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ORIGINAL ARTICLE

Impact of chronic urticaria on quality of life and work in Japan: Results of a real-world study

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ABSTRACT

Little attention has been given to the burden of chronic urticaria (CU) in Japan compared with other skin diseases, such as atopic dermatitis (AD) and psoriasis. The primary objective of the RELEASE study was to evaluate the real-life quality-of-life impairment in CU patients in Japan. Data were collected from 1443 urticaria, 1668 AD and 435 psoriatic patients; 552 urticaria patients who presented urticaria symptoms for over 6 weeks were defined as CU. The mean Dermatology Life Quality Index (DLQI) total score was 4.8, 6.1 and 4.8 in CU, AD and psoriatic patients, respectively. Disease control of urticaria evaluated by the Urticaria Control Test (UCT) and DLQI exhibited a strong correlation with a Spearman's rank correlation coefficient of −0.7158. CU and AD patients had relatively higher scores in all Work Productivity and Activity Impairment – General Health subscales except for absenteeism. At the time of the survey, approximately 64% of CU patients reported UCT scores of <12 and demonstrated higher work productivity loss and activity impairment versus patients with UCT scores of ≥12. Patients with lower UCT scores also displayed a higher percentage of dissatisfaction with their health state and the treatment they received. Approximately 85% of patients with CU had visited dermatology clinics, and less than 20% had visited hospital, indicating existence of a highly burdened population outside specialized centers. These results highlight the unmet medical needs of CU patients, suggesting the need to increase awareness of CU burden among both physicians and patients and to pursue improved real-life patient care.

Key words: chronic urticaria, Japanese, quality of life, questionnaires, urticaria.

INTRODUCTION

Chronic urticaria (CU) is characterized by the recurrent appearance of wheals and/or angioedema for more than 6 weeks.[1] The point prevalence of CU has been reported to be 0.5–1%.[2] According to a national patient survey conducted by the Ministry of Health, Labor and Welfare in Japan in 2014, nearly 228 000 patients were reported to have urticaria.[3] An epidemiological survey in Japan by Tanaka *et al.*[4] reported that approximately half of the total urticaria population had chronic spontaneous urticaria (CSU).

Existing evidence indicates that chronic symptoms of urticaria have a detrimental effect on the quality of life (QoL) including daily activities and emotional well-being.[5–7] Additionally, CU affects many aspects of QoL comparable with or worse than other chronic skin disorders such as atopic dermatitis or psoriasis.[7,8]

However, most previously published data on urticaria patients originated from highly selected patient populations treated at specialized centers, which tend to treat patients who suffer from severe disease, and may not reflect the average patient profiles.[9,10]

Recently, an online survey in Germany (ATTENTUS), in which data were collected from 9055 participants diagnosed with CU in real-life setting, reported the existence of a highly burdened population outside specialized centers. This German survey also revealed that 13–35% of patients with CU (depending on the length of time of being affected by symptoms) apparently gave up visiting their doctor to discuss impairments and rather chose self-treatment, highlighting the importance of better awareness of the disease and available treatment options for improved patient care.[11]

In Japan, limited studies have been conducted to evaluate the CU burden, while the burden of atopic dermatitis and psoriasis has been reported and widely recognized.[12–14] Thus, burden of CU is often disregarded compared with atopic dermatitis and psoriasis. Moreover, CU patients refractory to antihistamines and other conventional medications had few treatment options and often stopped visiting health-care providers (HCP). Omalizumab, an anti-immunoglobulin E monoclonal antibody, is a new treatment option that was approved in Japan on 24 March 2017 for the treatment of CSU, providing an opportunity to manage refractory CSU. Therefore, investigation of the real-life patient journey and impact of CU in

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Japanese patients is required to understand needs for a new treatment.

This cross-sectional, non-interventional, observational, web-based survey was conducted in Japan to assess the real-life burden in CU patients, together with atopic dermatitis and psoriatic patients to compare the degree of the burden. For the assessment of disease activity in patients with urticaria, European Academy of Allergology and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA²LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO) guidelines recommend the use of Urticaria Activity Score (UAS).[15] However, the UAS is a daily diary which has to be completed prospectively by patients and therefore not practical for a one-time survey. The RELEASE study employed the Urticaria Control Test (UCT), another recommended tool which retrospectively assesses the overall control of urticaria for the past 4 weeks with a simple scoring system.[16] Online survey is considered an appropriate method to investigate a real-life setting, as it facilitates data collection from a broad population including patients who currently do not visit physicians. However, online surveys are unlikely to capture the severest symptoms of past experience, as questionnaires, such as UCT and health-related QoL, principally collect data at current condition. This RELEASE study therefore included questionnaires to collect data on severest symptoms experienced in the past.

Herein, we present the patient demographics, disease activity, health-related QoL and health-care resource utilization results from the RELEASE study.

METHODS

Survey design and patients

In the RELEASE study, data were collected between 15 April and 30 May 2017 and patients were recruited through the patient panel of Rakuten Research with support from Social Survey Research Information Co. Ltd. Information on sociodemographics, use of health-care system and health-related QoL were included in the questionnaire (Fig. S1). The study was approved by a central ethics committee before initiating contact with patient panel members.

Inclusion criteria were patients who: (i) had been previously diagnosed with urticaria, psoriasis and/or atopic dermatitis and had visited physicians within the past 12 months; (ii) were willing to participate in an online survey in order to help increase the knowledge of disease; and (iii) able to provide informed consent. Patients under 20 years of age were a small portion of the panel (<1%) and not recruited to this survey.

Patients with urticaria were asked to report the physicians' diagnosis of urticaria and the subtypes among the following options: acute urticaria, chronic spontaneous (idiopathic) urticaria (defined by appearance of spontaneous symptoms without obvious cause), mechanical urticaria, cold/heat urticaria, solar urticaria, cholinergic urticaria, allergy-induced urticaria, non-allergy-induced urticaria, angioedema (diagnosed as angioedema/Quincke's edema) and other urticaria. CU was defined as the presence of chronic symptoms (wheals/itching/angioedema) persisting for over 6 weeks. In addition to the total urticaria patients, data analysis was performed for urticaria subgroups of CU, angioedema, and others who had urticaria other than CU or angioedema.

Study objectives

The primary objective was to evaluate the QoL impairment in patients with CU measured by the Dermatology Life Quality Index (DLQI) and the Work Productivity and Activity Impairment – General Health (WPAI-GH). The secondary objective was to identify CU patient journey and the impact of CU on patient life, with assessing variables such as demographic characteristics (e.g. age at first onset of symptoms, duration of symptoms), frequency of consultation with HCP, HCP specialty, proportions of patients satisfied with overall health status and medical treatment, any diagnosis of specified urticaria types, prescription of medication (oral steroids and antihistamines), disease control as reflected in UCT and impairments associated with urticaria. Moreover, correlation between UCT and QoL or characterized impairments was evaluated. The exploratory objective was to assess the impact of atopic dermatitis and psoriasis on patient life with some of the above assessment tools used for CU, and to compare the impact on QoL and work productivity among three skin diseases.

Patient-reported outcomes

Three patient-reported outcomes, namely DLQI,[17,18] the WPAI-GH[19] and UCT,[16] were used to assess patient QoL, work productivity and urticaria control, respectively.

The DLQI is a 10-question dermatology QoL questionnaire with a recall period of 7 days. The overall score ranges from 0 (no impact on patient's life) to 30 (most severe impact).[17] The WPAI-GH assesses the impact on work in the past 7 days and has four subscales: (i) absenteeism; (ii) presenteeism; (iii) work productivity loss; and (iv) activity impairment.[19] The scores for these subscales are expressed as impairment percentages; higher scores reflect more absence from work and greater impairment on work and daily activities. UCT is a four-item instrument, which assesses urticaria control over the previous 4 weeks.[16] Each UCT item is rated on a Likert-like scale (scored with 0–4 points). The total score ranges from 0 (no disease control) to 16 (complete disease control). A score of less than 12 indicates uncontrolled symptoms and a score of less than 8 indicates poor symptom control.

In addition, patients were asked to complete the same questionnaires (DLQI, WPAI-GH and UCT) but with recalling any 4-week duration experiencing severest symptoms in the past 12 months, namely past QoL, past work productivity and past urticaria control, respectively. Information on sociodemographics, previous/current use of health-care system and satisfaction with medical care were collected from all eligible patients who met the study criteria.

