

# Minimal clinical important difference (MCID) of the Thai Chronic Urticaria Quality of Life Questionnaire (CU-Q<sub>20</sub>L)

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## Summary

**Background:** Chronic urticaria (CU) has negative impacts on patients' daily lives. The Chronic Urticaria Quality of Life Questionnaire (CU-Q<sub>20</sub>L) evaluates quality of life impairment attitudes among chronic urticaria patients. Although the CU-Q<sub>20</sub>L has been validated in several languages, the minimal clinical important difference (MCID) of the CU-Q<sub>20</sub>L has never been determined.

**Objective:** This study aimed to investigate the validity, reliability, responsiveness to change, and MCID of the Thai CU-Q<sub>20</sub>L.

**Methods:** The Thai CU-Q<sub>20</sub>L was translated with permission from the authors of the original Italian version. The Thai CU-Q<sub>20</sub>L, the validated Thai Dermatology Life Quality Index (DLQI), and the Urticaria Activity Score were assessed for 166 patients to evaluate validity and internal consistency. The three questionnaires were then administered to 124 patients to determine the test-retest reliability, responsiveness, and MCID of the Thai CU-Q<sub>20</sub>L.

**Results:** The Thai CU-Q<sub>20</sub>L contained only three domains, whereas the Italian version revealed six domains. Nevertheless, the total variance of the Thai CU-Q<sub>20</sub>L (60.5%) was very close to that of the Italian version (60.0%). The validity of the Thai CU-Q<sub>20</sub>L was shown by strong correlations between CU-Q<sub>20</sub>L and DLQI scores. The Thai CU-Q<sub>20</sub>L also had high internal consistency and

test-retest reliability. Distribution-based, receiver operating characteristic analysis, and anchor-based approaches yielded MCID values of 3.9–8.0, 15, and 21.1, respectively.

**Conclusions:** The Thai CU-Q<sub>20</sub>L is a valid and reliable instrument. We propose that a difference in the Thai CU-Q<sub>20</sub>L score of 15 (MCID) is the smallest change patients perceive as a meaningful improvement. (*Asian Pac J Allergy Immunol* 2016;34:137-45)

**Keywords:** chronic urticaria, Chronic Urticaria Questionnaire (CU-Q<sub>20</sub>L), minimal clinical important difference (MCID), reliability, validation

## Introduction

Chronic urticaria (CU) is a common skin condition characterised by the occurrence of itchy wheals with or without angioedema lasting for at least 6 weeks. It is recognised as a disease with a strong negative influence on patients' well-being and health-related quality of life (HRQoL). To manage the disease effectively, treatment should focus on both the disease burden and the HRQoL of patients. It has been suggested that disease-specific questionnaires may be better than general dermatologic disease questionnaires for assessing both of these factors.

Developed in 2005, the Italian version of the Chronic Urticaria Quality of Life Questionnaire (CU-Q<sub>20</sub>L) is the first urticarial-specific questionnaire to assess HRQoL impairment in patients with chronic spontaneous urticaria.<sup>1</sup> The Urticaria Activity Score (UAS) was first used in 2008 to assess disease activity in CU patients.<sup>2</sup> The European Academy of Allergy and Clinical Immunology, the EU-funded network of excellence, the Global Allergy and Asthma European Network, the European Dermatology Forum, and the World Allergy Organisation accept the CU-Q<sub>20</sub>L and the UAS as the standard measurements that should be used to assess and monitor CU patients.<sup>3</sup> Over the

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Submitted date: 15/5/2015

Accepted date: 24/7/2015



last decade, the CU-Q<sub>2</sub>oL's validity, reliability, and responsiveness to change have been demonstrated in several different languages, including Brazilian-Portuguese, Bulgarian, German, Greek, Iranian, Persian, Polish, Spanish, and Turkish.<sup>4-11</sup> However, the interpretability, or minimal clinically important difference (MCID), of CU-Q<sub>2</sub>oL has never been investigated. Outcome measures should be able to interpret and detect change over time. The MCID, a crucial piece of information for patient care and therapeutic intervention, is the smallest change that patients consider to be worthwhile. This study aimed to investigate the validity, reliability, responsiveness to change, and interpretability (MCID) of the Thai version of the CU-Q<sub>2</sub>oL questionnaire.

