
Development of a daily diary for patients with chronic idiopathic urticaria

Susan D. Mathias, MPH*; Stephen C. Dreskin, MD, PhD†; Allen Kaplan, MD‡; Sarbjit S. Saini, MD§; Sheldon Spector, MD||; and Karin E. Rosén, MD, PhD¶

Background: Chronic idiopathic urticaria (CIU) is a disease characterized by itching and skin hives or wheals of unknown cause that vary in size and last for at least 6 weeks. The criterion standard for measuring disease activity is the urticaria activity score (UAS). However, content validity of the UAS has not been previously reported.

Objectives: To identify outcomes important to patients with CIU, create an urticaria patient daily diary based on the UAS and input from patients, and assess its content validity.

Methods: A qualitative research study was conducted in 2 stages using one-on-one telephone interviews of patients with CIU. In stage 1, patients were asked to discuss the impact of CIU on aspects of their life and to evaluate the content of the UAS. On the basis of this information, a patient daily diary, including UAS items, was developed. In stage 2, patients were interviewed to determine whether the urticaria patient daily diary was comprehensive and easily understood.

Results: Stage 1 interviews showed that CIU has an extensive impact on patients, from the primary symptoms of itching, hives, and angioedema to the broader aspects of sleep and health-related quality of life. Stage 2 interviews demonstrated the content validity of the urticaria patient daily diary and resulted in minor modifications to the diary. When the urticaria patient daily diary was administered in conjunction with the Dermatology Life Quality Index and Medical Outcomes Study Sleep Scale, patients considered the assessment to be comprehensive, although some recommendations were made to include more items on emotional issues and other aspects of angioedema.

Conclusions: The final urticaria patient daily diary is an easy-to-administer, comprehensive assessment of symptoms for CIU patients. Future research is needed to establish its additional psychometric properties.

Ann Allergy Asthma Immunol. 2010;105:142–148.

INTRODUCTION

Chronic idiopathic urticaria (CIU) is a disease characterized by itching and skin hives or wheals of unknown cause that vary in size and last for at least 6 weeks.¹ There are different naming conventions in the United States and Europe in relation to the CIU population (ie, chronic urticaria with a non-specific cause in the United States is referred to as *CIU*, whereas in some European countries and according to the new European guidelines, this condition is referred to as *chronic spontaneous urticaria*).²

Affiliations: * Health Outcomes Solutions, Winter Park, Florida; † University of Colorado Denver, Aurora, Colorado; ‡ Medical University of South Carolina, Charlotte, South Carolina; § Johns Hopkins University, Baltimore, Maryland; || California Allergy and Asthma Medical Group, Los Angeles, California; and ¶ Genentech Inc, South San Francisco, California.

Disclosures: Ms Mathias is an employee of Health Outcomes Solutions, which was paid by Genentech Inc to undertake this study. Dr Dreskin has worked as a consultant for Genentech Inc. Dr Saini has received grants from and worked as a consultant for Genentech Inc and Novartis. Dr Spector has received honoraria or investigator grants from AstraZeneca, Genentech Inc, Novartis, Glaxo, Merck, Sanofi-Aventis, and Pfizer. Dr Rosén is an employee of Genentech Inc.

Financial Support: Genentech Inc and Novartis Pharmaceutical Corp sponsored this study and the original manuscript.

Received for publication April 20, 2010; Received in revised form June 11, 2010; Accepted for publication June 16, 2010.

© 2010 Published by Elsevier Inc. on behalf of American College of Allergy, Asthma & Immunology.
doi:10.1016/j.anai.2010.06.011

Patients with CIU experience daily or almost daily outbreaks with their associated itching and subcutaneous swelling or angioedema for many years. Although the origin of CIU is uncertain, there is some evidence that CIU could result from autoimmune causes.³ First-line treatment is typically with nonsedating histamine₁ (H₁)-antihistamines. These drugs have documented effectiveness and a low adverse event profile.⁴ Older, first-generation antihistamines are not recommended as first-line agents for routine management because of their anticholinergic and sedative effects and their drug interactions, although they may be used in regions of the world where nonsedating antihistamines are unavailable. For nonresponding patients, the antihistamine dose may be increased up to 4-fold. For patients who are still nonresponsive, an alternate nonsedating or sedating antihistamine may be tried or a leukotriene antagonist may be added to their regimen. For symptoms that still persist, other nonapproved agents, such as cyclosporine, dapsone, or omalizumab, have been added. However, these treatments have not been approved for treating CIU in the United States. These treatment guidelines are a result of consensus reached during panel discussions at the Third International Consensus Meeting on Urticaria in 2008.