Statistical analysis

Data obtained from patients who completed all the questionnaires were analyzed with the descriptive methods using Hideyoshi Dplus version 2011 (Social Survey Research Information,

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Tokyo, Japan) and Excel Statistics (BellCurve for Excel; Social Survey Research Information). Means, medians, standard deviation (SD), and minimum and maximum values are reported for quantitative measurements, whereas absolute and relative frequencies are presented for categorical measurements. The data presented in tables were rounded off to the first decimal points.

RESULTS

Demographic characteristics

Overall, data were collected from 1443, 1668 and 435 patients with urticaria, atopic dermatitis and psoriasis, respectively (Table S1). Among urticaria patients, 552 and 17 were identified with CU and angioedema, respectively, whereas 879 patients were identified with other forms of urticaria. The CU patients were divided into three categories based on the disease control; 63.9% with UCT score of less than 12 (sum of 24.8% with UCT <8 and 39.1% with UCT of 8–11) and 36.1% with UCT of 12 or more at the time of survey, and 90% with UCT of less than 12 (sum of 56.5% with UCT <8 and 33.5% with UCT of 8–11) and 10% with UCT of 12 or more under the severest conditions within the past 1 year (Table 1).

In the CU group, the mean age of patients was 45.2 years, and the male : female ratio was 4:6. The atopic dermatitis group had a mean age of 43.1 years, and a male : female ratio of 5:5, while the psoriatic group had a mean age of 52.9 years, higher than the other groups, and a male : female ratio of 8:2. In the CU group, the mean age at the onset of CU was 34.5 years, with most of them occurring between the age of 20–40 years. CU lasted for 10.7 years on average. Approximately 53% of the CU patients suffered from symptoms for 10–12 months/year (Table 1). The demographic characteristics of the total urticaria population are presented in Table S2.

DLQI score

The mean (±SD) DLQI total score was 4.8 (±5.1), 6.1 (±5.5) and 4.8 (±4.9) in patients with CU, atopic dermatitis and psoriasis, respectively (Fig. 1a). In the subgroup analysis of the CU group, patients with a UCT score of less than 8 showed the highest mean (±SD) DLQI total score (10.5 ± 6.1) followed by patients with a UCT score of 8–11 (4.0 ± 3.0) and a UCT score of 12 or more (1.7 ± 2.1; Fig. 1b). Among urticaria patients, those with angioedema had a higher mean (±SD) DLQI total score (10.1 ± 8.7) compared with CU (4.8 ± 5.1) and others (4.0 ± 4.7; Fig. S2a). For the DLQI subscales, patients reported higher scores on symptoms and feelings scale in all disease groups (Fig. S2b).

The mean (±SD) total score of past QoL was 8.4 (±6.4), 9.0 (±6.9) and 6.5 (±5.9) in patients with CU, atopic dermatitis and psoriasis, respectively (Fig. S3a). In the CU group, patients with past urticaria control score of less than 8 showed the highest past QoL total score (11.2 ± 6.5) compared with other subgroups (Fig. S3b). Among urticaria patients, those with angioedema had the highest past QoL total score (16.2 ± 9.4; Fig. S3c).

Table 1. Patient demographics

Characteristics	Chronic urticaria (n = 552)	Atopic dermatitis (n = 1668)	Psoriasis (n = 435)
Age (years), mean ± SD	45.2 ± 11.3	43.1 ± 10.6	52.9 ± 10.9
Female, %	59.2	49.2	20.5
Age of disease onset (years), mean ± SD	34.5 ± 14.4	14.2 ± 14.8	36.8 ± 15.8
Duration of disease (years), mean ± SD	10.7 ± 12.1	28.8 ± 13.2	16.1 ± 12.8
Months per year suffering from skin symptoms, %			
>1	10.5	6.5	11.5
2–3	16.8	12.4	8.3
4–6	12.3	15.1	9.2
7–9	7.6	7.9	6.7
10–12	52.7	58.2	64.4
Current employment, %	74.1	77.3	75.4
Disease control/severity			
Current UCT (total score), mean ± SD	10.1 ± 3.7	–	–
Current UCT <8/8–11/≥12, %	24.8/39.1/36.1	–	–
Past UCT (total score), mean ± SD	7.0 ± 3.5	–	–
Past UCT <8/8–11/≥12, %	56.5/33.5/10.0	–	–
JDA category* (n = 1668) mild/moderate/severe/most severe, %	–	47.4/30.7/13.2/5.3	–
BSA* (n = 357), mean ± SD	–	–	9.0 ± 14.8

*Unknown: atopic dermatitis, 2.6%; psoriasis, 17.9%. BSA, body surface area; JDA, Japan Dermatological Association; SD, standard deviation; UCT, Urticaria Control Test.

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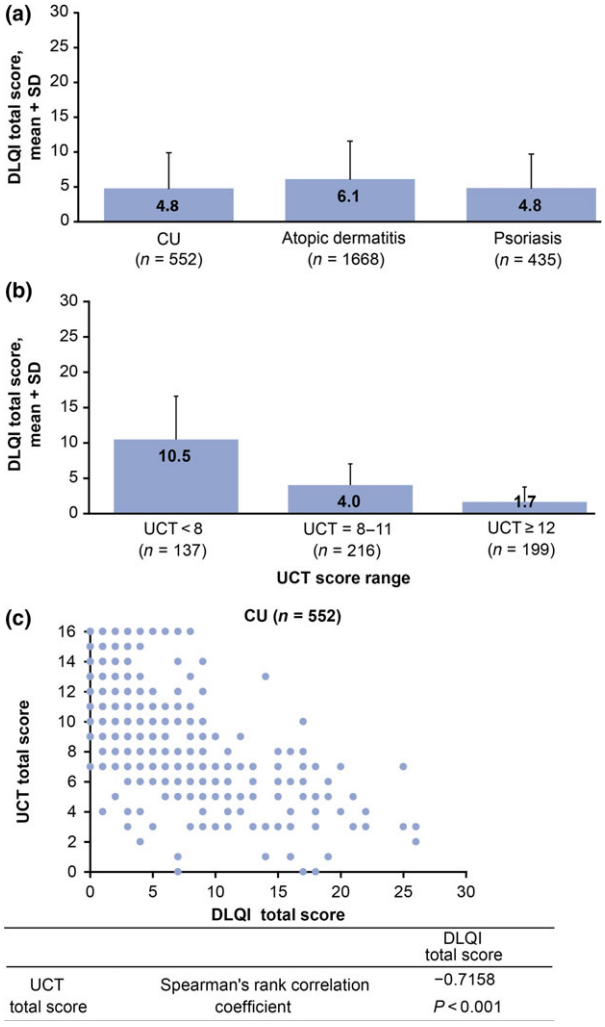

Figure 1. DLQI score. (a) Total score. (b) DLQI scores according to UCT score range in CU patients. (c) Correlation between UCT and DLQI. The aim of this questionnaire was to measure how much the patient's skin problem had affected their life over the last week. CU, chronic urticaria; DLQI, Dermatology Life Quality Index; SD, standard deviation; UCT Urticaria Control Test.

Disease control of urticaria and DLQI exhibited a strong correlation with the rank correlation coefficient of −0.7158 (Fig. 1c). A similar finding was observed between past urticaria control and past QoL with the rank correlation coefficient of −0.6915 (Fig. S3d).

WPAI-GH

Overall, compared with patients with psoriasis, patients with CU and atopic dermatitis had relatively higher scores in all WPAI-GH subscales except for absenteeism. Moreover, in the CU group, patients with a UCT score of less than 8, indicating poor symptom control, demonstrated highest presenteeism, work productivity loss and activity impairment (Table 2). There was no difference in absenteeism. Similar observations were noted for past work productivity (Table S3).

Visit to HCP

Nearly 30% of CU patients frequently consulted HCP, more than 50% sometimes consulted and less than 20% hardly ever consulted HCP. No major difference was found in the frequency of consultation among the three diseases (Fig. S4). Approximately 85% of CU patients had visited dermatology clinics, and less than 20% of patients visited hospital (Fig. 2). Similarly, approximately 89.3% of atopic dermatitis patients and 80.7% of psoriatic patients had visited dermatology clinics. Most patients with any of these diseases responded as being currently visiting HCP.