## Methods

### *Original (Italian) CU-Q<sub>2</sub>oL questionnaire*

The Italian version of the CU-Q<sub>2</sub>oL questionnaire comprises 23 items categorised into six domains: pruritus (two items), impact on daily activities (six), sleep problems (five), limitations (three), look (five), and swelling (two).<sup>1</sup> For each item, patients were asked to choose between five response values (scored 0–4) indicating the intensity of each item in the last 2 weeks. A total summed score across all items was calculated and transformed into scores ranging from 0 to 100, with a score of 100 indicating the worst HRQoL impairment.

### *Translation of the CU-Q<sub>2</sub>oL questionnaire*

The original Italian version of the CU-Q<sub>2</sub>oL was translated into Thai by two people who spoke both Thai and Italian natively. The first draft of the Thai version of the questionnaire was reviewed for comprehensibility of items by physicians who specialised in allergies. After these physicians reached consensus, the Thai version was back-translated into Italian by two native speakers of Italian. The original and back-translated Italian versions were then reviewed by the original Italian authors and the Thai research team to detect any misconceptions or misinterpretation introduced in the translation process. After a consensus conference, the Thai version of the CU-Q<sub>2</sub>oL was tested with 10 CU patients, and no points of misunderstanding were detected. Then, the final Thai CU-Q<sub>2</sub>oL was administered to CU patients for the study.

### *Subjects and measurements*

Data were collected from October 2014 to December 2014 at the Allergy Clinic in the

Department of Dermatology at Siriraj Hospital. This study was approved by the Siriraj Institutional Review Board, Faculty of Medicine, Siriraj Hospital. The target sample size for validation was 166. All patients aged over 18 years who had CU were invited to participate in the study. A complete history of possible causes, physical examination, necessary tests and laboratory investigations were performed in all patients. Screening for food allergy or intolerance was investigated by an elimination diet for 3 weeks. All suspected drugs used were discontinued or replaced with chemically unrelated drugs. Skin prick testing, drug provocation tests and oral food challenge tests were performed if necessary. For physical urticaria, provocative tests were performed as follows: Dermographism was evaluated by firm stroking of the skin, performed using a dermatographometer with a pressure of 4900 gm/cm<sup>2</sup>, which induced linear itchy wheals within minutes. Delayed pressure urticaria was diagnosed by using sandbags joined by a rope weighing 15 pounds each placed over one shoulder for 15 minutes, which resulted in a palpable wheal at the application site 2–8 hours later. Cold urticaria was made by application of an ice cube in a thin plastic bag to the skin of the forearm for 20 minutes which caused wheals to occur within 15 minutes at the test site, on rewarming of the skin. Cholinergic urticaria was diagnosed by the patient being asked to run on the spot to the point of perspiration. A positive response was defined by subsequent pruritic erythematous punctuate whealing, within 5–15 minutes. Adrenergic urticaria was confirmed by intradermal injection of noradrenaline (3-10 ng in 0.02 ml saline); a small red papule in a halo of blanched skin was considered positive. Solar urticaria was made by phototest and confirmed by exposure to natural sunlight.

Laboratory investigations included complete blood count, urinalysis, erythrocyte sedimentary rate, stool examination and other investigations that were necessary for the individuals, including urea nitrogen, creatinine, aspartate aminotransferase, alanine transferase, alkaline phosphatase, bilirubins, total protein, albumin, hepatitis B surface antigen, anti-hepatitis C virus, free T3, free T4, thyroid stimulating hormone using immunoassay method (cobas® by Roche Diagnostics, Mannheim, Germany), anti-thyroid autoantibodies (i.e. anti-thyroglobulin and anti-thyroid peroxidase; chemiluminescence immunoassay; Abbott, USA), antinuclear antibodies, cryoglobulins, serum

