

ORIGINAL ARTICLE

Skin & Eye Disease

Prevalence and clinical characteristics of chronic spontaneous urticaria in pediatric patients

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Abstract

Background: Data on the prevalence and disease management of chronic urticaria (CU) and chronic spontaneous urticaria (CSU) in the pediatric population are scarce. This study assessed the prevalence of CU and CSU, and disease management among pediatric patients (0-17 years).

Methods: A physician-based online survey was conducted in 5 European countries (United Kingdom, Germany, Italy, France, and Spain) assessing the annual diagnosed prevalence, disease characteristics, and treatment patterns in the target population. Results are based on physician responses and analyzed using descriptive statistics. Prevalence estimates were calculated based on the number of CU/CSU pediatric patients diagnosed, seen, and treated by the respondents and extrapolated to the total pediatric population from each country.

Results: Across 5 European countries, the one-year diagnosed prevalence of CU and CSU in pediatric patients was 1.38% (95% CI, 0.94-1.86) and 0.75% (95% CI, 0.44-1.08), respectively. Angioedema was reported in 6%-14% of patients. A large proportion of CSU pediatric patients (40%-60%) were treated with H1-antihistamines at approved dose and 16%-51% received H1-antihistamines at higher doses. Approximately 1/3 of pediatric CSU patients remained uncontrolled with H1-antihistamines at approved/higher doses. Other prescribed treatments were oral corticosteroids (10%-28%) and topical creams (15%-26%).

Conclusions: This study revealed a prevalence of CSU among pediatric population comparable to adults and also suggested an unmet need for approved treatments for inadequately controlled pediatric CSU patients. It is truly of concern that harmful (oral steroids) or insufficient (topical creams) treatments were frequently used despite better and guideline-recommended alternatives.

KEYWORDS

angioedema, chronic spontaneous urticaria, chronic urticaria, Europe, pediatric, prevalence, treatment patterns

1 | INTRODUCTION

Chronic urticaria (CU) is a debilitating disease characterized by itching hives, angioedema, or both for more than 6 weeks^{1,2} and has two forms, chronic spontaneous urticaria (CSU) and chronic inducible urticaria (CINDU).² CSU has spontaneous appearance of urticaria symptoms (ie, hives, angioedema, or both) due to known or unknown causes.² CSU is believed to affect 0.5%-1% of the global population at any given time, and it accounts for approximately two-thirds of all cases of CU.¹

In children, urticaria commonly presents as a single acute episode lasting a few days to weeks, and a small proportion of patients are generally reported to progress to a chronic form of the disease.³ The underlying causes of CU were reported to be similar in children and adults. Subtle changes in clinical characteristics had been observed between children and adults, for example, shorter time to remission, more frequent association with infection, and less frequent occurrence of angioedema in children.^{2,4,5} CU and CSU have a greater impact on health-related quality of life (HRQoL) in pediatric patients compared to other chronic diseases of childhood including epilepsy and diabetes.⁶ Moreover, these conditions could significantly affect children's learning capacity, with time missed from school and negative impact on work for caregivers and parents.⁷

The international EAACI/GA²LEN/EDF/WAO guidelines have recommended a stepwise treatment approach for CSU management in pediatric patients similar to adult patients.² They recommend second-generation non-sedating H1-antihistamines as the first-line treatment, followed by their weight-adjusted up-dosing if symptoms persist for more than 2 weeks. The use of first-generation sedating H1-antihistamines is particularly discouraged for children, as they are more sensitive to higher doses of sedating H1-antihistamines than adults and consequently are more likely to experience side effects.⁸ In refractory patients, the current guidelines² recommend the use of omalizumab, leukotriene receptor antagonists (LTRAs), or ciclosporin as an add-on therapy to H1-antihistamines. Short-course systemic corticosteroids can be administered during acute exacerbations.

While there is increasing information about the epidemiology, clinical characteristics, and treatment of CU and CSU in adults, there is little published information about these conditions in the pediatric population.^{4,9-11} Very few studies have reported the prevalence of CU and CSU in pediatric patients.¹²⁻¹⁴ Moreover, these studies were small in size and had limited information regarding geographic variations in prevalence of CU and CSU in the pediatric population.

The objectives of this study were to identify one-year diagnosed prevalence of CU and CSU, as well as, to assess disease characteristics and treatment patterns of CSU in pediatric patients in 5 European countries (United Kingdom (UK), Germany, France, Italy, and Spain).