Satisfaction with health state

Satisfaction with the current health state was similar among the three disease groups with 31.7%, 25.5% and 28.7% of CU, atopic dermatitis and psoriatic patients, respectively, reporting dissatisfaction (Fig. 3a). Percentage of dissatisfaction increased for the health state under severest conditions within the past 1 year, with the highest percentage (73.7%) seen in patients with CU among three diseases (Fig. 3b).

Satisfaction with treatment

The most important factor for treatment choice common to the three diseases was efficacy. Nearly 80% of patients responded that efficacy was most important (data not shown). Overall, 22.8% of CU, 17.7% of atopic dermatitis and 29.4% of psoriatic patients were not satisfied with the current treatment (Fig. 4a). The most common reason for not being satisfied with current treatment was lack of control. The percentage of patients who mentioned this reason was higher in psoriatic patients (Fig. 4b). Sixty-seven percent of CU patients reported that they had been prescribed antihistamines, whereas 43% were prescribed oral corticosteroids. In addition, nearly 30% of urticaria patients were not aware of the specifics of the medications they had received (Fig. S5).

Assessment of satisfaction in CU patients by UCT score range

Chronic urticaria patients with lower UCT scores displayed a higher percentage of dissatisfaction with their health state and the treatment they received. Among CU patients with UCT scores of less than 8, 53.3% of patients showed dissatisfaction with their health state and only 2.9% were satisfied (Fig. 5a); 47.4% of patients showed dissatisfaction with treatment they received and only 6.6% were satisfied (Fig. 5b). Moreover, a higher percentage of dissatisfaction with their health state and received treatment (81.7% and 52.9%, respectively) was noted in CU patients with past urticaria control score of less than 8 (Fig. S6). Approximately 60% of CU patients chose "I often have trouble sleeping at night because the skin itches so badly" as the most annoying urticaria symptom, and 40% chose "I feel impaired in my daily activities at work or school in terms of my ability to concentrate or my mobility" (Fig. S7).

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Table 2. WPAI-GH scores

WPAI-GH (%)	Chronic urticaria				Atopic dermatitis	Psoriasis
	Overall	UCT <8	UCT 8–11	UCT ≥12		
Absenteeism						
n	409	103	148	158	1289	328
Mean ± SD	2.4 ± 9.0	2.9 ± 9.0	1.7 ± 6.9	2.8 ± 10.7	3.0 ± 12.2	2.9 ± 12.3
Presenteeism						
n	404	103	143	158	1268	319
Mean ± SD	21.2 ± 24.6	34.5 ± 25.8	21.4 ± 23.6	12.4 ± 20.6	22.4 ± 25.2	15.4 ± 22.7
Work productivity loss						
n	404	103	143	158	1268	319
Mean ± SD	20.2 ± 23.4	33.2 ± 25.3	20.5 ± 22.1	11.4 ± 19.0	21.2 ± 23.8	14.8 ± 21.9
Activity impairment						
n	552	137	216	199	1668	435
Mean ± SD	27.4 ± 27.2	43.9 ± 26.6	26.1 ± 25.5	17.5 ± 24.0	27.7 ± 27.4	20.2 ± 25.1

SD, standard deviation; UCT, Urticaria Control Test; WPAI-GH Work Productivity and Activity Impairment – General Health.

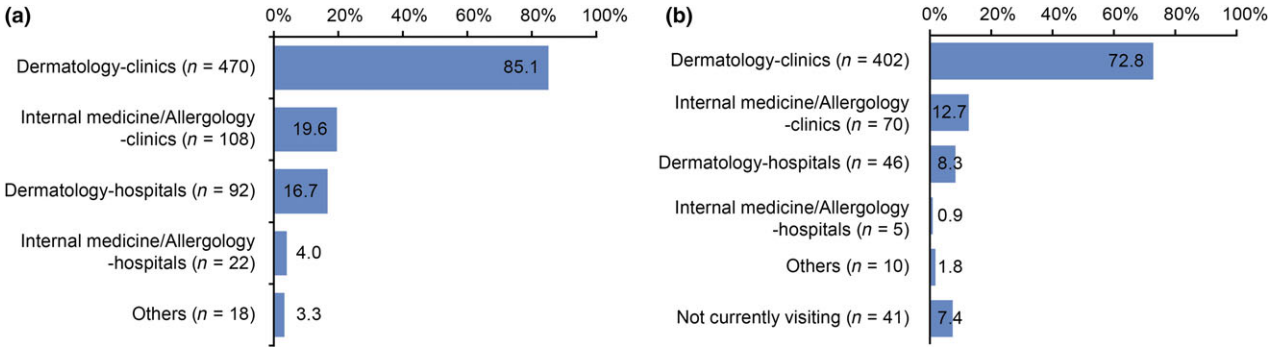

Figure 2. Visit to HCP by CU patients. (a) HCP (ever visited). (b) HCP (currently visiting). Patients were asked: Q. "Which physicians did you already see for your skin problems? Multiple choices can be made"; Q. "Which physician is currently treating you for your skin problems? Multiple choices can be made". CU, chronic urticaria; HCP, health-care providers.

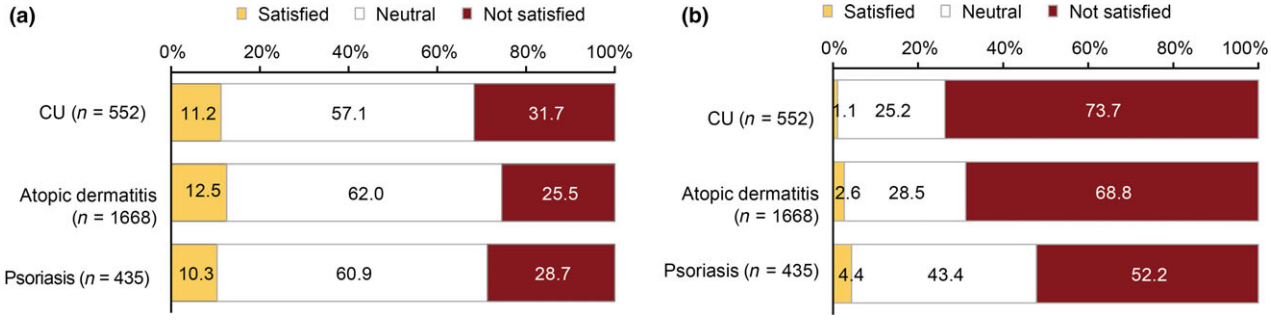

Figure 3. Satisfaction with health state. (a) Satisfaction with health state/current. (b) Satisfaction with health state/under the severest condition within the past 1 year. Patients were asked: Q. "Overall, are you satisfied with current health state?"; Q. "How much were you satisfied with your health state when you experienced the severest symptoms?". CU, chronic urticaria.

DISCUSSION

This web-based survey was conducted in Japan to collect data on the CU burden and the use of health-care system in real-life clinical practise. The demographic characteristics of Japanese patients with chronic skin disorders reported in the RELEASE study are mostly comparable with the findings reported in previous publications,[20,21] supporting the reliability of the results of this study. Additionally, in this survey the peak age of CU occurrence was between 20 and 40 years, which is consistent

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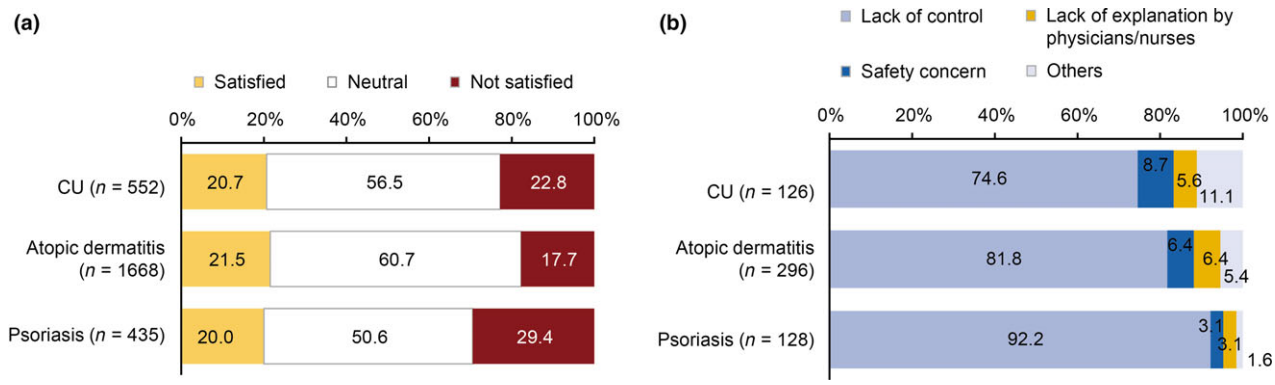

Figure 4. Satisfaction with treatment. (a) Satisfaction with treatment. (b) Reason for not being satisfied with treatment. Data on the reason for not being satisfied with treatment were obtained from those who selected "not satisfied with treatment". Patients were asked: Q. "Are you satisfied with the current medical care you receive?"; Q. "Why are you unsatisfied with the medical care?". CU, chronic urticaria.