complement level, chest and sinus X-ray studies. The autologous serum skin test was performed by the intradermal injection of 50 µl undiluted autologous serum into the volar aspect of the forearm together with the simultaneous injection of controls including saline and 10 µg/ml histamine. The test was positive at 30 minutes if the serum-injected site manifested a wheal with a diameter at least 1.5 millimetres greater than that of the saline wheal.<sup>2,12,13</sup> After thorough examinations, all patients with chronic spontaneous urticaria (unidentified causes of recurrent urticaria occurring at least twice a week for at least 6 weeks) were recruited to our study. The second and third visits, with a 2-week interval between them, were set to follow-up the patients. All patients obtained proper treatment during appointments. Patients with other dermatological diseases were excluded from the research.

On the first day (day 0), patients were asked to sign the consent form. The information regarding three different questionnaires were explained to the patients; (i) the Thai CU-Q<sub>2</sub>oL (ii) the UAS, and (iii) the Thai Dermatology Life Quality Index (DLQI). The UAS is a specific questionnaire to determine the disease severity of CU patients over one week (UAS7). It assesses different degrees of urticarial severity by calculating scores for 7 consecutive days. The UAS7 sums each four-point scale (scored 0–3) of intensity of pruritus and number of wheals, with a minimum of 0 and a maximum of 6 points per day. Therefore, the highest total possible UAS7 score is 42.<sup>2</sup> The DLQI is a HRQoL questionnaire for general dermatologic diseases that was developed by Finlay and Khan.<sup>14</sup> It comprises 10 questions corresponding to six domains: Symptoms and feeling, Daily activities, Leisure, Work and school, Personal relationships, and Treatment. The total DLQI score ranges from 0 to 30. Dr Finlay previously gave formal permission to the first author to validate and use the Thai version of the DLQI questionnaire.<sup>15</sup> After the patients understood how to complete the three questionnaires, they were asked to fill in the UAS7 for 7 consecutive days by themselves before the second visit.

On the second visit (day 14), the UAS7 was collected, and the Thai versions of the CU-Q<sub>2</sub>oL and the DLQI were completed by the patients at the Allergy Clinic. Another UAS7 was given to each patient to complete for the next 7 consecutive days before returning to the hospital for the third visit. On the third visit (day 28), the UAS7 was collected, and

the Thai versions of the CU-Q<sub>2</sub>oL and the DLQI were again completed by the patients.

### Statistical analysis

Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) were the reference for how measurement properties should be defined and analysed.<sup>16</sup> PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA) was used for the analysis.

#### 1. Validity

- **Cross-cultural validity** is the degree to which the performance of the Thai CU-Q<sub>2</sub>oL items can adequately reflect the performance of the original CU-Q<sub>2</sub>oL items. Exploratory factor analysis was used to determine scales with proper item division of the Thai CU-Q<sub>2</sub>oL. Principal component analysis with varimax rotation was employed. An eigenvalue  $\geq 1$  was chosen as the criterion to retain domains. Each item was classified into the domain when loading with a domain loading  $\geq 0.5$ .<sup>17,18</sup>

- **Construct validity** measures the degree to which a measurement relates to a relevant metric. The relationships between the Thai CU-Q<sub>2</sub>oL and the Thai DLQI and between the Thai CU-Q<sub>2</sub>oL and the UAS7 were evaluated using Pearson's correlation coefficient. Correlation coefficient values of  $<0.3$ ,  $0.3-0.6$ , and  $>0.6$  indicated weak, moderate, and strong correlations, respectively.<sup>19</sup>

- **Known-group validity** is the ability of a measure to discriminate between groups that are theoretically known to differ. The ability of the Thai CU-Q<sub>2</sub>oL to distinguish patients with three different urticarial severities and different HRQoL impairment was investigated using the Kruskal-Wallis test. UAS7 scores were used to classify disease severity of the patients as mild (score of 0–14), moderate (score of 15–22), or severe (score of 23–42).<sup>8</sup> DLQI scores were used to differentiate five levels of HRQoL impairment: no effect (score of 0–1), small effect (score of 2–5), moderate effect (score of 6–10), large effect (score of 11–20), and extremely large effect (score of 21–30).<sup>20</sup>