The discomfort associated with CIU can have a major impact on patients' health-related quality of life (HRQOL) and has also been associated with increases in symptoms of anxiety and depression compared with healthy controls.⁵

Health status scores for patients with CIU are similar to the scores of patients with coronary artery disease in terms of feeling a lack of energy, social isolation, and emotional upset.⁶ A number of clinical trials in patients with CIU have found those treatments that are able to improve symptoms and reduce the number of wheals also lead to significant improvements in overall HRQOL, sleep, and ability to undertake daily activities.^{7,8}

The criterion standard for measuring chronic urticaria activity is the urticaria activity score (UAS).⁹ The UAS was developed specifically for use in CIU patients and has been used in H₁-antihistamine clinical development.¹⁰ Furthermore, the current European Academy of Allergology and Clinical Immunology, Global Allergy and Asthma European Network, European Dermatology Forum, and World Allergy Organization guidelines recommend the use of the UAS for assessing disease activity and response to treatment.^{8,9}

The UAS asks patients to rate the intensity of pruritus, the number of hives, and the size of their largest hive. Intensity of pruritus (0–3) and number of hives (0–3) are added together to create a daily UAS score (0–6 points per day). A validation study found that patients preferred documenting the 2 components of the daily UAS compared with other symptom qualities, such as swelling number and erythema size, and that UAS scores correlated positively with patients' HRQOL, particularly when UAS scores were averaged during at least 4 days.⁸ The UAS may be used in conjunction with quality-of-life measures, such as the Dermatology Life Quality Index (DLQI)¹¹ or the Chronic Urticaria Quality of Life Questionnaire,¹² to provide a more comprehensive assessment of patient-reported outcomes in CIU.

Despite its increasing use, the content validity of the UAS has not been previously reported. Content validity is the extent to which an instrument thoroughly and appropriately assesses the concept it is intended to measure.^{13,14} For a health care instrument, it is important to assess the patient's perspective.^{13,15} The first step in establishing content validity is to define the concept, and the second step is to verify that selected items appropriately represent the concept. The fundamental approach to establishing content validity is through qualitative research.

The objective of this study was to undertake a qualitative research study from the patient's perspective. The study was conducted in 2 stages. The first stage focused on defining the concept (ie, identifying outcomes that are important to patients with CIU). Patients were asked to evaluate the content of the UAS and to evaluate the impact of CIU on other aspects of a patient's life, such as sleep, activity limitations, and overall HRQOL. On the basis of the feedback from this investigation, a urticaria patient daily diary, including slightly modified UAS items, was then developed. Stage 2 of the study was conducted to determine whether the urticaria patient daily diary is considered comprehensive and easily understood by CIU patients.

METHODS

Patients with CIU from 10 allergy clinics located throughout the United States were recruited for participation in both stages of the study. Clinics included academic centers and private practice sites. Potentially eligible participants were identified through their physician's office and were contacted and screened for eligibility. To be eligible, participants had to meet the following criteria: age between 18 and 75 years, diagnosed as having CIU more than 3 months ago (defined as hives and itch for at least 3 days in a 7-day period for 6 consecutive weeks), self-reported moderate to severe itching, more than 10 hives, currently symptomatic despite taking H₁-antihistamines, ability to speak and read English, willingness to sign an informed consent form and take part in 1 or 2 telephone interviews lasting no more than 1 hour, no diagnosis of atopic dermatitis or other skin condition(s) that cause itching, and not currently taking omalizumab or steroids. Once deemed eligible, a telephone interview date and time were scheduled. Telephone interviews were conducted by 1 of 3 trained interviewers using a semistructured interview guide (available from the authors on request). Power calculations are not typically conducted for qualitative research; rather, the appropriate sample size is based on the concept of theoretical saturation.¹⁶ Theoretical saturation occurs when a concept is so well developed that further elicitation of data results in minimal or no new information that would elaborate or challenge the concept. When qualitative research is being conducted to assess content validity, saturation is reached when enough data have been collected to fully describe the depth and range of concepts and categories explaining a particular phenomenon, such as the symptoms of CIU, and to understand the relationships among the concepts and categories.¹⁶ Therefore, transcripts were reviewed and analyzed continuously after the conduct of several interviews, and enrollment continued until no new issues or concepts were identified.