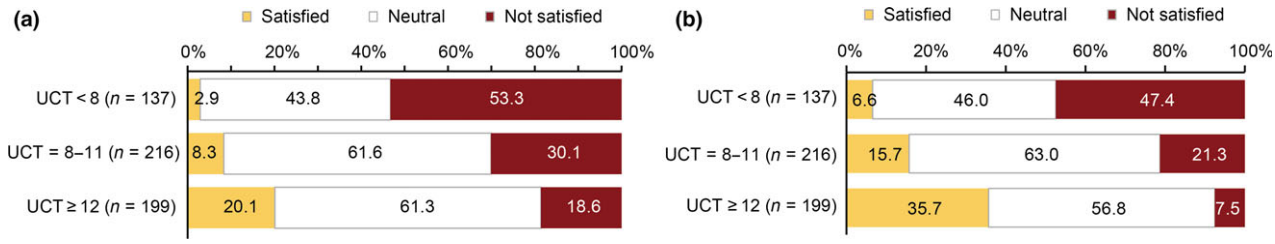

Figure 5. Satisfaction assessment/current by UCT score range in CU patients. (a) Satisfaction with health state. (b) Satisfaction with treatment. CU, chronic urticaria; UCT, Urticaria Control Test.

with the previous findings.[2,11,22,23] The duration of CU reported in this survey (10.7 years) was similar to that of the ATTENTUS study (11.5 years)[11] and slightly longer than that in other studies.[24,25] This may indicate a wider spectrum of the recruited patients in the real-life setting studies, namely the ATTENTUS and RELEASE study, compared with the studies at specialized centers. Prevalence of angioedema in the current study was lower than previously published report in Japan.[4] This may be because of a higher proportion of patients with severe and sustained symptoms at specialized centers than those in the general patient population.

The comprehensive guidelines for urticaria published by the Japanese Dermatological Association and the EAACI/GA^{2}LEN/EDF/WAO emphasize the importance of patient QoL for the choice of additional treatment in cases refractory to antihistamines.[1,26] Although a statistical comparison among the three diseases is not relevant in this study setting, it was observed that the CU patients in Japan experienced QoL impairment similarly to patients with atopic dermatitis and psoriasis, as indicated by the DLQI score. This confirms a significantly impaired QoL in the wide spectrum of CU patients, as well as in the specialized centers that have been previously reported.[6,27,28]

In addition, this RELEASE study evaluated disease control of urticaria using UCT for the first time in Japan and revealed that approximately 64% of CU patients at the time of survey displayed a UCT score of less than 12, indicating uncontrolled symptoms. Those CU patients with lower UCT scores showed higher DLQI total scores compared with patients with high UCT scores. Percentage of dissatisfaction with their health state and with the treatment was also higher in those patients. UCT has been reported as a valid and reliable tool for screening disease control in patients with CU due to its simple scoring system, easy interpretation and retrospective approach. Also, there was a strong correlation between UCT scores and health-related assessments, such as UAS (consisting of numbers of wheals and intensity of itching), Patient's Global Assessment (PatGA-VAS) and Chronic Urticaria Quality of Life Questionnaire (CU-Q_2oL, a validated urticaria-specific questionnaire).[16] Moreover, Weller *et al.*[16] reported that the screening accuracy of the UCT to identify CU patients with insufficiently controlled disease was high. The results of this survey highlighted the large proportion of CU patients with a UCT score of less than 12 and the higher DLQI dissatisfaction in those patients, indicating the need to provide appropriate treatment options to the patients with uncontrolled symptoms.

The UCT and health-related QoL questionnaires principally collect data on the condition at the time of the survey. Unlike a study with patients visiting hospital, an online survey in a preregistered patient panel likely misses the timing of severest

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conditions. Thus, this RELEASE study included questionnaires on disease control and patient QoL under the severest conditions in the past. Most CU patients (90.0%) demonstrated past urticaria control scores of less than 12 for the severest conditions. Mean total score of past QoL (identical items with DLQI) was 8.4 in CU patients, which greatly increased from the DLQI score at the time of survey (4.8). Moreover, the percentage of dissatisfaction with the health state under the severest conditions within the past 1 year was higher in the CU patients (73.7%) than that of atopic dermatitis (68.8%) and psoriasis (52.2%). Altogether, those results indicated a larger gap between the time of severest condition and the time of the survey in CU patients compared with atopic dermatitis and psoriasis, implying intermittent appearance of urticaria relative to other skin diseases. Although one should carefully interpret the data owing to the lack of clinical validation and recall bias on past status, the results suggested the importance of the information on the severest condition for recognition of true impact of uncontrolled urticaria on QoL, especially in the case of an online survey.

In line with the results of an observational study (AWARE) in Scandinavian countries,[29] CU patients in the current survey displayed an impairment of work productivity. Of note, presenteeism score was worse in patients with uncontrolled symptoms in CU patients, while this was not the case with absenteeism. A similar observation was reported in a previous study.[30] Impairment at work caused by CU may be mainly due to reduced on-the-job effectiveness.

In the ATTENTUS study performed in Germany, 41.5% of CU patients had been treated in a clinic, indicating that a highly burdened CU population receives medical care outside specialized hospitals.[11] This RELEASE study reported that a higher percentage of the CU patients (85.1%) had visited dermatology clinics, and patients visiting hospitals was less frequent (<20%). This suggests that a substantial population of patients with CU do not visit specialized hospitals in a real-life setting despite dissatisfaction with their health state and their medical treatment. The advertisement of a survey purely through an online banner, namely the ATTENTUS survey, was more likely to make patients with the uncontrolled symptoms respond, compared with those whose symptoms were well controlled, likely causing participant selection bias. In contrast, this RELEASE survey recruited patients through the patient panel from a large pool of preregistered Japanese web panelists, minimizing selection bias. Although inclusion criteria was more strict in the RELEASE survey than that of the ATTENTUS study because of the requirement of a visit to a HCP in the past 12 months, the higher percentage of CU patients treated in clinics in the RELEASE study may be due to a wider spectrum of participants than that of the ATTENTUS study, and also possibly a difference of medical care systems between the countries.

This study also revealed that 41.3% of the patients with urticaria were prescribed oral corticosteroids, which are not recommended by the EAACI/GA^{2}LEN/EDF/WAO guidelines and should only be limited to short-time use by the Japanese guideline for the management of urticaria.[1,31] Despite the noticeable use of corticosteroids, approximately 32% and 23% of CU patients were not satisfied with their current health state and the treatment they received, respectively, highlighting high unmet needs in effective treatment options.

In this RELEASE study, more than 50% of CU patients claimed to have disturbed sleep at night because of itch. Because CU patients' struggle in daily life can be underestimated owing to the outbreak of hives that typically disappear within a day, this study provides insights into the importance of patient-reported QoL assessments.

Limitations of this survey include that diagnoses provided by physicians were dependent on self-reports by each survey participant, and that this survey contained the information recalled by patients regarding the severest condition from the past. Moreover, this study recruited patients with various conditions ranging from mild to severe, making it difficult to simply interpret the "average" within the analysis groups. Thus, the subgroup analysis was performed on CU patients based on their UCT scores.

This web-based survey revealed the burden of CU in Japan purely from the patients' perspective with varied distribution of patients from local clinics to specialized medical centers. Many Japanese patients with CU experienced impairment of QoL and work productivity, similar to patients with atopic dermatitis and psoriasis. QoL impairment was correlated with uncontrolled urticaria symptoms. In addition, many CU patients, especially those with uncontrolled symptoms, were unsatisfied with their current health state and medical care. These results highlight the unmet medical needs of CU patients, suggesting that it is important to increase the awareness of CU burden among both physicians and patients and to pursue improved real-life patient care.