#### 2. Reliability

- **Internal consistency** is the degree of correlation among items of measurement. Cronbach's  $\alpha$  reliability coefficient was used to analyse the internal consistency. The interpretation of Cronbach's  $\alpha$  was as follows:  $<0.6$  = unacceptable,  $0.60-0.65$  = undesirable,  $0.65-0.70$  =



minimally acceptable, 0.70-0.80 = respectable, 0.80-0.90 = excellent, and  $>0.9$  = excessive consistency.<sup>5,21</sup>

- **Test-retest reliability** measures how consistent scores remain across multiple administrations. Stable patients (no change in disease severity assessed by UAS7 over a 2-week interval) should exhibit consistency in the Thai CU-Q<sub>2</sub>oL between two administrations (2<sup>nd</sup> and 3<sup>rd</sup> visits). Changes in UAS7 scores between the 2<sup>nd</sup> and 3<sup>rd</sup> visits were used to define stable patients. These changes ranged from 0 to 4. Intraclass correlation coefficient (ICC) values of  $<0.4$ ,  $0.4-0.75$ , and  $>0.75$  indicate poor, average, and strong reliability, respectively.<sup>22</sup>

### 3. Responsiveness and interpretability

- **Responsiveness to change** is the ability of an instrument to detect clinical change over time. We expected at least a moderate correlation between score changes in the Thai CU-Q<sub>2</sub>oL and the Thai DLQI. Receiver operating characteristic (ROC) and area under the curve (AUC) were used to investigate the ability of the Thai CU-Q<sub>2</sub>oL to detect changes in patients' HRQoL impairment over time. Area under the curves (AUCs) of 1, 0.9, 0.8, 0.7, and 0.5 were considered perfect, excellent, good, fair, and no better than chance, respectively.<sup>23</sup>

- **Interpretability** is the ability of an instrument to be interpreted from quantitative scores or changes in scores, with a qualitative meaning. The MCID is interpreted as the smallest difference in scores that patients perceive as important.<sup>24,25</sup> We wished to investigate the smallest reduction in Thai CU-Q<sub>2</sub>oL that patients recognised as a meaningful improvement, using three different methods:

(i) Distribution method (MCID-1): The distribution method refers to the numerical distribution of values. The standard error of measurement (SEM)<sup>26,27</sup> and half of the standard deviation (SD) of the measure of interest are the most widely adopted distribution statistics to represent MCID values.<sup>28</sup> SEM is the SD of CU-Q<sub>2</sub>oL at baseline  $\times$  (1-reliability of the instrument)<sup>1/2</sup>. Either Cronbach's  $\alpha$  or test-retest correlation can be used for the reliability values.

(ii) ROC analysis (MCID-2): Previous studies have shown that the changes in scores of 5 and between 2.2 (for inflammatory skin diseases) or 3.1 (for chronic idiopathic urticaria) were the values used to define the MCID of DLQI.<sup>28,29</sup> Accordingly, three response criteria were examined for evaluating the Thai CU-Q<sub>2</sub>oL: changes in the DLQI score  $\geq 3$ ,

changes in the DLQI score  $\geq 4$ , and changes in the DLQI score  $\geq 5$ . Those patients whose condition worsened over the 2-week interval were excluded from this analysis. The ROC analysis was used to derive the AUC for each response criterion. The Thai CU-Q<sub>2</sub>oL value with the highest AUC and  $\geq 80\%$  for sensitivity and specificity was the best defined MCID-2.

(iii) Anchor-based approach (MCID-3): The anchor-based approach compares score changes with an "anchor" as a reference. We used DLQI as an anchor and compared the change in CU-Q<sub>2</sub>oL scores with the change in DLQI scores. From the analysis of MCID-2, the criterion that had the highest AUC was used to define responders. Patients who had either less of a change in DLQI scores than those of the responder group or no change in their DLQI scores were defined as non-responders. Patients whose condition had worsened over the 2-week interval were excluded from this analysis. The MCID-3 was the difference in mean change of the Thai CU-Q<sub>2</sub>oL between "responders" and "non-responders".