2 | METHODS

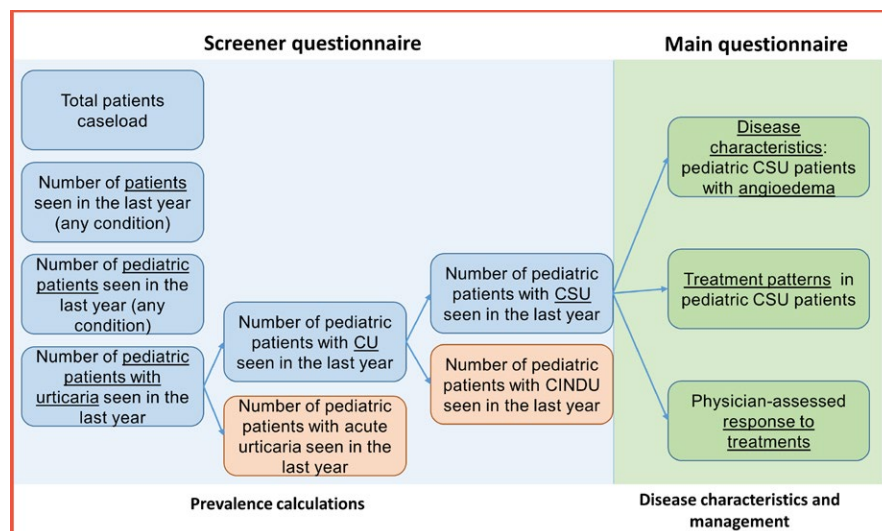
2.1 | Study design

An online survey (screening and main questionnaire) was conducted during September and October 2015 with physicians recruited from large, representative, national panels in UK, Germany, France, Italy, and Spain (Figure 1).

2.2 | Respondent selection

General practitioners, dermatologists/allergists, and pediatricians with 2-30 years of medical practice from primary, secondary, and tertiary healthcare settings were considered eligible and asked to answer the screener questionnaire and were randomly selected to take part in the survey. For the main questionnaire, physicians who treated at least 5 pediatric patients with any condition and at least 1 pediatric patient with CU and CSU in the calendar year 2014 were included. For each country, the total sample (screen out and completes) is representative of the target physician population in that country with respect to geographic region distribution and medical specialty as per national statistics.

FIGURE 1 Study design. CU, chronic urticaria; CSU, chronic spontaneous urticaria; CINDU, chronic inducible urticaria. For calculation of CU prevalence, patients with acute urticaria were excluded. For calculation of CSU prevalence, patients with CINDU were excluded [Colour figure can be viewed at wileyonlinelibrary.com]



2.3 | Screening and main questionnaire

Both questionnaires (see supporting information) referred to a period of 12 months counting for the calendar year 2014. The screening questionnaire contained questions related to the total patients' caseload and the number of pediatric patients seen for any condition and specifically for CU and CSU (Figure 1). In the main questionnaire, the questions focused on CSU disease characteristics including the presence of angioedema, treatment patterns, and physician-assessed response to treatments (Figure 1). Inadequately controlled patients were defined as those who, despite the prescribed treatment, were still symptomatic, presenting hives, itch, and/or angioedema, and required a change in the treatment.

2.4 | Outcomes

Three main outcomes were reported: (i) one-year diagnosed prevalence estimates of CU and CSU in the pediatric population in the year 2014; (ii) estimates for the proportions of patients with the presence of angioedema related to CSU as reported by the respondent physicians based on their record or recall; and (iii) estimates for the proportions of pediatric CSU patients receiving different treatment options as reported by physicians based on their record or recall, as well as, the proportions of patients inadequately controlled despite receiving H1-antihistamine treatment at approved/higher doses.

2.5 | Statistical analysis

The diagnosed prevalence of CU and CSU in 2014 in the pediatric population was calculated as per below equations:

$$\text{Prevalence of CU} = \frac{[\text{Pediatric population with CU during the year of survey}]}{[\text{Pediatric population during the same time period in each country}]} \times 100$$

$$\text{Prevalence of CSU} = \frac{[\text{Pediatric population with CSU during the year of survey}]}{[\text{Pediatric population during the same time period in each country}]} \times 100$$

In above equations, the nominator value, that is, "pediatric population with CU or CSU during the year of survey," was calculated by summing up the total number of pediatric patients diagnosed, seen, and treated with CU or CSU during the calendar year 2014 by each physician included in the sample. The results from the sample, which include average patient load per physician and the distribution of means, were used to make inferences about the total eligible population of physicians from each country. Statistical calculations combining sample size and variability (standard deviation) were used to generate a confidence interval (95% CI) for all the prevalence estimates.

The total pediatric population in each country within the same time period (denominator value) was obtained from Eurostat.¹⁵ The other outcomes, namely treatment patterns, response to treatments, and the presence of angioedema, were reported as

proportions. Outcomes were reported for each of the 5 countries and per three different pediatric age groups (0-6 years, 7-11 years, and 12-17 years).

3 | RESULTS

A total of 2074 physicians completed the screener questionnaire (UK: 370, Germany: 454, France: 457, Italy: 392, and Spain: 401), and 1127 physicians completed the main questionnaire (UK: 225, Germany: 225, France: 226, Italy: 226, and Spain: 225).

