (equal); Investigation (equal); Visualization (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Chris Rutkowski:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Visualization (supporting); Writing-original draft (supporting). **Petra Staubach:** Conceptualization (supporting); Data curation (supporting); Investigation (supporting); Visualization (supporting). **Lauri Ann van der Poel:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (supporting); Supervision (supporting); Writing-original draft (supporting). **Torsten Zuberbier:** Conceptualization (supporting); Data curation (supporting); Visualization (supporting). **Tabi Anika Leslie:** Conceptualization (lead); Data curation (lead); Investigation (equal); Supervision (lead); Writing-original draft (equal); Writing-review & editing (equal).

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/pai.13674.

ORCID

Sophia Tsabouri https://orcid.org/0000-0001-7584-5401
Stefania Arasi https://orcid.org/0000-0002-8135-0568
Burcin Beken https://orcid.org/0000-0001-7677-7690
Martin K. Church https://orcid.org/0000-0002-1639-9410

Montserrat Alvaro-Lozano https://orcid.org/0000-0002-5528-8043
Carlo Caffarelli https://orcid.org/0000-0001-7710-6995
Carsten Flohr https://orcid.org/0000-0003-4884-6286
Sherief R. Janmohamed https://orcid.org/0000-0002-8700-480X
George N. Konstantinou https://orcid.org/0000-0003-1371-6764
Susanne Lau https://orcid.org/0000-0002-5189-4265
Sebastien Lefevre https://orcid.org/0000-0002-8806-6623
Charlotte G. Mortz https://orcid.org/0000-0001-8710-0829
Giovanni Pajno https://orcid.org/0000-0002-6897-4587
Helena Pite https://orcid.org/0000-0002-7300-928X
Krzysztof Rutkowski https://orcid.org/0000-0002-2350-8697
Lauri-Ann Van der Poel https://orcid.org/0000-0002-1797-3381
Torsten Zuberbier https://orcid.org/0000-0002-1466-8875