## Results

Of the 166 patients with chronic spontaneous urticaria, 131 (79%) were female and 35 (21%) were male. Table 1 demonstrates the demographic data of our patients. The mean age of the patients was  $41.8 \pm 13.8$  years. The average duration of disease was 2 years, with a range of 2 months to 34 years. On the third visit, 126 patients completed the CU-Q<sub>2</sub>oL, UAS7, and DLQI for the second time.

### Cross-cultural validity

Exploratory factor analysis demonstrated a three-domain structure, which described 60.5% of the variance of the 23 items (Table 2). All items except items 17 and 20 were important components, with a minimum factor loading of 0.5. Items 17 and 20 loaded to domain II with a loading factor of 0.30 and III with a loading factor of 0.26. Two items (items 17 and 20) were assigned to three domains each. Cronbach's  $\alpha$  correlations were highest when items 17 and 20 were loaded to domain II and III, respectively.

### Construct validity

There was a strong correlation between the total DLQI score and the total CU-Q<sub>2</sub>oL score ( $r = 0.76$ ,  $p < 0.0001$ ). Correlations between each corresponding domain of DLQI and CU-Q<sub>2</sub>oL were found to be strong and statistically significant (all  $r$  values



**Table 1.** Demographic data of 166 patients with chronic spontaneous urticaria (CSU)

	N (%)
<b>Sex</b>	
- female	131 (78.9)
- male	35 (21.1)
<b>Education</b>	
- primary school degree	11 (6.6)
- high school degree	41 (24.7)
- bachelor degree	78 (46.7)
- master degree	33 (19.9)
- doctor of philosophy degree	3 (1.8)
<b>Urticaria Activity Score</b>	
- mild (0-14)	136 (81.9)
- moderate (15-22)	13 (7.8)
- severe (23-42)	17 (10.2)
<b>Dermatology Life Quality Index</b>	
- no effect (0-1)	57 (34.3)
- small effect (2-5)	56 (33.7)
- moderate effect (6-10)	33 (19.8)
- very large effect (11-20)	15 (9.0)
- extremely large effect (21-30)	5 (3)
<b>Treatments</b>	
- antihistamine alone	138 (83.1)
- antihistamine + prednisolone	7 (4.2)
- antihistamine + monteleukast	6 (3.6)
- antihistamine + hydroxychloroquine	3 (1.8)
- antihistamine + prednisolone + monteleukast	5 (3.0)
- antihistamine + monteleukast + cyclosporine	3 (1.8)
- antihistamine + prednisolone + cyclosporine	2 (1.2)
- antihistamine + prednisolone + monteleukast + hydroxychloroquine	2 (1.2)

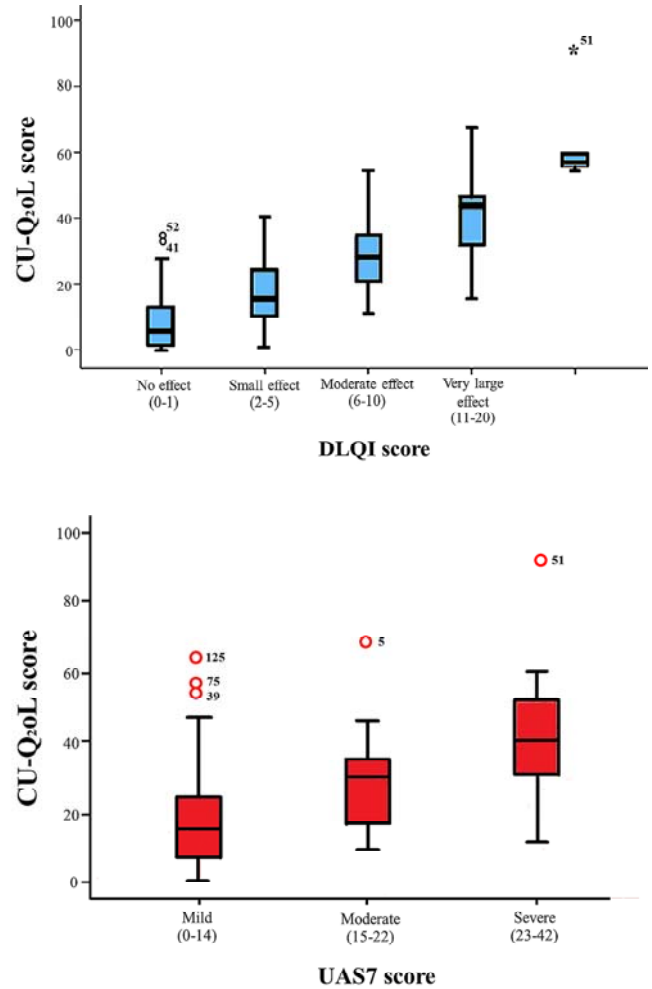
$\geq 0.63$ ,  $p < 0.0001$ ). There was moderate correlation between the CU-Q<sub>2</sub>oL score and the disease activity score (UAS7) ( $r = 0.59$ ,  $p < 0.0001$ ).