3.1 | Prevalence of CU

The estimated number of pediatric patients (aged 0-17 years) suffering from CU in the year 2014 was 825.774 across the 5 countries surveyed. Based on the total pediatric population during this same time period, the prevalence of CU in the pediatric population was estimated to be 1.38% (Table 1). The CU prevalence varied from 1.11% to 1.52%, with the highest prevalence observed in France and lowest in Germany (Table 1). The CU prevalence was numerically higher in older age groups (aged 7-11 and 12-17 years) compared to the youngest age group (aged 0-6 years) (Table 1). The differences in prevalence of CU among different countries and age groups were not statistically significant.

3.2 | Prevalence of CSU

The estimated number of CSU pediatric patients was 450.123 in five European countries, resulting in prevalence of 0.75% across the five European countries (Table 2). Prevalence of CSU ranged from 0.58% to 0.86% with the highest prevalence observed in Italy and lowest in Germany (Table 2). The CSU prevalence was numerically higher in older age groups (aged 7-11 and 12-17 years) compared to the youngest age group (aged 0-6 years) in Germany, France, Italy, and Spain (Table 2). These numerical differences among the different countries and age groups were not statistically significant.

3.3 | Presence of angioedema in CSU patients

Physicians reported that 5%-14% of their pediatric patients with CSU had angioedema (Figure 2). The estimates of angioedema were numerically higher in the oldest age group (12-17 years) compared to younger age groups (0-6 years and 7-11 years), although the differences were not statistically significant (Figure 2).

3.4 | Treatment patterns among CSU patients

A large proportion of pediatric CSU patients (>40% in UK, Germany and Italy; >60% in France and Spain) were treated with H1-antihistamines at the approved dose (Figure 3). H1-antihistamines at higher than approved doses were prescribed in 16%-51% of pediatric patients across the countries (Figure 3). Other frequently prescribed

TABLE 1 Annual diagnosed CU prevalence in pediatric population in five European countries in 2014

	EU5	UK	Germany	France	Italy	Spain
Estimated # of CU patients (0-17 y)	825.774	185.923	145.504	222.576	146.294	125.477
Age (y)	CU prevalence (in percentage)					
0-17	1.38 (95% CI 0.94-1.86)	1.37 (95% CI 0.71-2.02)	1.11 (95% CI 0.82-1.40)	1.52 (95% CI 1.08-1.96)	1.44 (95% CI 1.01-1.87)	1.51 (95% CI 1.06-1.96)
0-6	0.92 (95% CI 0.49-1.36)	1.05 (95% CI 0.56-1.55)	0.67 (95% CI 0.40-0.94)	1.10 (95% CI 0.55-1.64)	0.76 (95% CI 0.34-1.18)	0.99 (95% CI 0.57-1.42)
7-11	1.73 (95% CI 1.08-2.38)	1.99 (95% CI 0.84-3.14)	1.47 (95% CI 1.04-1.90)	1.83 (95% CI 1.29-2.38)	1.61 (95% CI 1.09-2.12)	1.65 (95% CI 1.11-2.20)
12-17	1.61 (95% CI 1.08-2.14)	1.21 (95% CI 0.64-1.79)	1.26 (95% CI 0.90-1.62)	1.69 (95% CI 1.20-2.17)	2.03 (95% CI 1.37-2.68)	1.92 (95% CI 1.32-2.51)

TABLE 2 Annual diagnosed CSU prevalence in pediatric population in five European countries in 2014

	EU5	UK	Germany	France	Italy	Spain
Estimated # of CSU patients (0-17 y)	450.123	110.305	76.029	117.352	86.849	59.588
Age (y)	CSU prevalence (in percentage)					
0-17	0.75 (95% CI 0.44-1.08)	0.81 (95% CI 0.23-1.39)	0.58 (95% CI 0.42-0.74)	0.80 (95% CI 0.54-1.07)	0.86 (95% CI 0.54-1.18)	0.72 (95% CI 0.48-0.96)
0-6	0.53 (95% CI 0.19-0.87)	0.84 (95% CI 0.09-1.59)	0.37 (95% CI 0.19-0.56)	0.54 (95% CI 0.32-0.75)	0.4 (95% CI 0.18-0.63)	0.41 (95% CI 0.17-0.65)
7-11	0.89 (95% CI 0.50-1.29)	0.97 (95% CI 0.37-1.57)	0.67 (95% CI 0.43-0.91)	1.06 (95% CI 0.71-1.40)	0.89 (95% CI 0.47-1.30)	0.87 (95% CI 0.53-1.21)
12-17	0.90 (95% CI 0.54-1.26)	0.64 (95% CI 0.22-1.06)	0.71 (95% CI 0.54-0.89)	0.87 (95% CI 0.45-1.28)	1.34 (95% CI 0.84-1.83)	0.96 (95% CI 0.64-1.28)

treatments were oral corticosteroids (10%-28% of patients), topical creams (15%-26% of patients), and leukotriene receptor antagonists (LTRA; 4%-18% of patients) (Figure 3). A very small proportion of patients also received ciclosporin or omalizumab (<5%) (Figure 3).