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SUPPORTING INFORMATION

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

Figure S1. Survey design. *Patients with chronic urticaria were defined as those who remain chronically symptomatic for 6 weeks or longer. DLQI, Dermatology Life Quality Index; HCP, health-care providers; WPAI-GH, Work Productivity and Activity Impairment – General Health.

Figure S2. DLQI score. (a) DLQI total score by urticaria subgroups. (b) DLQI item score. *Maximum score, 3. The aim of this questionnaire was to measure how much the patient's skin problem had affected their life over the last week. CU, chronic urticaria; DLQI, Dermatology Life Quality Index; SD, standard deviation.

Figure S3. Past QoL total score. (a) Past QoL total score by CU, atopic dermatitis and psoriasis. (b) Past QoL total score by past urticaria control score range in CU patients. (c) Past QoL total score by urticaria subgroups. (d) Correlation between past urticaria control and past QoL (CU [n = 552]). The aim of this questionnaire was to measure how much the patient's skin problem had affected their life when they were under the severest condition within the past 1 year. CU, chronic urticaria; QoL, quality of life; SD, standard deviation.

Figure S4. Discussion on symptoms with HCP. CU, chronic urticaria; HCP, health-care providers

Figure S5. Prescribed medications for urticaria subgroups. (a) Antihistamines. (b) Oral corticosteroids. Patients were asked: Q. "Have you already been prescribed an antihistamine product for the urticaria symptoms?"; Q. "Have you already been prescribed an oral corticosteroid product for the urticaria symptoms?". CU, chronic urticaria.

Figure S6. Satisfaction assessment under the severest condition within past 1 year by past urticaria control score range (CU). (a) Satisfaction with health state. (b) Satisfaction with treatment. CU, chronic urticaria.

Figure S7. Characterization of impairments associated with urticaria. CU, chronic urticaria.