Study Design

Figure 1 contains a schema of the study design and includes high-level changes to the urticaria patient daily diary during the stages of the study.

Stage 1

Patients were mailed a study packet containing an introductory letter explaining study procedures, a self-administered questionnaire containing the initial version of the urticaria patient daily diary and several demographic and clinical questions, 2 copies of the informed consent form, and a preaddressed, postage-paid envelope to return the study materials. Patients were asked to read and sign the 2 copies of the informed consent form and to complete the self-administered urticaria patient daily diary and background questionnaire before taking part in the scheduled telephone interview. The urticaria patient daily diary included the UAS, which contained 3 items that ask respondents to rate itch severity, number of hives, and the size of the largest hive (in centime-

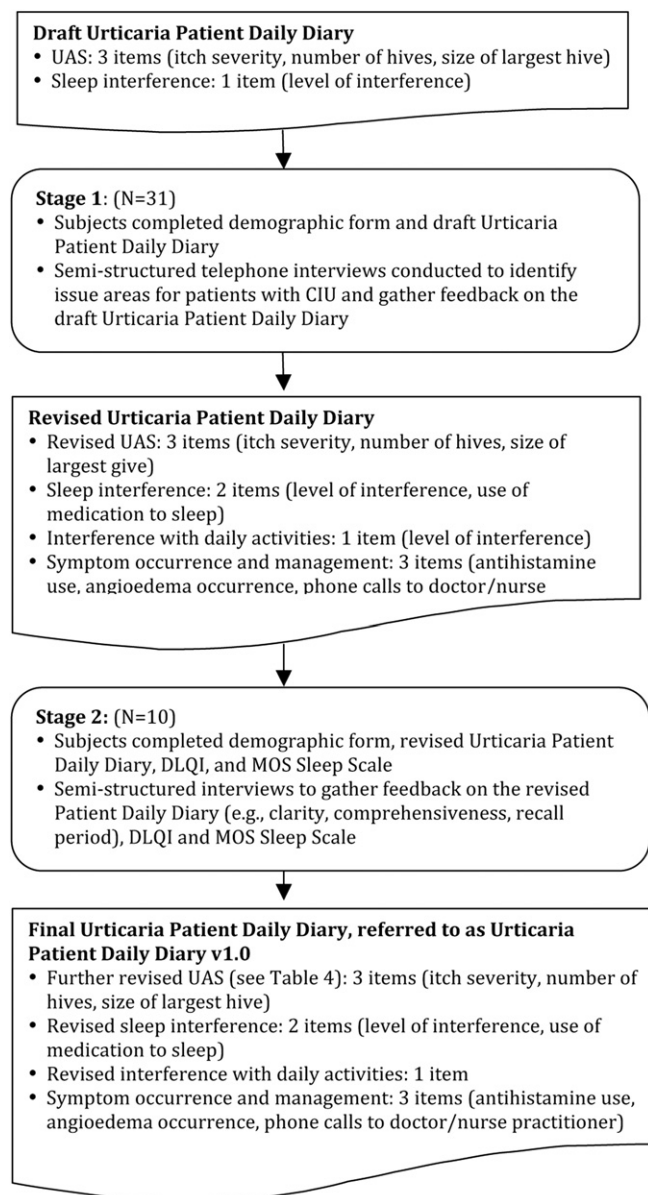


Figure 1. Study design. CIU indicates chronic idiopathic urticaria; DLQI, Dermatology Life Quality Index; MOS, Medical Outcomes Study; and UAS, urticaria activity score.

ters). A fourth item was added regarding sleep interference. The single, general item on sleep interference, developed by experts in outcomes research, was included to explore the importance and relevance of sleep interference among patients with CIU.