Approximately 1/3 of pediatric CSU patients remained uncontrolled with H1-antihistamines at approved or higher doses. Uncontrolled CSU was generally higher in the oldest age group (12-17 years) (Figure 4).

4 | DISCUSSION

This is the first study that assessed the prevalence of CU and CSU in the pediatric population in five European countries (France, Germany, Italy, Spain, and UK) using a representative online physician survey. The prevalence of CU and CSU in pediatric patients was found to be 1.38% and 0.75%, respectively, across these countries. These findings suggest that the prevalence of CU and CSU in the pediatric population is similar to that of the adult population.

Very limited information is available in the literature regarding the epidemiology of CU and CSU in pediatric patients. The retrospective, population-based study conducted by Cantarutti et al in Italy reported the prevalence of CU in children aged 0-14 years over

the time period 2006-2012.¹² The observed prevalence increased over the years, with prevalence estimates of 0.38% (95% CI 0.3-0.4) in 2006 and 0.84% (95% CI 0.8-0.9) in 2012. In our study, the prevalence of CU in Italy was higher [1.44 (95% CI 1.01-1.87)] compared to that reported by Cantarutti and coworkers, which may be mainly due to the different time period (2014) and age group (0-17 years) considered in our analysis. A retrospective claims database analysis conducted by Broder et al estimated the prevalence of CSU in children aged ≤11 years at 0.14% in the United States.¹³ These findings obtained from a claims database might be underestimating the true prevalence due to the absence of a single specific International Classification of Diseases (ICD) code for the diagnosis of CSU and therefore the need to use an algorithm to define CSU cases. Our study was not conducted in the United States and was based on data collected from clinicians; therefore, no direct comparison can be made.

The prevalence of CU and CSU in the pediatric population might be underestimated in different studies, as it is likely to happen that some of the CU and CSU cases in children and in adolescents might not come to specialists and are possibly treated by parents using over-the-counter medications. Hence, a general population-based survey might provide more accurate estimates of the prevalence of the disease. For example, a recently conducted cross-sectional study

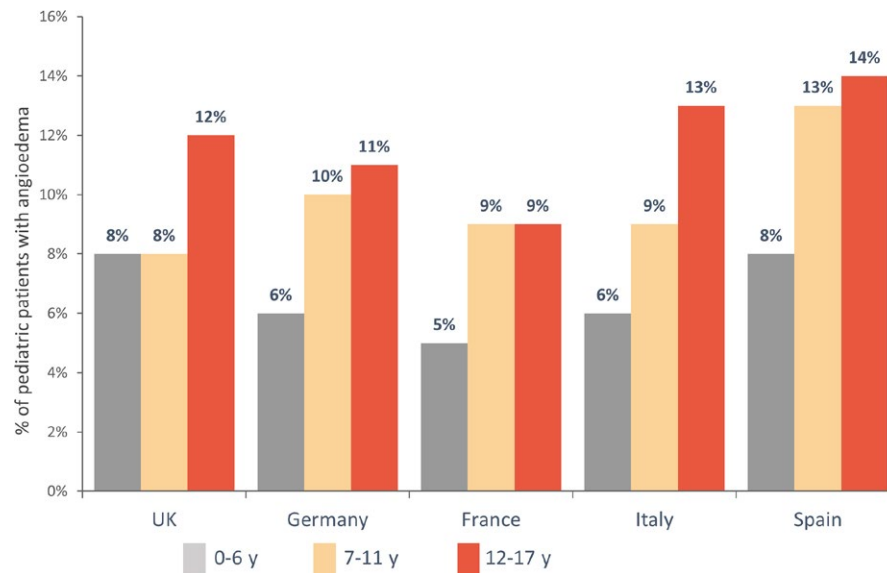


FIGURE 2 Proportion of CSU pediatric patients suffering from angioedema related to CSU as reported by physicians [Colour figure can be viewed at wileyonlinelibrary.com]