Table S1. Data collection and sample size

Table S2. Characteristics of the total urticaria group

Table S3. Past work productivity

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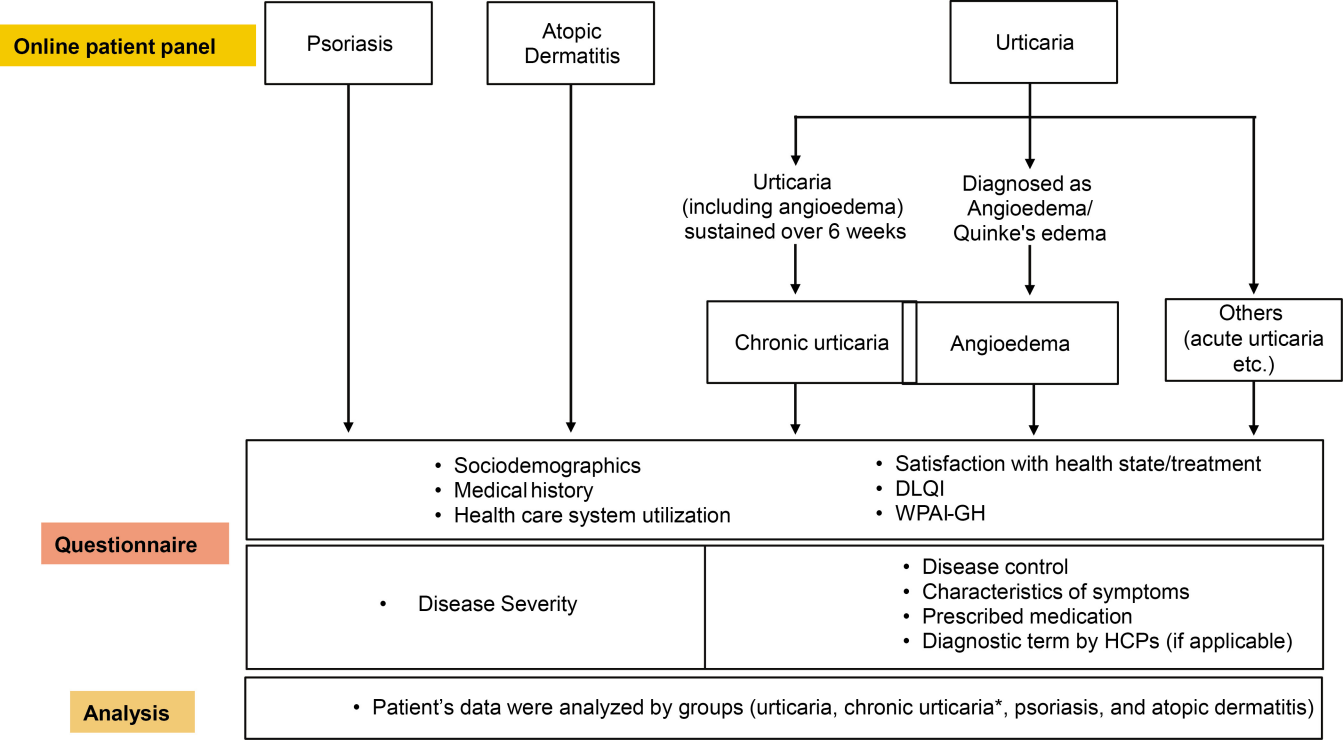
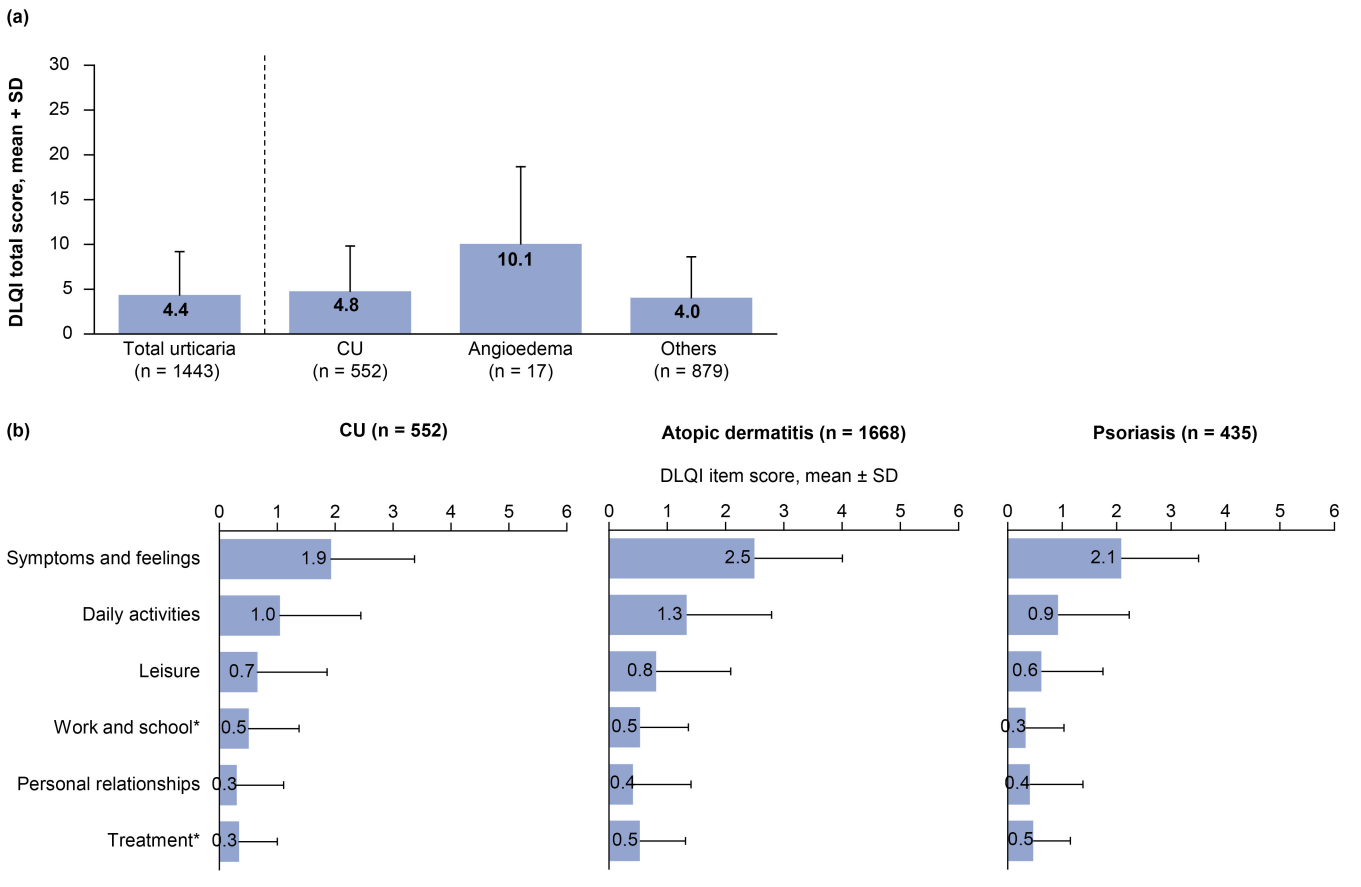
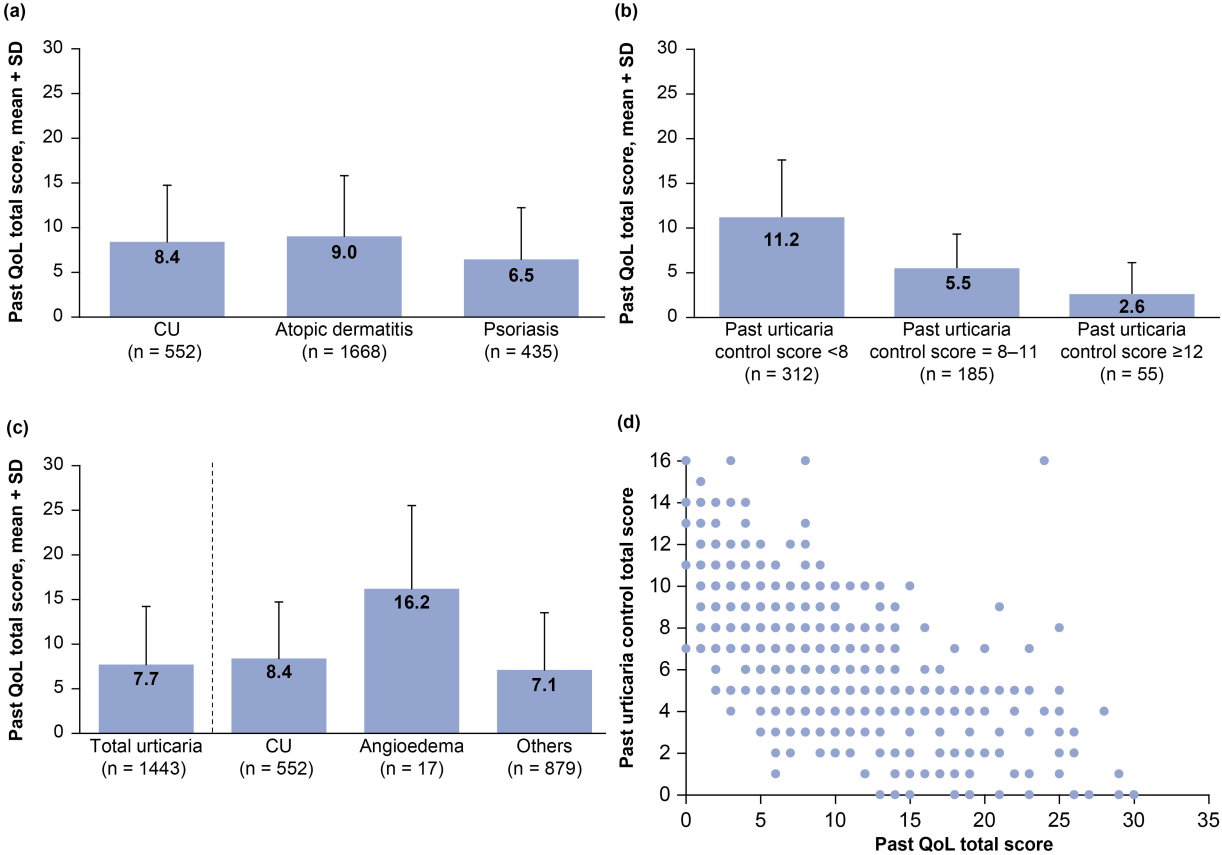
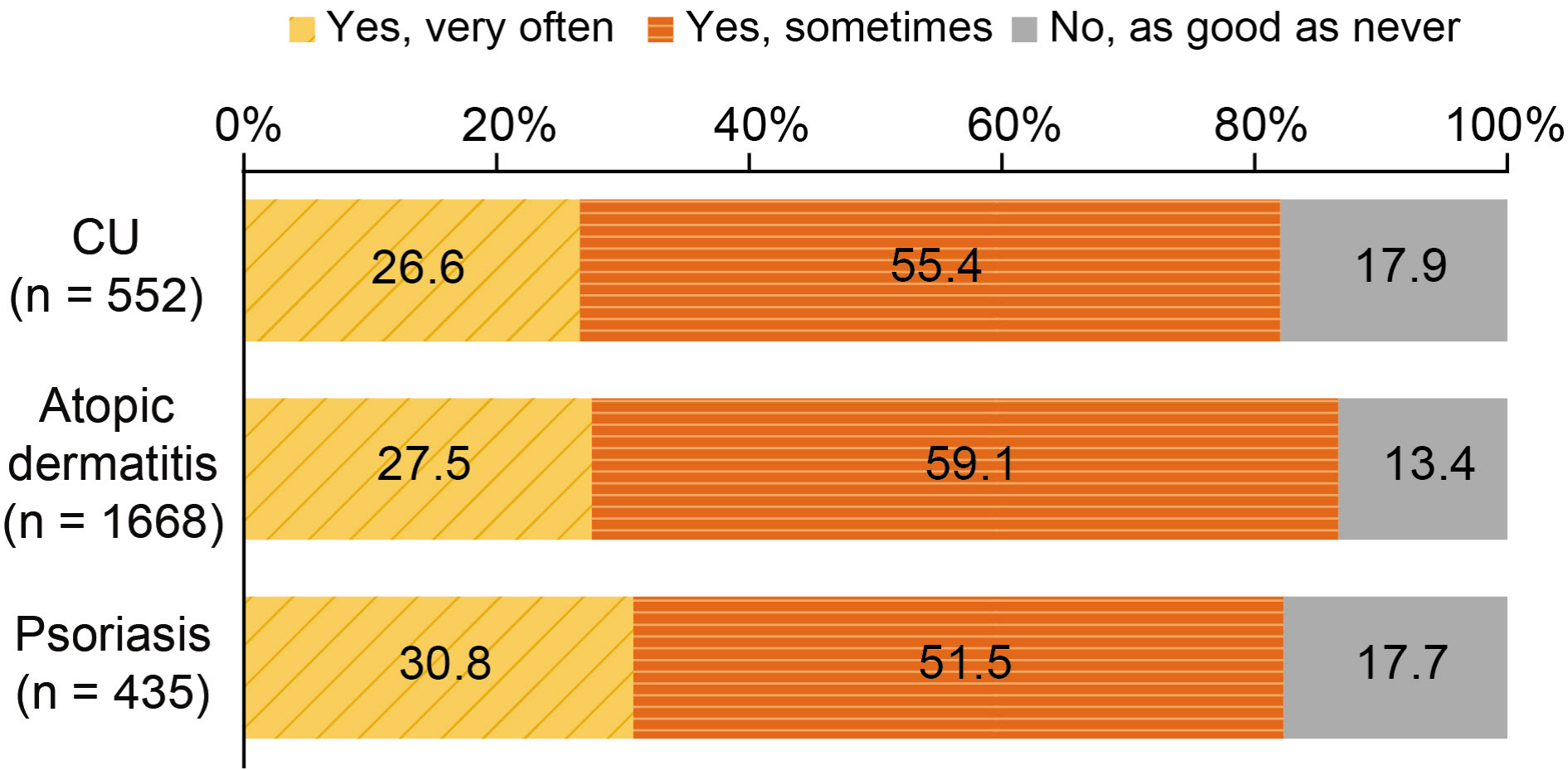
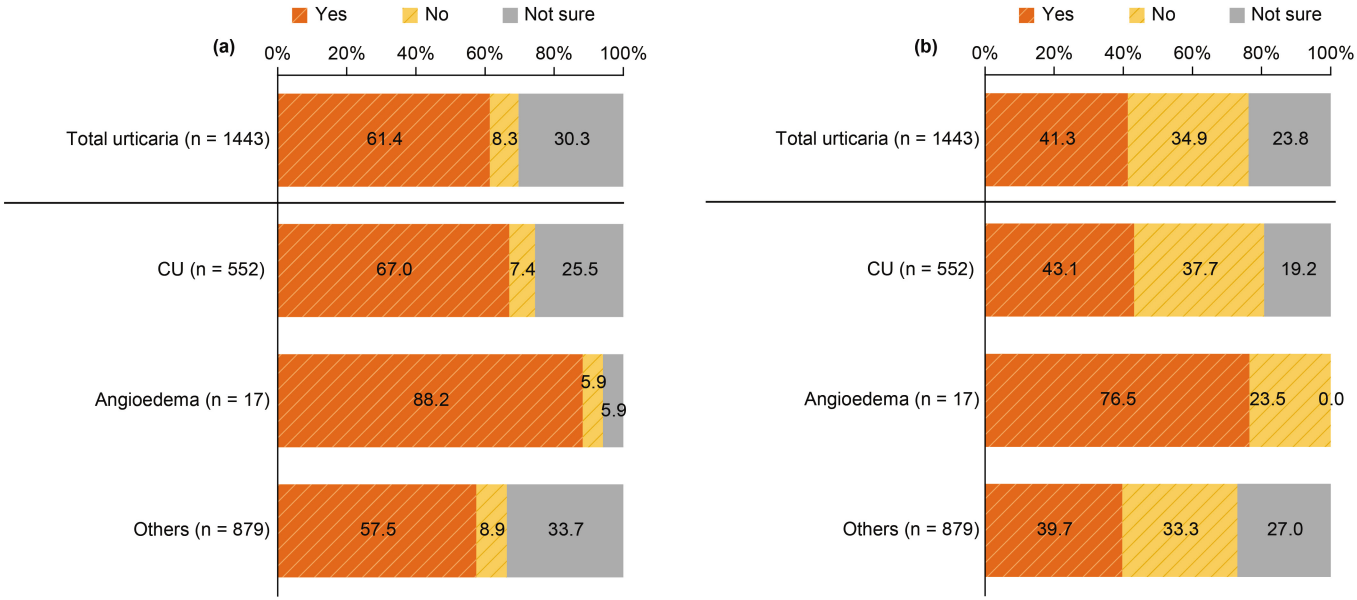