The interview guide included questions regarding CIU diagnosis and current treatment plan, symptoms at the time of diagnosis and current symptoms, the impact of CIU and CIU symptoms on overall HRQOL and daily activities, the impact of CIU and CIU symptoms on psychosocial issues (social

life, work life, family life, and emotional issues), the impact of CIU and CIU symptoms on sleep, and the frequency and bother of hives, itching, and angioedema. In general, responses were on a scale ranging from 0 to 10. For instance, severity ratings ranged from 0 (not at all severe) to 10 (extremely severe), and bother was measured on a scale from 0 (not at all bothered) to 10 (extremely bothered). The interview concluded with questions about the relevance of the urticaria patient daily diary and whether any changes were recommended, including the addition of supplemental items. For stage 1, theoretical saturation was achieved and no new study participants were enrolled after 31 interviews were completed.

Stage 2

On the basis of stage 1 interviews, revisions were made to the urticaria patient daily diary. To ensure that the revised diary was understood, patients with CIU took part in the second stage of the study. In-depth cognitive debriefing telephone interviews were conducted in stage 2 to assess the content validity of the revised urticaria patient daily diary. The patient daily diary was administered in conjunction with the Medical Outcomes Study (MOS) Sleep Scale and the DLQI so that patients could evaluate the instrument in the context of a comprehensive patient-reported outcome assessment. Although the MOS Sleep Scale and the DLQI could not be revised regardless of the feedback received, they were included so that respondents could consider the comprehensiveness of the complete set of questions, taking into account the content of the diary with these 2 questionnaires.

The semistructured discussion guide for this second stage of the study included questions regarding how easy or difficult it is to recall specific CIU symptoms during a 12- and 24-hour period, whether the wording for the UAS questions related to itch and hives were clear and understandable, the appropriateness of the sleep interference and daily activities questions, and the overall comprehensiveness of the diary (and the additional 2 questionnaires). For stage 2, theoretical saturation was achieved after 10 individuals were interviewed. Nine of those 10 individuals had also participated in stage 1 interviews.

The study was approved by a central institutional review board. Patients received a small honorarium for participation in each interview.

Statistical Analysis

All interviews were recorded and transcripts from each interview were prepared and reviewed by the project team. Each transcript was reviewed and analyzed qualitatively for content; items not well understood were reworded.

RESULTS

Demographic and clinical characteristics for the 2 samples are presented in Table 1. Most patients were female, white, and married and had at least a college degree. The time since diagnosis varied considerably. Approximately half of the patients were taking 3 or more CIU medications. On average,

Table 1. Demographic and Clinical Characteristics^a

Characteristics	Stage 1 (n = 31)	Stage 2 (n = 10)
Female, No. (%)	26 (84)	8 (80)
Age, mean (SD), y	46.0 (16.1)	40.5 (17.3)
Race/ethnicity, No. (%)		
White	26 (84)	9 (90)
African American	2 (6)	0 (0)
Asian or Pacific Islander	1 (3)	0 (0)
Native American or Alaskan Native	0 (0)	0 (0)
Other	2 (6)	1 (10)
Marital status, No. (%)		
Married	18 (58)	6 (60)
Living together with a partner	3 (10)	1 (10)
Widowed, divorced, or separated	6 (19)	1 (10)
Single or never married	4 (13)	2 (20)
Income, No. (%)		
<\$50,000	7 (23%)	2 (20%)
\$50,000–\$99,999	7 (23%)	0 (0%)
≥\$100,000	12 (39%)	6 (60%)
No response	5 (16%)	2 (20%)
Education level, No. (%)		
High school or less	1 (3)	0 (0)
Some college	9 (29)	2 (20)
College degree	14 (45)	5 (50)
Graduate or professional degree	7 (23)	3 (30)
Time since diagnosis		
Diagnosed in the last year	9 (29)	4 (40)
Diagnosed between 2 and 5 years ago	13 (42)	5 (50)
Diagnosed >5 years ago	9 (29)	1 (10)
Current number of chronic idiopathic urticaria medications		
≥3	17 (55)	5 (50)
≤2	14 (45)	5 (50)

^a Percentages may not total 100% because of rounding.

stage 1 interviews lasted 40 to 45 minutes, whereas stage 2 interviews were shorter, lasting approximately 30 minutes.