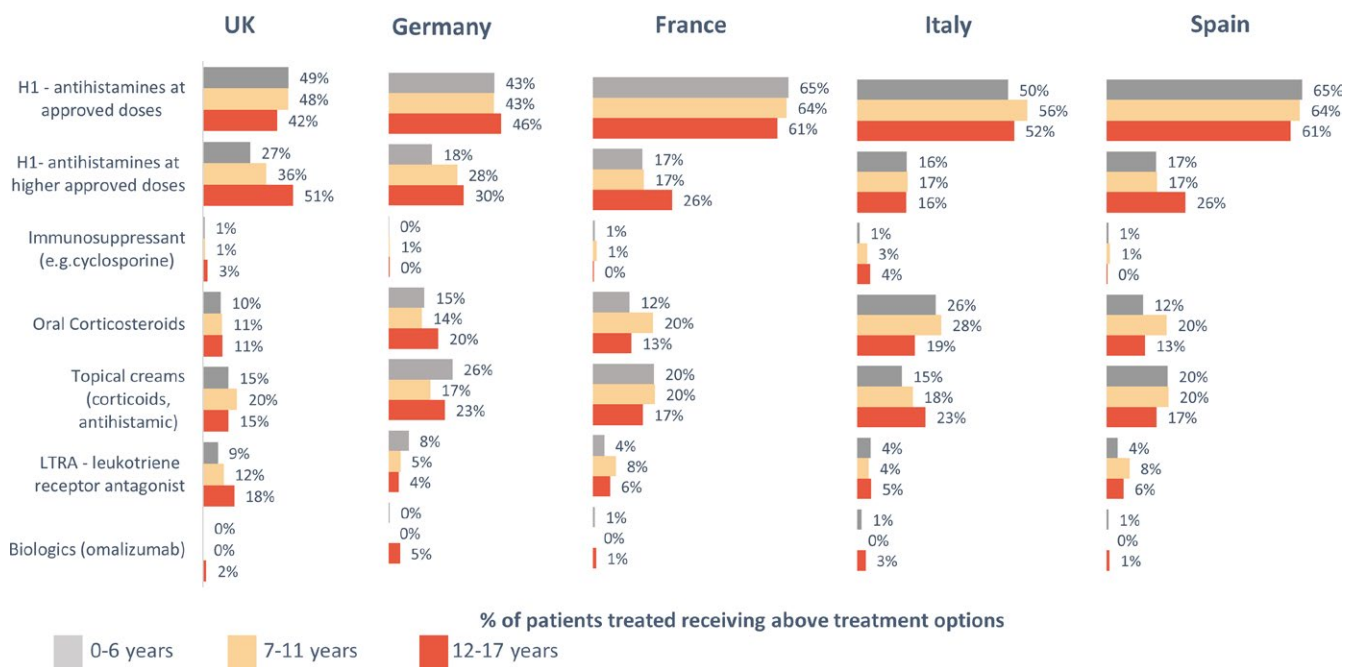


FIGURE 3 Percentage of CSU pediatric patients receiving different treatments as reported by physicians [Colour figure can be viewed at wileyonlinelibrary.com]

in Korea, which included 4076 children aged 4-13 years from 3 kindergartens and 6 elementary schools, reported a CU prevalence of 1.8% in this population.¹⁶

Although we did not specifically assess the prevalence of chronic inducible urticaria (CINDU) in this study, the assumption that all CU patients who did not have CSU were CINDU patients resulted in a prevalence rate of 0.63. Future studies are required to assess the prevalence of CINDU in the pediatric population.

The presence of angioedema is an important prognostic factor to predict the course of disease in CSU patients.¹ A study by Volonakis

et al investigated 226 pediatric CU patients aged 1-14 years for the presence of angioedema and reported that wheals along with angioedema were present in 15% of patients.¹⁷ Our study found that 5%-14% of pediatric CSU patients develop angioedema. In contrast, in adult CSU patients, rates of angioedema are considerably higher, ranging from 33 to 67% in different studies.¹⁸⁻²²

Interestingly, in adult patients with CSU, a recent real-world study in inadequately controlled CSU patients has found that 32.8% of patients reported angioedema without having it recorded in the medical forms, indicating a disagreement in reporting of angioedema