#### Known-group validity

The mean UAS7 and DLQI scores were  $8.8 \pm 9.6$  (range: 0–42) and  $4.67 \pm 5.3$  (range: 0–23), respectively. The statistically significant differences in the CU-Q<sub>2</sub>oL total score among the three UAS7 groups and five DLQI groups were found (Figure 1,  $p < 0.0001$ ).

#### Internal consistency and test-retest reliability

Internal consistency was excellent, with Cronbach's  $\alpha > 0.85$ . The ICCs for the CUQ<sub>2</sub>oL total score and each of the three domain scores between two administrations were calculated for 44 patients, revealing average to strong reliability (Table 3).



**Figure 1.** The significant differences in the CU-Q<sub>2</sub>oL scores among the five DLQI groups and the three UAS7 groups.

(a) Correlation between Chronic Urticaria Quality of Life Questionnaire (CU-Q<sub>2</sub>oL) and Dermatology Life Quality Index (DLQI)

(b) Correlation between Chronic CU-Q<sub>2</sub>oL and Urticaria Activity Score-7 (UAS7)

#### Responsiveness to change and interpretability (MCID)

The correlation between the difference of the Thai CU-Q<sub>2</sub>oL and the difference of DLQI scores was moderate ( $r = 0.60$ ,  $p < 0.0001$ ). The MCID-1 values of the Thai CU-Q<sub>2</sub>oL using the distribution method were 8.0 (half of the SD), 3.9 (SEM) using the Cronbach's  $\alpha$  value, and 7.9 (SEM) using the ICC value. Table 4 demonstrates that the change in the DLQI score of  $\geq 5$  had the greatest discriminative power among the three response criteria. ROC



**Table 2.** Cross-cultural validity of the Thai Chronic Urticaria Quality of Life Questionnaire (CU-Q<sub>2</sub>oL)

Domains	Initial Eigenvalues					
	Extraction sums of squared loadings			Rotation sums of squared loadings		
	Total	% of variance	Cumulative %	Total	% of variance	Cumulative %
I	10.05	43.71	43.71	5.09	22.11	22.11
II	2.16	9.41	53.12	4.65	20.21	42.32
III	1.67	7.33	60.45	4.17	18.13	60.45