Stage 1

The findings from stage 1 interviews were used primarily to identify the outcomes that are most important to patients with CIU. When asked what aspects of their life were most affected by CIU, patients provided a wide range of responses, demonstrating the broad impact of CIU on all areas of HRQOL. Patients reported physical symptoms; interference with usual activities, social and emotional functioning, sleep, and work; and reduced overall HRQOL. Some of the more relevant direct patient quotes in Table 2 provide insight as to how CIU affects each of these aspects of life.

With regard to sleep, patients were asked during the telephone interview, “How often do you typically wake up because of your skin condition?” On average, patients reported waking 1.2 (SD, 1.4) times during a typical night due to CIU, with some patients not waking at all (n = 7) and some patients waking up at least once an hour (n = 2) or just taking

“catnaps” (n = 2). Patients were also asked, “On a scale from 0 to 10, where 0 is ‘extremely poor’ and 10 is ‘excellent,’ how would you rate the quality of your sleep?” The average response was 6.2 (SD, 2.6). In addition, patients were asked, “On a scale from 0 to 10, where 0 is ‘not at all’ and 10 is ‘extremely bothered,’ how much does itching bother you at nighttime?” The average response was 5.1 (SD, 3.7).

Symptom-related questions in the stage 1 telephone interview guide focused on frequency, severity, and bother of hives, itch, and angioedema (Table 3). Itching and hives occurred most frequently, each occurring, on average, approximately 5 days during the prior week. Itching and hives occurred daily for 55% and 57% of patients, respectively. Angioedema occurred less frequently. Sixty-two percent of patients did not experience any angioedema episodes in the prior week, whereas 18% of patients experienced 3 or more episodes. As indicated in Table 3, a wide range of severity and bother was reported for each of the symptoms. Mean severity scores were 5.2 for hives, 6.0 for itch, and 5.3 for angioedema, whereas mean bother scores were 4.8 for hives, 5.4 for itch, and 5.8 for angioedema.

Regarding the UAS, all 31 patients reported that it was easy to understand and that the response options were appropriate; however, some useful feedback was received. For example, it became clear that *pruritus* is not a familiar term to patients and that *itch* should be included as a descriptor. In addition, patients indicated a preference for words for *greater than* and *less than* rather than the symbols < and >, and patients indicated a preference for measuring hive size in inches rather than centimeters. (Because the urticaria patient daily diary will be used internationally, we retained the use of the term centimeters in the diary and recommend providing patients with a ruler for measuring hive size that uses the metric system.)

Some issue areas that were reported by CIU patients are not captured by the DLQI or the initial draft of the urticaria patient daily diary. For example, patients reported frustration from not knowing the cause of CIU, what may lead to an outbreak, or when an outbreak may occur. Patients also reported loss of mobility and normal functioning of their hands and fingers due to swelling and severe itching, as well as activity limitations and emotional exhaustion.

On the basis of the stage 1 findings, a revised urticaria patient daily diary was created, including the wording suggestions for the UAS items mentioned herein. The item on sleep interference was retained, and an item regarding the use of medication to help with sleep was added. The urticaria patient daily diary was augmented further with an item on interference with daily activities and 3 items on symptom occurrence and management: the first pertaining to the use of antihistamines for CIU symptoms, the second pertaining to the occurrence of angioedema, and the third pertaining to calling a physician or nurse practitioner because of CIU. The urticaria patient daily diary was designed to be completed every 12 hours for the UAS items of itch (severity) and hives (number and largest size) and every 24 hours for the inter-