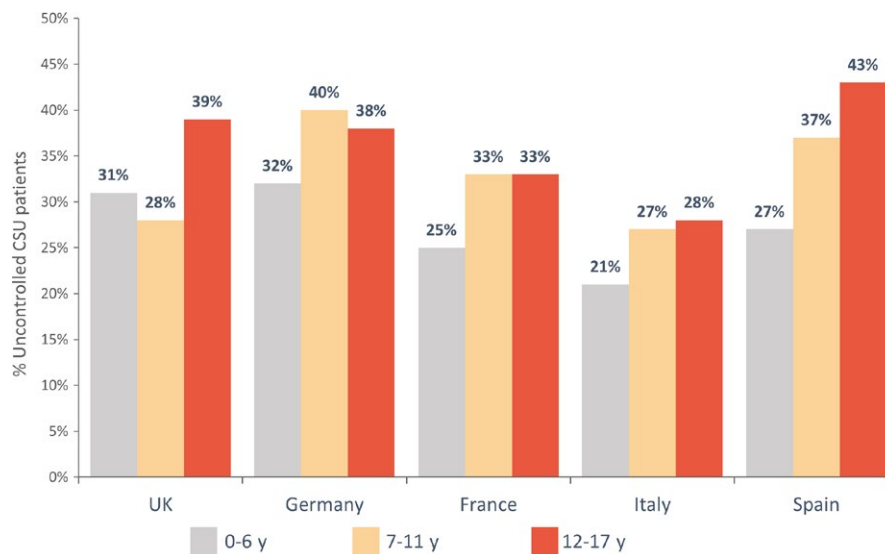


FIGURE 4 Percentage of uncontrolled CSU patients despite receiving H1-antihistamines treatments (at approved or higher doses) as reported by physicians [Colour figure can be viewed at wileyonlinelibrary.com]

between physicians and patients.²³ This group of patients reported a similar negative impact of angioedema as the patients with confirmed angioedema. Hence, angioedema might be underestimated in clinical practice. This could also hold true for our study which assessed the presence of angioedema in the pediatric population as reported by physicians at rates ranging from 5% to 14%.

Published data regarding the overall treatment patterns and response to treatment in the pediatric population are scarce. Although treatment recommendations for the management of pediatric patients are based on extrapolation of data obtained in adult patients,^{2,4} such extrapolations need to be done with caution. Many independent studies in the medical literature have emphasized the point that extrapolation of adult data to children may not be accurate.^{24,25} For example, drugs such as H1-antihistamines that are used in the treatment of CSU can be metabolized and excreted differently in children compared with adults.²⁶

The current study reported the full range of drugs prescribed in the real world to treat CSU in the pediatric population, as well as, physician reported response to treatments. A large proportion of patients were treated with H1-antihistamines at approved/higher doses, but at least one-third of patients were inadequately controlled, suggesting a high unmet need for effective second-line treatments in the pediatric CSU patients. The present analysis also revealed that a high proportion of patients received oral corticosteroids and topical creams. However, guidelines recommend only short-term use of oral corticosteroids to treat exacerbations in CSU and no topical treatments.² There is a need to increase awareness among physicians, who treat children and adolescents with CSU, about treatment guidelines in CSU.

The present study has several limitations. Findings from this study were based on physicians' recall and were not confirmed through medical record abstraction. As prevalence estimates were

obtained as reported by physicians, there could be possible chances of overestimation, as well as, underestimation of prevalence. Even if the study design tried to avoid double counting, there is always a risk that the same patient visited more than one physician for the same medical problem, leading to the overestimation of prevalence. On the other hand, it might occur that some of the patients did not visit any physicians and were treated by over-the-counter medications by parents or visited other specialty physicians not included in the present study, leading to the underestimation of prevalence (for this reason, we report the data as diagnosed prevalence). This study did not distinguish between sedating and non-sedating H1-antihistamines. As this study was a physician-based survey, disease characteristics as reported by patients and caregivers were not assessed.

In conclusion, the present study demonstrated that the prevalence of CU and CSU in the pediatric population could be higher than estimated and comparable to that in the adult population. A large number of pediatric patients are inadequately controlled with currently prescribed treatments, and there is a high unmet need for approved second-line effective treatments of CSU for this population. It is truly worrying that both harmful (oral steroids) and insufficient (topical creams) treatments were frequently used despite better and guideline approved alternatives. Awareness of treatment guidelines among physicians could lead to better adherence to guidelines and thus facilitate improved care for patients. In the future, more studies are required to further understand the epidemiology, disease burden, and management of CU and CSU in pediatric patients.

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CONFLICT OF INTEREST

Maria-Magdalena Balp, Charis Papavassilis, and Thomas Severin are employees of Novartis Pharma AG, Basel, Switzerland. Alexandra Chirilov is an employee of GfK SE, Nuremberg, Germany. Veruska Carboni is an employee of GfK Switzerland AG, Risch-Rotkreuz, Switzerland. Haijun Tian is employee of Novartis Pharmaceuticals Corporation, East Hanover NJ, USA. Karsten Weller received honoraria for educational lectures from Dr. R. Pflieger, Essex pharma (now MSD), Uriach, UCB, Novartis, Shire, Viropharma, and Moxie. In addition, he received honoraria for consulting from Novartis and he is or was involved in clinical research projects of Dr. R. Pflieger, Essex pharma (now MSD), Faes, Uriach, Novartis, Shire, and Viropharma. Torsten Zuberbier is affiliated with organizations like WHO-Initiative ARIA, DGAKI, ECARF, GA²LEN, and WAO in various capacities; he received research grants and/or honoraria for consulting from AstraZeneca, AbbVie, ALK, Almirall, Astellas, Bayer Health Care, Bencard, Berlin Chemie, FAES, HAL, Henkel, Kryolan, Leti, L'Oreal, Meda, Menarini, Merck, MSD, Novartis, Pfizer, Sanofi, Stallergenes, Takeda, Teva, UCB. Marcus Maurer is or was a Speaker and/or Advisor for and/or have received research funding from Almirall Hermal, Bayer, Schering Pharma, Biofrontera, Essex Pharma, Genentech, GSK, Merckle Recordati, Moxie, Novartis, Sanofi Aventis, Schering-Plough, Leo, MSD, Shire, Symbiopharm, UCB, Uriach, and Viropharma.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Supplementary Material

A list of screener and main questionnaires has been given below.