Online patient panel
Psoriasis
Atopic Dermatitis
Urticaria
Urticaria (including angioedema) sustained over 6 weeks
Diagnosed as Angioedema/ Quinke's edema
Chronic urticaria
Angioedema
Others (acute urticaria etc.)
Questionnaire
• Sociodemographics
• Medical history
• Health care system utilization
• Satisfaction with health state/treatment
• DLQI
• WPAI-GH
• Disease Severity
• Disease control
• Characteristics of symptoms
• Prescribed medication
• Diagnostic term by HCPs (if applicable)
Analysis
• Patient's data were analyzed by groups (urticaria, chronic urticaria*, psoriasis, and atopic dermatitis)

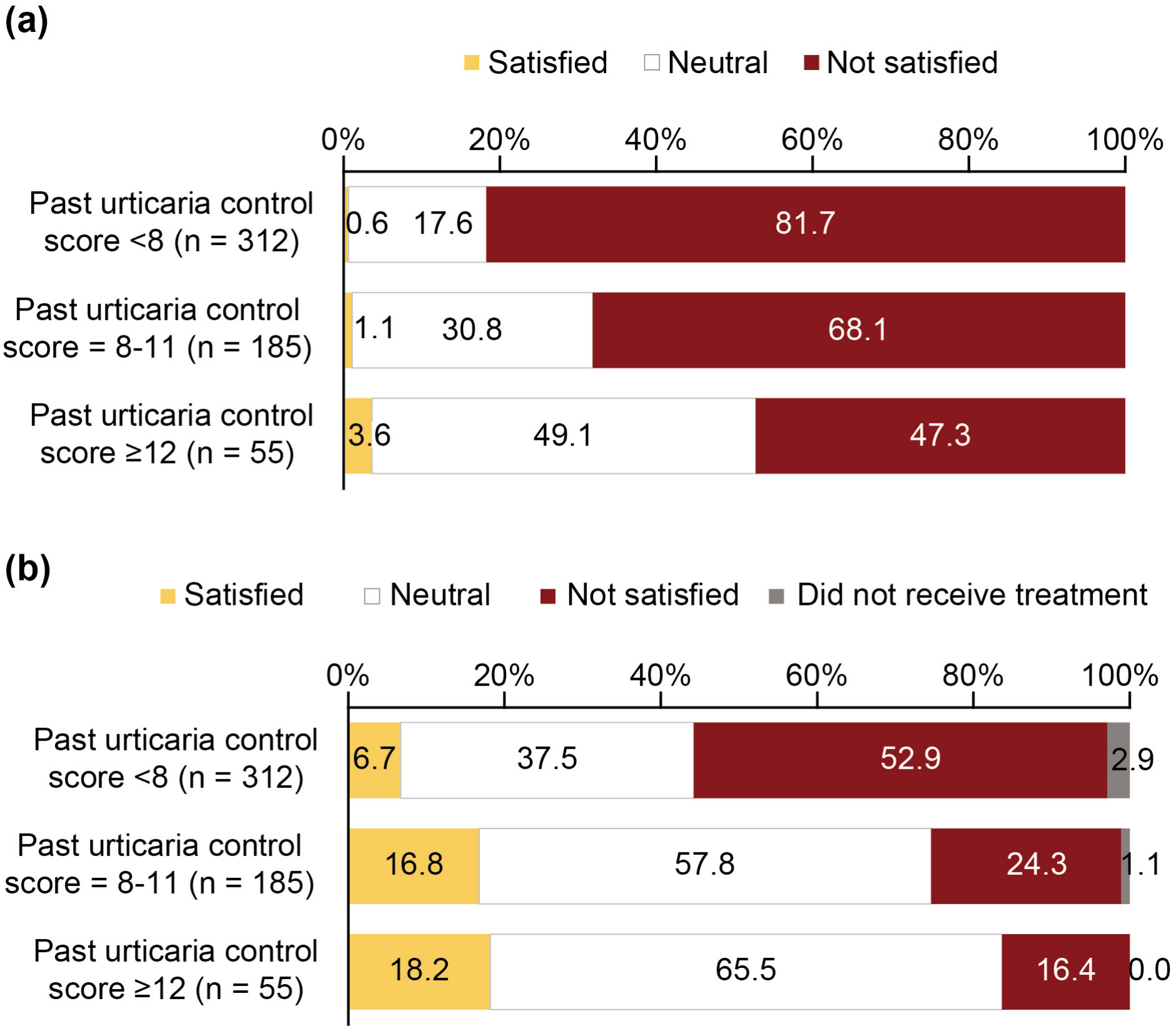

(a)
DLQI total score, mean + SD
30
25
20
15
10
5
0
4.4
4.8
10.1
4.0
Total urticaria (n = 1443)
CU (n = 552)
Angioedema (n = 17)
Others (n = 879)
(b)
CU (n = 552)
Atopic dermatitis (n = 1668)
Psoriasis (n = 435)
DLQI item score, mean ± SD
0 1 2 3 4 5 6
Symptoms and feelings
Daily activities
Leisure
Work and school*
Personal relationships
Treatment*
1.9
1.0
0.7
0.5
0.3
0.3
2.5
1.3
0.8
0.5
0.4
0.5
2.1
0.9
0.6
0.3
0.4
0.5



		Past QoL total score
Past urticaria control total score	Spearman's rank correlation coefficient	−0.6915 P<0.001


Yes, very often
Yes, sometimes
No, as good as never
0%
20%
40%
60%
80%
100%
CU (n = 552)
26.6
55.4
17.9
Atopic dermatitis (n = 1668)
27.5
59.1
13.4
Psoriasis (n = 435)
30.8
51.5
17.7