Table 2. Aspects of Life Most Affected by Chronic Idiopathic Urticaria

Life aspect	Direct quotes from patient interviews
Physical symptoms	"I could barely walk because my feet hurt so bad." "(The) itching, it will drive you insane."
Usual daily activities	"Swelling – it's the most uncomfortable." "As far as my house, everything went undone." "I don't want to leave the house when I have an outbreak."
Social functioning	"I had to cut back on a lot of activities that I enjoyed personally." "My friendships, they took a decline because I was just incapacitated." "I can't go to the beach, I can't go to the pool . . . I stay indoors."
Work functioning	"The redness of my skin . . . it scares people" "There is no way a person can actually hold a job down and work." "I have stayed home from work a couple of times when it was really bad."
Emotional functioning	". . . there were times that I just couldn't focus on the work. It was a bit distracting." "Emotionally, I would say sometimes I am severely depressed." "Sometimes I feel like I'm having panic (over the outbreaks)"
Sleep	". . . sometimes it's embarrassing" "Generally at night it gets a lot worse . . . and that makes it very, very difficult to sleep." "Before, I was up every 2 hours . . . I could hardly sleep I was just – just really a wreck."
Overall impact on quality of life	"A great deal (My quality of life was horrible)." "Quite a bit . . . always the scratching and itching or just feeling insecure . . ." "A little bit . . . mild effect because I know how to treat when I see it coming"

ference items related to sleep and daily activities, as well as the symptom management items. The appropriateness of these recall periods was evaluated during stage 2 interviews.

Stage 2

The findings from stage 2 suggest that the urticaria patient daily diary is not burdensome for patients. Average time for completion of the daily diary was 6 to 7 minutes. All patients reported that the length was "just right," with 1 patient further commenting that it was so brief that we "could add more." All patients reported that the urticaria patient daily diary was easy to understand and that the response options were appropriate and useful. Furthermore, all 10 patients reported that it was "easy" to recall the symptoms of hives and itch during the past 12 hours.

Feedback from the 10 study participants warranted consideration of additional changes to the urticaria patient daily diary. For the sleep interference question, minor rewording of the response options was suggested to clarify that the impact of CIU on sleep was being assessed, rather than sleep in general. The response options were changed from (1) mild, not troublesome, adequate sleep; (2) moderate, awoke occasionally, average sleep; and (3) substantial, severe interference, poor sleep to (1) mild, little impact on sleep; (2) moderate, awoke occasionally, some impact on sleep; and (3) substantial, woke up often, severe impact on sleep. For the interference with daily activities item, the suggestion was made to add examples of daily activities, so "work life and social life" were added in parentheses. In addition, for in-

Table 3. Symptom Frequency, Severity, and Bother

Symptom	Mean (SD)	Median	Minimum, maximum
Hives			
No. of days in past week (n = 30 ^a)	4.9 (2.8)	7	0 (n = 6), 7 (n = 17)
Severity ^b (n = 25)	5.2 (2.7)	5	1 (n = 2), 10 (n = 1)
Bother ^c (n = 25)	4.8 (2.8)	4.5	0 (n = 1), 9.75 (n = 1)
Itch			
No. of days in past week (n = 31)	5.2 (2.4)	7	0 (n = 3), 7 (n = 17)
Severity (n = 27)	6.0 (2.8)	6	2 (n = 3), 10 (n = 3)
Bother (n = 26)	5.4 (2.7)	5	1 (n = 3), 10 (n = 2)
Angioedema			
No. of days in past week (n = 29)	1.0 (1.3)	0	0 (n = 15), 4 (n = 2)
Severity (n = 15)	5.3 (2.8)	5	2 (n = 3), 10 (n = 1)
Bother (n = 14)	5.8 (3.2)	5	2 (n = 2), 10 (n = 3)

^a Sample size differs from n = 31 because some respondents provided text vs numeric responses, even after probing.

^b Severity measured on a scale from 0 (not at all severe) to 10 (extremely severe).

^c Bother measured on a scale from 0 (not at all bothered) to 10 (extremely bothered).

Table 4. Questions on Itch and Hives

Question	Patient feedback	Item modification
Severity of itch	Clear and easy No difficulty reported	None
No. of hives	Difficult if hives cluster or “run together” Difficult if hives are on patient’s back	Added instructions to clarify how to count clustered hives Added instructions suggesting the patient have someone else count hives if on their back
Size of largest hive	Generally, not much difficulty, but several commented that it could be difficult to single out a hive when they are clustered	Added instructions to clarify that a group of hives should not be measured as one hive

creased clarity, a minor revision was made to 1 of the daily activity response options (changed from “1 – mild, not troublesome, little impact on daily activities” to “1 – mild, little impact on daily activities”).