SCREENER QUESTIONNAIRE

- S1. Please select the region where your primary practice is located?
- S2a. What is your **primary** medical specialty?
- S2b. Do you have a **secondary specialty**?
- S2c. What is your **secondary specialty**?
- S3. How many years have you been practicing your specialization since completing residency?
- S4a. Which of the following best describes your **primary** practice setting?
- S5. What is the name of your place of practice?
- S5a. Approximately, could you please indicate the average number of beds of your place of practice?

PATIENT CASELOAD:

- S6. In the **past year**, approximately, how many patients, have you personally seen and clinically managed **for any condition**?
- S6a. In the **past year**, how many **pediatric patients**, including adolescents (**patients aged 0 to 17 years inclusive**), have you personally seen and clinically managed **for any condition**?
- S6b. What proportion of them falls into these 3 age categories?
- 0-6 years old
- 7-11 years old
- 12-17 years old
- S7. In the **past year**, how many pediatric patients, including adolescents (**patients aged 0 to 17 years inclusive**), have you personally seen with **urticaria** (including patients personally diagnosed/treated/managed and patients referred on for treatment)?

Q1. Of the pediatric patients you have **personally seen** for **urticaria in the past year**, how many suffered from **chronic urticaria (CU*)**?

And how many suffered from **acute urticaria (AU**)**? (Including patients personally treated/managed and patients referred on for treatment).

For the common understanding of the question and types of urticaria, we would like to use the definitions as per International Guideline (the EAACI/GA2LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update).

***CHRONIC URTICARIA** is defined as urticaria with daily or almost daily appearance of pruritus and wheals with or without angioedema for 6 weeks or more. Chronic urticaria is further subdivided into chronic spontaneous urticaria (CSU) and chronic inducible urticaria.

****ACUTE URTICARIA** is defined as urticaria lasting for less than 6 weeks.

Q1b. And of the pediatric patients you have **personally seen with chronic urticaria in the past year**, how many were diagnosed predominantly with **chronic spontaneous urticaria (CSU*)**?

And how many were diagnosed predominantly with **chronic inducible urticaria (CINDU**)**?

For the common understanding of the questions and types of urticaria, we would like to use the definitions as per International Guideline (the EAACI/GA2LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update).

***CHRONIC SPONTANEOUS URTICARIA (CSU)** is defined as spontaneous, daily, or almost daily occurrence of itchy hives, with or without angioedema, lasting for 6 weeks or more. Spontaneous means the occurrence of the wheals without a known trigger such as physical urticaria or stress/physical exercise in the sense of cholinergic urticaria, or intake of a food to which the patient has a known hypersensitivity.

****CHRONIC INDUCIBLE URTICARIA (CINDU)** is defined as urticaria induced by a well-known trigger such as pressure, water, sun, or exercise/stress (cholinergic urticaria)

MAIN QUESTIONNAIRE

SECTION 1- CU MARKET SIZING

Let's start with Chronic Urticaria.

Doctor you have previously mentioned that, **in the past year**, you have seen **pediatric patients affected by chronic urticaria (CU)** (including patients personally diagnosed/treated/managed and patients referred on for treatment).

Q2. Of those pediatric patients you have seen for **chronic urticaria**, how many...:

	# CU patients
a) ... did you personally diagnose and manage	_____ #
b) ...were diagnosed by another physician and sent to you for management	_____ #
c) ...did you personally diagnose and refer to	_____ #

another physician for management	

Q3. Of those patients, **approximately**, how many fell into these 3 age categories?

	_____ # CU patients	Q3a 0-6 years old	Q3b 7-11 years old	Q3c 12-17 years old
a) ... did you personally diagnose and manage	_____ #	_____ #	_____ #	_____ #
b) ... were diagnosed by another physician and sent to you for management	_____ #	_____ #	_____ #	_____ #
c) ...did you personally diagnose and refer to another physician for management	_____ #	_____ #	_____ #	_____ #

SECTION 2- CSU POPULATION SIZING

We will now talk about Chronic Spontaneous Urticaria.