Item no.	Item name	Domains		
		I	II	III
7	Sleep	<b>0.677</b>	0.447	0.156
8	Free time	<b>0.593</b>	0.494	0.297
11	Falling asleep	<b>0.877</b>	0.101	0.090
12	Waking up at night	<b>0.847</b>	0.214	0.057
13	Tired	<b>0.818</b>	0.157	0.239
14	Concentration	<b>0.630</b>	0.224	0.371
1	Pruritus	0.469	<b>0.589</b>	0.110
2	Wheals	0.345	<b>0.692</b>	0.161
3	Eyes swelling	0.031	<b>0.767</b>	0.025
4	Lips swelling	0.047	<b>0.710</b>	0.064
5	Work	0.383	<b>0.720</b>	0.291
6	Physical activities	0.342	<b>0.736</b>	0.286
9	Social relationship	0.464	<b>0.557</b>	0.378
10	Eating	0.433	<b>0.518</b>	0.231
17	Limit foods	0.329	0.300	0.335
15	Nervousness	0.493	0.231	<b>0.533</b>
16	Bad mood	0.494	0.305	<b>0.578</b>
18	Embarrassed by signs	0.078	0.217	<b>0.852</b>
19	Embarrassed in public	0.028	0.274	<b>0.835</b>
20	Cosmetics	0.168	0.237	0.261
21	Limits clothes	0.237	0.045	<b>0.619</b>
22	Sports	0.125	0.276	<b>0.619</b>
23	Medication side-effects	0.122	0.146	<b>0.680</b>

The threshold for assignment of an item to a factor was preset to  $\geq 0.5$  (bold values). Items 17 and 20 were exceptions.

analysis showed that the reduction in the Thai CU-Q<sub>2</sub>oL score of  $\geq 15$  was the best defined MCID-2 as both sensitivity and specificity of this value were high (sensitivity 83.3% and specificity 82.4%). For MCID-3, 17 patients had changes in their DLQI scores  $\geq 5$  and were defined as responders (Table 5). Fifty-four patients were non-responders ( $0 \leq$  changes in their DLQI scores  $< 5$ ). Fifty-three patients were excluded from the analysis because their condition worsened. The mean score change of the Thai CU-Q<sub>2</sub>oL

between responders and non-responders (MCID-3) was 21.1.

## Discussion

Our study demonstrated that the Thai CU-Q<sub>2</sub>oL was semantically equivalent to the original version of the questionnaire. However, the Thai and Brazilian-Portuguese versions of CU-Q<sub>2</sub>oL contained only 3 domains, whereas the original Italian version, as well as the German, Greek and Polish versions,



**Table 3.** Internal consistency and test-retest reliability of the Thai CU-Q<sub>2</sub>oL

Scale	Items	Mean score (0–100)*	SD*	Cronbach's $\alpha$ * (n = 166)	Intraclass coefficients** (n = 44)
Total score		19.91	15.9	0.94	0.76
Domain I (sleep, leisure, concentration)	7, 8, 11, 12, 13, 14	23.19	21.7	0.91	0.74
Domain II (symptoms, eating, limits)	1, 2, 3, 4, 5, 6, 9, 10, 17	19.09	16.6	0.89	0.66
Domain III (mental status, looks, impact on life activities)	15, 16, 18, 19, 20, 21, 22, 23	18.37	17.5	0.85	0.77

\* These values were derived from the data of 166 patients who completed the Thai DLQI and the Thai CU-Q<sub>2</sub>oL for the first time.

\*\* The ICC values were analyzed from the data of 44 patients who had stable disease severity and completed both questionnaires again within a 2-week interval.

revealed six domains because of different language structures.<sup>1, 5-8</sup> The items for each of the six domains of the Italian version were previously described elsewhere. In the Thai version, domain I (six items) included the scales of sleep problems and impact on life activities of the Italian version, and domain II (nine items) related to pruritus, swelling, and limitations. Domain III (eight items) covered the aspects of sleep problems, limitations, and looks.

Nevertheless, the total variance of the Thai CU-Q<sub>2</sub>oL was 60.5%, which was very close to that of the Italian version (60.0%).