For the questions on itch and hives that comprise the original UAS, feedback and item modifications from the stage 2 interviews are summarized in Table 4. No difficulties were reported and no changes were made for the item on severity of itch. For the items pertaining to hives (number and size), additional instructions were added for increased clarity regarding how to count clustered hives and hives located on the patient’s back (ie, in a place hard to reach). In addition to the item modifications, a slight change was also made to the instructions for these items. For increased clarity, “in the morning” and “in the evening” were changed to “every morning” and “every evening.”

During the stage 2 interviews, patients identified areas not covered in the modified UAS, DLQI, and MOS Sleep Scale that may be of interest for future research. Several patients mentioned that they would include more questions related to the emotional aspects of the condition, particularly the anxiety related to the appearance of hives and anxiety surrounding the anticipation of an outbreak or an episode of angioedema. There was also a suggestion to include more about the severity and impact of angioedema, rather than just the occurrence of angioedema.

The MOS Sleep Scale and DLQI were not the focus of this investigation and have previously been shown to be valid and reliable. Nevertheless, it is worth reporting that overall, patients reported both instruments to be comprehensive. Regarding the MOS Sleep Scale, some patients noted that there may be issues related to sleep and medication use and that some reported sleep problems may not be due to CIU. Finally, several patients noted that mood, depression, self-esteem, and emotions are relevant issues that are not captured in the questionnaires.

DISCUSSION

This qualitative research study was conducted in 2 stages to identify outcomes important to patients with CIU and to assess the content validity of the urticaria patient daily diary, including the UAS. Results from stage 1 showed that CIU has an extensive impact on patients, from the symptoms of itch-

ing, hives, and angioedema to the broader aspects of HRQOL. Stage 1 provided evidence that the UAS, with minor modifications, was a promising instrument for symptom assessment in CIU patients, although further evidence of content validity was required. The domains of the DLQI represent many of the aspects of HRQOL that patients considered important: symptoms and feelings, daily activities, leisure, work and school activities, personal relationships, and treatment issues. However, a few additional issue areas were reported by CIU patients that are not captured by the DLQI or the UAS, including mobility, activity limitations, emotional exhaustion, and frustration. These issues represent important topics for future research.

Results from stage 2 provide evidence of the content validity of the urticaria patient daily diary, including the revised UAS, although additional changes were still necessary. The instrument is considered clear and easy to understand, with response options that are appropriate and useful. Patient feedback obtained in stage 2 resulted in additional minor modifications to the instrument, primarily to the wording of response items and instructions. When the urticaria patient daily diary was administered in conjunction with the DLQI and MOS Sleep Scale, patients considered the assessment to be comprehensive, although some recommendations were made to include more items on emotional issues and other aspects of angioedema.

The final urticaria patient daily diary is an easy-to-administer, comprehensive assessment of symptoms for CIU patients. The final urticaria patient daily diary includes more detailed instructions for the UAS and the addition of an item on sleep interference, an item on interference with daily activities, and 3 items on symptom occurrence and management.

For a more comprehensive assessment of outcomes that are considered important by CIU patients, one should consider administering the urticaria patient daily diary in conjunction with a disease-specific HRQOL instrument, such as the DLQI. Future research is needed to evaluate the reliability, construct validity, responsiveness, and interpretability of the components of the urticaria patient daily diary.

There are inherent limitations in conducting one-on-one in-depth interviews. For instance, only a small sample of English-speaking adults in the United States were invited to

participate, which limits generalizability. Generalizability is also limited given that the interview population was primarily female, white, and highly educated. In addition, all participants were adults; therefore, these findings may not be generalized to a pediatric population. If the diary were to be used with adolescents, additional cognitive debriefing should be conducted to confirm that the wording is appropriate and readily understood within this population. Selection bias may be present because the participants were individuals who agreed to discuss issues in an interview setting. However, given that the interview did not include highly sensitive issues, there is no reason to believe that participants would not answer truthfully. Finally, it is possible that participation in stage 1 may have influenced responses of participants in stage 2. For example, probing questions in the stage 1 interview may have brought new issues to the forefront of patients' minds for stage 2.