Doctor, before you mentioned that in the past year you have personally seen:

- Pediatric patients **with Chronic Spontaneous Urticaria (CSU*)**;
- Pediatric patients with **chronic inducible urticaria (CINDU**)**

***CHRONIC SPONTANEOUS URTICARIA (CSU)** is defined as spontaneous, daily, or almost daily occurrence of itchy hives, with or without angioedema, lasting for 6 weeks or more. Spontaneous means the occurrence of the wheals without a known trigger such as physical urticaria or stress/physical exercise in the sense of cholinergic **urticaria, or intake of a food to which the patient has a known hypersensitivity.**

****CHRONIC INDUCIBLE URTICARIA (CINDU)** is defined as urticaria induced by a well-known trigger such as pressure, water, sun, or exercise/stress (cholinergic urticaria)

Q4. Of those patients you have seen for **chronic inducible urticaria**, what proportion of them fell into these 3 age breaks?

	0-6 years old	7-11 years old	12-17 years old	
_____ # CINDU patients seen in the past year	_____ %	_____ %	_____ %	Total =100%

96 Q5. Of those patients you have seen for **chronic spontaneous urticaria**, how many...

	_____ # CSU patients
a) ... did you personally diagnose and manage	_____ #
b) ... were diagnosed by another physician and sent to you for management	_____ #
c) ...did you personally diagnose and refer to another physician for management	_____ #

97
98
99 Q6. Of those patients, **approximately**, how many fell into these 3 age categories?
100

	_____ # CSU patients	Q8.1 0-6 years old	Q8.2 7-11 years old	Q8.3 12-17 years old
a) ... did you personally diagnose and manage	_____ #	_____ #	_____ #	_____ #
b) ... were diagnosed by another physician and sent to you for management	_____ #	_____ #	_____ #	_____ #
c) ...did you personally diagnose and refer to another physician for management	_____ #	_____ #	_____ #	_____ #

101
102
103 **SECTION 3: TREATMENT**

104 Q7. Of the pediatric patients you **have personally and clinically treated/managed** for **chronic**
105 **spontaneous urticaria, in the past year**, what proportion received the following treatment options in
106 each age category?
107

	0-6 years old	7-11 years old	12-17 years old
1. H1- antihistamines at approved doses	_____ %	_____ %	_____ %
2. H1- antihistamines at higher approved doses	_____ %	_____ %	_____ %
3. Immunosuppressant (e.g cyclosporine)	_____ %	_____ %	_____ %
4. Oral Corticosteroids)	_____ %	_____ %	_____ %

5. Topical creams (corticoids, antihistaminic)	_____ %	_____ %	_____ %
6. LTRA – leukotriene receptor antagonist	_____ %	_____ %	_____ %
7. Biologics (omalizumab)	_____ %	_____ %	_____ %
8. Alternative treatments (homeopathic / TCM / ...)	_____ %	_____ %	_____ %
9. Wait & see / no active treatment	_____ %	_____ %	_____ %
10. Other treatments	_____ %	_____ %	_____ %

Q8. Please now focus on your patients with **chronic spontaneous urticaria** that you **treated with antihistamines (approved or higher approved daily doses)** in the past year.

What proportion of them were **insufficiently controlled* on antihistamines in each age category?**

** **By insufficiently controlled we intend a patient who, despite the prescribed treatment, results still symptomatic, presents hives and itch and requires a change in the treatment.***

IF NONE OF THEM PLEASE INSERT 0

	0-6 years old	7-11 years old	12-17 years old
Patients insufficiently controlled on antihistamines <u>(approved or multiple of approved daily doses)</u>	_____ %	_____ %	_____ %

Q9. Please now think of your patients **insufficiently controlled on antihistamines (approved or higher approved daily doses).**

Approximately, what proportion of them suffered from mild, moderate and severe CSU in each age break?

	0-6 years old	7-11 years old	12-17 years old
Mild	_____ %	_____ %	_____ %
Moderate	_____ %	_____ %	_____ %
Severe	_____ %	_____ %	_____ %
Don't know	○	○	○

Q10. Considering all your pediatric patients suffering from **chronic spontaneous urticaria** that you personally treated in the past year, approximately, what proportion of them also **presented angioedema related to CSU in each age category**?

IF NONE OF THEM PLEASE INSERT 0

	0-6 years old	7-11 years old	12-17 years old
CSU patient with angioedema	_____ %	_____ %	_____ %

Q11. On average, could you please indicate the **CSU disease duration** in your pediatric patients in each age break?

	0-6 years old	7-11 years old	12-17 years old
Less than 6 months	☐	☐	☐
6 months to 1 year	☐	☐	☐
Above 1 year	☐	☐	☐
Patient has never come back after 6 months	☐	☐	☐

Q12. What proportion of your pediatric **CSU** patients (0 to 17 years old) were diagnosed with another condition before the final **CSU** diagnosis was confirmed / given?

IF NONE OF THEM PLEASE INSERT 0

% of patients diagnosed with another condition	_____ %
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