The validated Thai DLQI was used as a relevant metric to compare with the Thai CU-Q<sub>2</sub>oL, because both instruments measured HRQoL impairment. Ten questions of the Thai DLQI were classified into three domains that corresponded to the three domains of the Thai CU-Q<sub>2</sub>oL. The validity of the

**Table 4.** The smallest change in the Thai CU-Q<sub>2</sub>oLscore (MCID-2) that patients perceived as a meaningful improvement by three different criteria of responders

Changes in Thai CUQ <sub>2</sub> oLscore	Changes in DLQI score					
	DLQI $\geq 3$ (responders = 27) *		DLQI $\geq 4$ (responders = 20) **		DLQI $\geq 5$ (responders = 17) ***	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
9.0	65.9	85.2				
10.0	65.9	77.8				
11.0	68.2	74.1				
12.0			70.6	90.0		
13.0			70.6	90.0		
14.0			80.4	85.0	77.8	88.2
15.0			84.3	75.0	83.3	82.4
16.0					83.3	82.4
17.0					85.2	70.6
18.0					87.0	70.6
19.0					87.0	70.6
20.0					88.9	70.6
21.0					92.6	52.9
AUC	0.78 (0.67–0.90)		0.87 (0.77–0.96)		0.90 (0.84–0.97)	

\*, \*\*, \*\*\* There were 44, 51, and 54 non-responders, respectively.

AUC = area under the curve



**Table 5.** Mean change in the Thai CU-Q2oL score between responders (change in DLQI scores  $\geq 5$ ) and non-responders

Total mean score		Mean change in score			
Baseline (n=166)	Week 2 (n=126)	Total different mean score (n=126)	Responder Mean (n=17)	Non-responder Mean (n=54)	MCID-3
19.9	13.6	6.3	7.3 (9.4)	28.4 (15.3)	21.1

Thai CU-Q2oL was demonstrated by the strong correlations between the corresponding domains of the Thai CU-Q2oL and the Thai DLQI. The total scores of both instruments had a strong correlation. Moreover, the mean scores of the Thai CU-Q2oL could differentiate patients with different levels of disease severity and HRQoL impairment. Patients with higher CU-Q2oL scores tended to have higher disease severity and HRQoL impairment. The reliability of each domain was investigated using Cronbach's  $\alpha$ , revealing excellent reliability. The values of the ICCs confirmed that the Thai CU-Q2oL was consistent across multiple administrations for stable patients.

To the best of our knowledge, this was the first study to investigate the MCID for the CU-Q2oL. The MCID-1 of the CU-Q2oL by distribution-based analysis in our study ranged from 3.9 to 8.0. However, it is generally recommended that the MCID value should be based on clinical relevance rather than statistical distribution.<sup>30</sup> In our study, MCID-2 and MCID-3 relied on clinical relevance, because both used reductions in the DLQI scores of  $\geq 5$  to define responders. Therefore, MCID-2 or MCID-3 should be used to represent the MCID of the Thai CU-Q2oL. ROC analysis showed that the MCID-2 value was 15, whereas the anchor-based approach resulted in an MCID-3 value of 21.1. However, ROC analysis illustrated that the MCID-3 (the smallest change in the Thai CU-Q2oL score of 21.1) had low specificity (Table 4). Thus, we proposed that the MCID-2 (score reduction in the Thai CU-Q2oL of at least 15 points) may indicate the smallest change that patients perceive as a meaningful improvement.

Responsiveness and MCID values may vary in different populations and contexts. It is recommended that multiple relevant anchors be employed to confirm responsiveness and determine the MCID. The limitation of our study was that we used only one anchor (the validated Thai DLQI) to compare with the Thai CU-Q2oL. Further studies in

other populations with other anchors, such as the Short Form 36 Health Survey, the Skindex-29, and the Satisfaction profile (SAT-P) are warranted to establish the MCID value of CU-Q2oL.<sup>31-35</sup>

In conclusion, our study investigated all measurement properties of the Thai CU-Q2oL, including validity, reliability, responsiveness to change, and interpretability (MCID). The results of our study, based on accepted methodological standards, have provided evidence that the Thai CU-Q2oL is a valid and reliable instrument for use in research and clinical practice. A reduction of 15 in the Thai CU-Q2oL score (MCID) is the smallest change that patients recognised as a meaningful improvement in our study.

### Acknowledgements

The authors would like to thank Assistant Professor Dr Chulaluk Komoltri for her advice on the statistical analysis.

### Conflict of interest

All authors declare that they have neither conflicts of interest nor financial support from pharmaceutical companies.

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