In conclusion, through one-on-one interviews with patients, important outcome areas in CIU were identified, including physical symptoms, usual daily activities, social functioning, work functioning, emotional functioning, sleep, and overall QOL. On the basis of input from patients, the urticaria patient daily diary was developed. Cognitive debriefing interviews demonstrated the content validity of the urticaria patient daily diary. Future research is needed to establish additional psychometric properties of the instrument, to evaluate the content validity in a pediatric population, and to further explore the emotional aspects of CIU and the impact of angioedema.

ACKNOWLEDGMENTS

We acknowledge the contributions of Betsy Tschosik, Health Outcomes Solutions, and James Zazzali, Genentech Inc, in preparing and reviewing the manuscript and the numerous study coordinators at each site who assisted with patient recruitment and enrollment.

REFERENCES

- Greaves MW. Chronic idiopathic urticaria. *Curr Opin Allergy Clin Immunol*. 2003;3:363–368.
- Zuberbier T, Asero R, Bindslev-Jensen C, et al. EAACI/GA²LEN/EDF/WAO guideline: definition, classification, and diagnosis of urticaria. *Allergy*. 2009;64:1417–1426.
- Kaplan AP, Greaves MW. Pathogenesis of chronic urticaria. *Clin Exp Allergy*. 2009;39:777–787.
- Zuberbier T, Asero R, Bindslev-Jensen C, et al. EAACI/GA²LEN/EDF/WAO guideline: management of urticaria. *Allergy*. 2009;64:1427–1443.
- Engin B, Uguz F, Yilmaz E, Ozdermir M, Mevlitoglu I. The levels of depression, anxiety and quality of life with chronic idiopathic urticaria. *J Eur Acad Dermatol Venereol*. 2008;22:36–40.
- O'Donnell BF, Lawlor F, Simpson J, Morgan M, Greaves MW. The impact of chronic urticaria on the quality of life. *Br J Dermatol*. 1997;136:197–201.
- Kapp A, Pichler WJ. Levocetirizine is an effective treatment in patients suffering from chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled, parallel, multicenter study. *Int J Dermatol*. 2006;45:469–474.
- Grob JJ, Auquier P, Dreyfus I, Ortonne JP. Quality of life in adults with chronic idiopathic urticaria receiving desloratadine: a randomized, double-blind, multicentre, placebo-controlled study. *J Eur Acad Dermatol Venereol*. 2008;22:87–93.
- Mlynek A, Zalewska-Janowska A, Martus P, Staubach P, Zuberbier T, Maurer M. How to assess disease activity in patients with chronic urticaria? *Allergy*. 2008;63:777–780.
- Chowdhury BA. Clinical development programs for chronic idiopathic urticaria indication for H₁-antihistamines. http://www.fda.gov/ohrms/dockets/ac/02/slides/3850S1_04_FDA-CHOWDHURY.ppt. Accessed February 10, 2010.
- Lennox RD, Leahy MJ. Validation of the dermatology index as an outcome measure for urticaria-related quality of life. *Ann Allergy Asthma Immunol*. 2004;93:142–146.
- Bairardini I, Pasquali M, Braidò F, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: Chronic Urticaria Quality of Life Questionnaire (CU-Q₂oL). *Allergy*. 2005;60:1073–1078.
- Fink A. *The Survey Handbook*. Thousand Oaks, CA: Sage Publications Inc; 1995.
- Churchill GA Jr. *Marketing Research: Methodological Foundations*. 5th ed. Ft. Worth, TX: The Dryden Press; 1991.
- Litwin MS. *How to Assess and Interpret Survey Psychometrics*. 2nd ed. Thousand Oaks, CA: Sage Publications Inc; 2003.
- Brod M, Tesler LE, Christensen TL. Qualitative research and content validity: developing best practices based on science and experience. *Qual Life Res*. 2009;18:1263–1278.

Requests for reprints should be addressed to:

Susan D. Mathias, MPH

Health Outcomes Solutions

PO Box 2343

Winter Park, FL 32790

E-mail: smathias@healthoutcomessolutions.com