REFERENCES

1. Maurer M, Gimenez-Arnau A, Ensina LF, Chu CY, Jaumont X, Tassinari P. Chronic urticaria treatment patterns and changes in quality of life: AWARE study 2-year results. *World Allergy Organ J*. 2020;13(9):100460. https://doi.org/10.1016/j.waojou.2020.100460
2. Goncalo M, Gimenez-Arnau A, Al-Ahmad M, et al. The global burden of chronic urticaria for the patient and society. *Br J Dermatol*. 2021;184(2):226-236. https://doi.org/10.1111/bjd.19561
3. Balp MM, Khalil S, Tian H, Gabriel S, Vietri J, Zuberbier T. Burden of chronic urticaria relative to psoriasis in five European countries. *J Eur Acad Dermatol Venereol*. 2018;32(2):282-290. https://doi.org/10.1111/jdv.14584
4. Itakura A, Tani Y, Kaneko N, Hide M. Impact of chronic urticaria on quality of life and work in Japan: results of a real-world study. *J Dermatol*. 2018;45(8):963-970. https://doi.org/10.1111/1346-8138.14502
5. Maurer M, Abuzakouk M, Berard F, et al. The burden of chronic spontaneous urticaria is substantial: real-world evidence from ASSURE-CSU. *Allergy*. 2017;72(12):2005-2016. https://doi.org/10.1111/all.13209
6. Thomsen SF, Pritzier EC, Anderson CD, et al. Chronic urticaria in the real-life clinical practice setting in Sweden, Norway and Denmark: baseline results from the non-interventional multicentre AWARE study. *J Eur Acad Dermatol Venereol*. 2017;31(6):1048-1055. https://doi.org/10.1111/jdv.14210
7. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA(2)LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy*. 2018;73(7):1393-1414. https://doi.org/10.1111/all.13397
8. United Nations publication "Standard Country or Area Codes for Statistical Use". https://unstats.un.org/unsd/methodology/m49/. Accessed January 5, 2021.
9. Hawro T, Ohanyan T, Schoepke N, et al. The urticaria activity score-validity, reliability, and responsiveness. *J Allergy Clin Immunol Pract*. 2018;6(4):1185-1190.e1. https://doi.org/10.1016/j.jaip.2017.10.001
10. Weller K, Groffik A, Church MK, et al. Development and validation of the urticaria control test: a patient-reported outcome instrument for assessing urticaria control. *J Allergy Clin Immunol*. 2014;133(5):1365-1372, 1372 e1-6. https://doi.org/10.1016/j.jaci.2013.12.1076
11. Volonakis M, Katsarou-Katsari A, Stratigos J. Etiologic factors in childhood chronic urticaria. *Ann Allergy*. 1992;69(1):61-65.
12. Maurer M, Church MK, Goncalo M, Sussman G, Sanchez-Borges M. Management and treatment of chronic urticaria (CU). *J Eur Acad Dermatol Venereol*. 2015;29(Suppl 3):16-32. https://doi.org/10.1111/jdv.13198
13. Balp MM, Weller K, Carboni V, et al. Prevalence and clinical characteristics of chronic spontaneous urticaria in pediatric patients. *Pediatr Allergy Immunol*. 2018;29(6):630-636. https://doi.org/10.1111/pai.12910
14. Powell RJ, Leech SC, Till S, et al. BSACI guideline for the management of chronic urticaria and angioedema. *Clin Exp Allergy*. 2015;45(3):547-565. https://doi.org/10.1111/cea.12494
15. Caffarelli C, Paravati F, El Hachem M, et al. Management of chronic urticaria in children: a clinical guideline. *Ital J Pediatr*. 2019;45(1):101. https://doi.org/10.1186/s13052-019-0695-x
16. Costa C, Goncalo M, Urticaria GGPdEd. [Diagnostic and therapeutic approach of chronic spontaneous urticaria: recommendations in Portugal]. *Acta Med Port*. 2016;29(11):763-781. Abordagem Diagnostica e Terapeutica da Urticaria Cronica Espontanea: Recomendacoes em Portugal. https://doi.org/10.20344/amp.8294
17. Curto-Barredo L, Yelamos J, Gimeno R, Mojal S, Pujol RM, Gimenez-Arnau A. Basophil activation test identifies the patients with chronic spontaneous urticaria suffering the most active disease. *Immun Inflamm Dis*. 2016;4(4):441-445. https://doi.org/10.1002/iid3.125
18. Hoffmann HJ, Santos AF, Mayorga C, et al. The clinical utility of basophil activation testing in diagnosis and monitoring of allergic disease. *Allergy*. 2015;70(11):1393-1405. https://doi.org/10.1111/all.12698
19. Sahiner UM, Civelek E, Tuncer A, et al. Chronic urticaria: etiology and natural course in children. *Int Arch Allergy Immunol*. 2011;156(2):224-230. https://doi.org/10.1159/000322349
20. Church MK, Weller K, Stock P, Maurer M. Chronic spontaneous urticaria in children: itching for insight. *Pediatr Allergy Immunol*. 2011;22(1 Pt 1):1-8. https://doi.org/10.1111/j.1399-3038.2010.01120.x
21. Church MK, Maurer M, Simons FE, et al. Risk of first-generation H(1)-antihistamines: a GA(2)LEN position paper. *Allergy*. 2010;65(4):459-466. https://doi.org/10.1111/j.1398-9995.2009.02325.x
22. Broder MS, Raimundo K, Antonova E, Chang E. Resource use and costs in an insured population of patients with chronic idiopathic/spontaneous urticaria. *Am J Clin Dermatol*. 2015;16(4):313-321. https://doi.org/10.1007/s40257-015-0134-8
23. Zuberbier T, Aberer W, Asero R, et al. Methods report on the development of the 2013 revision and update of the EAACI/GA2 LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2014;69(7):e1-e29. https://doi.org/10.1111/all.12370
24. European Medicines Evaluation Agency (EMEA). Omalizumab (Xolair) summary of product characteristics (SmPC). http://www.ema.europa.eu. Accessed June 30, 2017.
25. Maurer M, Eyerich K, Eyerich S, et al. Urticaria: collegium internationale allergologicum (CIA) update 2020. *Int Arch Allergy Immunol*. 2020;181(5):321-333. https://doi.org/10.1159/000507218
26. Khaleva E, Vazquez-Ortiz M, Comberiati P, et al. Current transition management of adolescents and young adults with allergy and asthma: a European survey. *Clin Transl Allergy*. 2020;10:40. https://doi.org/10.1186/s13601-020-00340-z
27. Roberts G, Vazquez-Ortiz M, Knibb R, et al. EAACI Guidelines on the effective transition of adolescents and young adults with allergy and asthma. *Allergy*. 2020;75(11):2734-2752. https://doi.org/10.1111/all.14459
28. Bauer A, Dickel H, Jakob T, et al. Expert consensus on practical aspects in the treatment of chronic urticaria. *Allergo J Int*. 2021;30(2):64-75. https://doi.org/10.1007/s40629-021-00162-w
29. Hacard F, Giraudeau B, d'Acremont G, et al. Guidelines for the management of chronic spontaneous urticaria: recommendations supported by the centre of evidence of the French society of dermatology. *Br J Dermatol*. 2021;185(3):658-660. https://doi.org/10.1111/bjd.20415

30. Song WJ, Choi M, Lee DH, et al. The KAAACI/KDA evidence-based practice guidelines for chronic spontaneous urticaria in Korean adults and children: part 1. definition, methodology and first-line management. *Allergy Asthma Immunol Res*. 2020;12(4):563-578. https://doi.org/10.4168/aair.2020.12.4.563
31. Katelaris C, Smith W & Choi J et al. ASCIA chronic spontaneous urticaria (CSU) position paper and treatment guidelines. https://www.allergy.org.au/images/stories/pospapers/ASCIA_HP_Position_Paper_CSU_2020.pdf.
32. Beck LA, Bernstein JA, Maurer M. A review of international recommendations for the diagnosis and management of chronic urticaria. *Acta Derm Venereol*. 2017;97(2):149-158. https://doi.org/10.2340/00015555-2496
33. Kulthanan K, Tuchinda P, Chularojanamontri L, et al. Clinical practice guideline for diagnosis and management of urticaria. *Asian Pac J Allergy Immunol*. 2016;34(3):190-200.
34. Kocatürk Göncü E, Aktan S, Atakan N, et al. The Turkish guideline for the diagnosis and management of urticaria-2016. *Turkderm - Arch Turk Dermatol Venerology*. 2016;50:82-98. https://doi.org/10.4274/turkderm.22438
35. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol*. 2014;133(5):1270-1277. https://doi.org/10.1016/j.jaci.2014.02.036
36. Hide M, Hiragun T, Japanese DA. Japanese guidelines for diagnosis and treatment of urticaria in comparison with other countries. *Allergol Int*. 2012;61(4):517-527. https://doi.org/10.2332/allergolint.12-RAI-0497

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Tsabouri S, Arasi S, Beken B, et al. A European survey of management approaches in chronic urticaria in children: EAACI pediatric urticaria taskforce. *Pediatr Allergy Immunol*. 2022;33:e13674. https://doi.org/10.1111/pai.13674