Yes
No
Not sure
(a)
0%
20%
40%
60%
80%
100%
Total urticaria (n = 1443)
61.4
8.3
30.3
CU (n = 552)
67.0
7.4
25.5
Angioedema (n = 17)
88.2
5.9
5.9
Others (n = 879)
57.5
8.9
33.7
(b)
Total urticaria (n = 1443)
41.3
34.9
23.8
CU (n = 552)
43.1
37.7
19.2
Angioedema (n = 17)
76.5
23.5
0.0
Others (n = 879)
39.7
33.3
27.0


(a)
Satisfied
Neutral
Not satisfied
0%
20%
40%
60%
80%
100%
Past urticaria control score <8 (n = 312)
0.6
17.6
81.7
Past urticaria control score = 8-11 (n = 185)
1.1
30.8
68.1
Past urticaria control score ≥12 (n = 55)
3.6
49.1
47.3
(b)
Satisfied
Neutral
Not satisfied
Did not receive treatment
0%
20%
40%
60%
80%
100%
Past urticaria control score <8 (n = 312)
6.7
37.5
52.9
2.9
Past urticaria control score = 8-11 (n = 185)
16.8
57.8
24.3
1.1
Past urticaria control score ≥12 (n = 55)
18.2
65.5
16.4
0.0

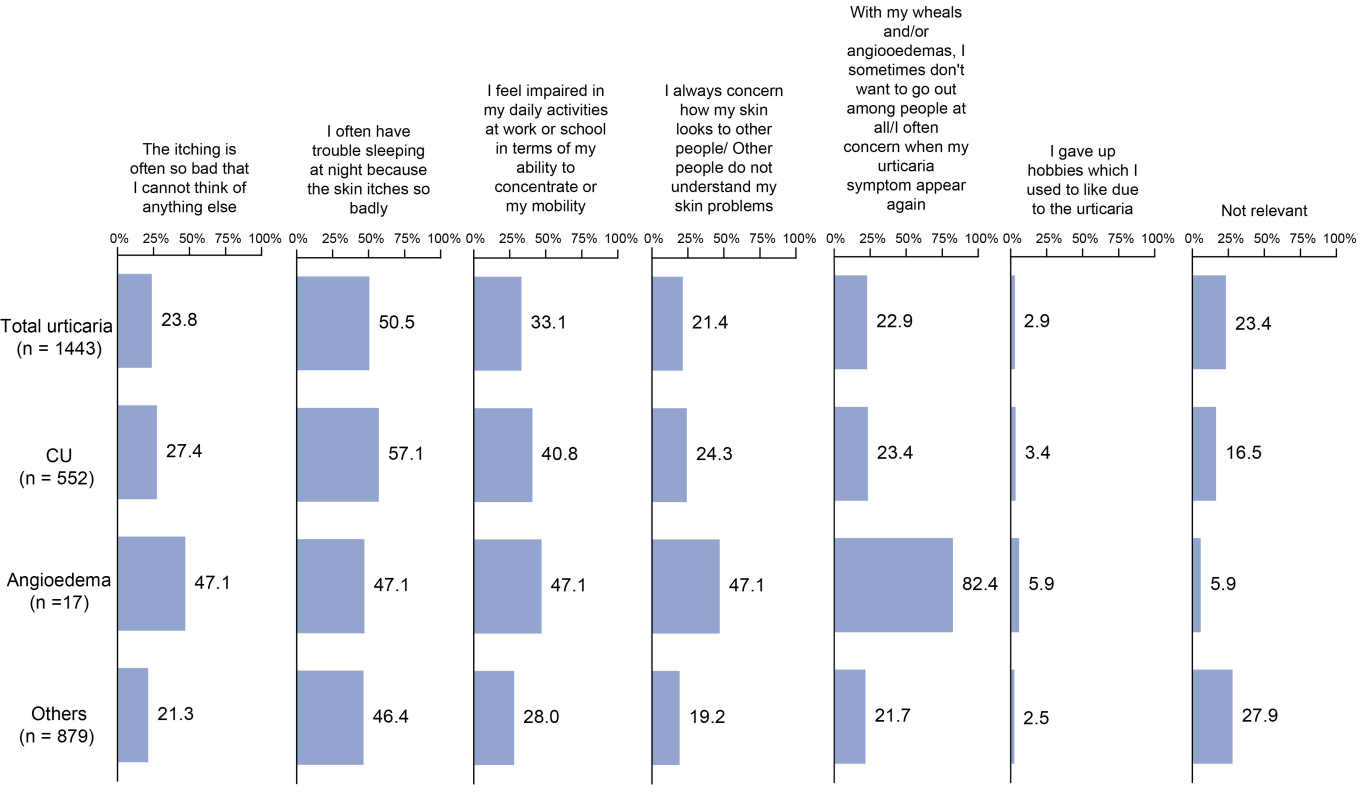

The itching is often so bad that I cannot think of anything else
I often have trouble sleeping at night because the skin itches so badly
I feel impaired in my daily activities at work or school in terms of my ability to concentrate or my mobility
I always concern how my skin looks to other people/ Other people do not understand my skin problems
With my wheals and/or angiooedemas, I sometimes don't want to go out among people at all/I often concern when my urticaria symptom appear again
I gave up hobbies which I used to like due to the urticaria
Not relevant
0% 25% 50% 75% 100%
Total urticaria (n = 1443)
23.8
50.5
33.1
21.4
22.9
2.9
23.4
CU (n = 552)
27.4
57.1
40.8
24.3
23.4
3.4
16.5
Angioedema (n =17)
47.1
47.1
47.1
47.1
82.4
5.9
5.9
Others (n = 879)
21.3
46.4
28.0
19.2
21.7
2.5
27.9

Table S1. Data collection and sample size

Parameters	Urticaria	Atopic dermatitis	Psoriasis	Total count inclusive overlaps
Total samples	1745	2048	580	4067
Total exclusion	302	380	145	745
Dummy disease	2	1	1	2
Validation Q	245	357	139	672
Inconsistent value	3	2	0	3
Other inconsistency*	52	20	5	68
Sample size for analysis	1443	1668	435	3322

*Excluded those who answered "never diagnosed as urticaria".

Table S2. Characteristics of the total urticaria group

Characteristics	Urticaria (n = 1443)
Age (years), mean ± SD	45.7 ± 11.6
Female, %	59.7
Age of disease onset (years), mean ± SD	32.8 ± 15.4
Duration of disease (years), mean ± SD	12.9 ± 13.1
Months/year suffering from skin symptoms, %	
>1 month	22.8
2-3 months	16.9
4-6 months	11.9
7-9 months	7.0
10-12 months	41.4
Current employment	73.5
Disease control	
UCT (total score)	10.8 ± 3.5
Urticaria diagnosis given by physicians, %	
Chronic spontaneous/idiopathic urticaria	53.0
Allergic urticaria	32.7
Cold/heat urticaria	17.4
Acute urticaria	17.1
Solar urticaria	7.1
Mechanical urticaria	3.5
Non-allergic urticaria	2.3
Cholinergic urticaria	2.1
Angioedema/Quinke's edema	1.2
Other diagnosis	4.3
Received a diagnosis, but I am not sure	10.5

SD, standard deviation; UCT, urticaria control test.

Table S3. Past work productivity

Past work productivity (%)		Chronic urticaria				Atopic dermatitis	Psoriasis
		Overall	Past urticaria control <8	Past urticaria control = 8-11	Past urticaria control ≥12		
Absenteeism	N	381	212	131	38	1163	307
	Mean ± SD	5.6 ± 16.3	8.0 ± 18.6	2.4 ± 10.7	3.2 ± 16.5	3.9 ± 13.7	3.0 ± 11.4
Presenteeism	N	354	200	120	34	1089	284
	Mean ± SD	33.1 ± 30.5	43.5 ± 30.7	22.2 ± 24.7	10.3 ± 20.8	29.6 ± 27.5	17.1 ± 23.7
Work productivity loss	N	354	200	120	34	1089	284
	Mean ± SD	4.2 ± 15.8	5.1 ± 17.1	2.4 ± 12.3	5.0 ± 18.8	0.2 ± 3.0	1.6 ± 8.6
Activity impairment	N	552	312	185	55	1668	435
	Mean ± SD	37.6 ± 31.1	48.2 ± 31.0	26.9 ± 24.8	13.5 ± 24.8	34.5 ± 29.8	21.9 ± 27.1

SD, standard deviation.