



Exploring the content validity of the EQ-5D-5L and four bolt-ons (skin irritation, self-confidence, sleep, social relationships) in atopic dermatitis and chronic urticaria

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Abstract

Background The objective of this study was to assess the content validity of the EQ-5D-5L and four bolt-ons: skin irritation, self-confidence, social relationships and sleep, for people with atopic dermatitis (AD) and chronic urticaria (CU).

Methods Adults with AD or CU in the United Kingdom, with varying levels of severity, participated in either online or in-person semi-structured interviews. During the interviews, participants were first asked about the symptoms and impacts of their condition. They were then asked to complete the EQ-5D-5L and four bolt-ons using ‘think-aloud’ and retrospective probing. Interviews were recorded, transcribed, then analysed using content and thematic analysis.

Results Thirty participants ($N=15$ with AD; $N=15$ with CU) were interviewed. Participants spontaneously reported itch (AD: 100%; CU: 93%), self-confidence (AD: 100%, CU: 47%), sleep (AD: 53%; CU: 53%), and social relationships (AD: 27%; CU: 60%). The skin irritation bolt-on was the most important or relevant dimension for 60% of AD and 73% of CU participants. For all participants, skin irritation and self-confidence bolt-ons improved the EQ-5D-5L’s comprehensiveness. Social relationships was more frequently ranked as the least relevant among the other bolt-ons.

Conclusions This study assessed the content validity of four EQ-5D-5L bolt-ons within two patient populations. Skin irritation, self-confidence and sleep bolt-ons showed good evidence of content validity for people with AD and CU, providing support for their application in other skin conditions. The value of a social relationships bolt-on was less clear. Quantitative psychometric research is recommended to further support the use of bolt-ons in CU and AD.

Keywords EQ-5D-5L · Bolt-ons · Content validity · Atopic dermatitis · Chronic urticaria · Itch · Self-confidence

Background

The EQ-5D is the most widely used generic preference-accompanied health status instrument [1]. Several health technology assessment (HTA) bodies, including the National Institute for Health and Care Excellence (NICE) in England and Wales, state a preference for the EQ-5D to be used to assess health-related quality of life (HRQoL) and provide evidence of the effectiveness or benefit of health technologies [2]. The assumption from the NICE guidance is that the measure is suitable for all conditions, but evidence has

emerged that the EQ-5D does not reflect the burden of some conditions [3–6]. This suggests that in certain diseases, the measure has limited content validity [7]. For this reason, some HTA bodies, such as the Institute for Quality and Efficiency in Health Care (IQWiG) in Germany [9], recommend using condition-specific HRQoL instruments. However, for many conditions, a validated condition-specific preference-based measure is not available to generate utility values. Therefore, adding bolt-on dimensions to the EQ-5D that are specific to a particular patient population is a way to improve the accuracy and precision of the generic instrument [8].

Bolt-ons describing self-confidence and skin irritation have been added to the EQ-5D-5L to better encapsulate the impact of HRQoL in psoriasis [10]. The development of these bolt-ons was based on qualitative interviews with individuals with psoriasis in the UK [10]. Further evaluation of

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the psychometric performance and content validity of these two bolt-ons has been conducted with psoriasis patients [10–12]. Recent studies have also shown the usefulness of the bolt-ons in other chronic conditions, myasthenia gravis (self-confidence bolt-on only) and chronic kidney disease [13, 14]. Another recent study explored the content validity of the EQ-5D-5L with the skin irritation and self-confidence bolt-ons in individuals with AD in Hungary [15].

AD is a chronic inflammatory disease characterised by dry, inflamed skin patches or plaques with lesions, which are particularly impactful during flare-ups [16, 17]. It is a common condition that often begins in childhood but can occur at any age, with a prevalence in Europe estimated to be up to 19% of children and 4.4% of adults [18]. Similarly, urticaria is an allergic skin condition that causes rashes or angioedema with a prevalence of 0.5% in adults in Europe [19, 20].

AD and CU significantly impact the HRQoL of people living with these skin conditions. Several studies have demonstrated that individuals with AD or CU can experience anxiety, shame, depression, low self-esteem, and an unwillingness to be seen in public [21–25]. Other reported areas of HRQoL impact include pain, sleep, relationships, and social outings [21, 26–31]. EQ-5D bolt-ons proposed for these dimensions of HRQoL may therefore be relevant and important for measuring the HRQoL impact of AD and CU.

This study aimed to explore the content validity (relevance, importance, comprehensiveness and comprehensibility) of the EQ-5D-5L and skin irritation and self-confidence bolt-ons in patients with AD and CU in the UK. Furthermore, as impacts on sleep and social relationships for people with AD [32, 33] and CU [21, 27] have been reported in previous literature, the study also explored the validity of two additional bolt-ons for these dimensions of HRQoL.

Methods

Study design

This cross-sectional study consisted of qualitative interviews with UK adults with AD or CU. The interviews included concept elicitation of symptoms and impacts of AD or CU, as well as cognitive debriefing of the EQ-5D-5L and skin irritation and self-confidence bolt-ons. Exploratory questions on the relevance of additional bolt-ons of sleep impact and social relationships were also included in the interviews [34]. The study was reviewed and approved by the University of Portsmouth ethics review committee (reference: 23/ETHICS/002). The study design, data analysis and reporting followed the Standards for reporting qualitative research (SRQR, see supplementary materials) [35].

Sample

Participants were recruited by a specialist recruitment agency using social media, a patient database, referrals from healthcare professionals, and patient associations. Recruitment continued until data saturation which was anticipated to be met after 15 interviews [36]. Participants were required to be 18 years or older, living in the UK, able to read and speak English, and have a self-reported diagnosis of AD or CU. Potential participants were excluded if they reported having any other dermatological conditions or systemic diseases associated with dermatological symptoms. Soft quotas based on self-reported condition severity (mild/moderate/severe) and ethnicity were used during recruitment to ensure heterogeneity in the samples. All participants received information on the study content, procedures, and their rights as participants, then provided informed consent prior to participation in the study.

Procedures

Interviews followed a semi-structured interview guide and were conducted by experienced interviewers (AKS, KG, AM, KW), trained on the study objectives and interview guide. The interviewers were all female qualitative researchers with a psychology undergraduate degree or above. Interviews were conducted in person or via video-conference using Zoom. Interviews were conducted between May to September 2023, lasted approximately 60 min (Mean = 56 min, SD = 13 min), and patients received a remuneration of £65 (online)/ £115 (in-person) for their participation in the study. All interviews were audio-recorded, transcribed verbatim and de-identified for analysis.

Figure 1 provides an overview of the interview procedures. Interviews began with a concept elicitation section in which participants were asked open-ended questions about their experiences with their skin condition, including the symptoms and impact on their HRQoL. Participants then completed the EQ-5D-5L (including the EuroQol visual analogue scale) whilst ‘thinking aloud’ to explain their reasoning as they responded. Probes explored the reasoning further, in addition to the relevance, comprehensiveness, comprehensibility, and importance of the dimensions. Participants then completed the EQ-5D-5L with the two psoriasis bolt-ons: skin irritation and self-confidence. Participants were then asked follow-up probe questions about the bolt-ons and to compare and evaluate the measures. After completing each measure participants were asked if they felt any aspects of HRQoL was missing from the instrument to assess instrument comprehensiveness. In order to assess comprehensibility, at these two time-points participants were also asked about the appropriateness of the wording and if there

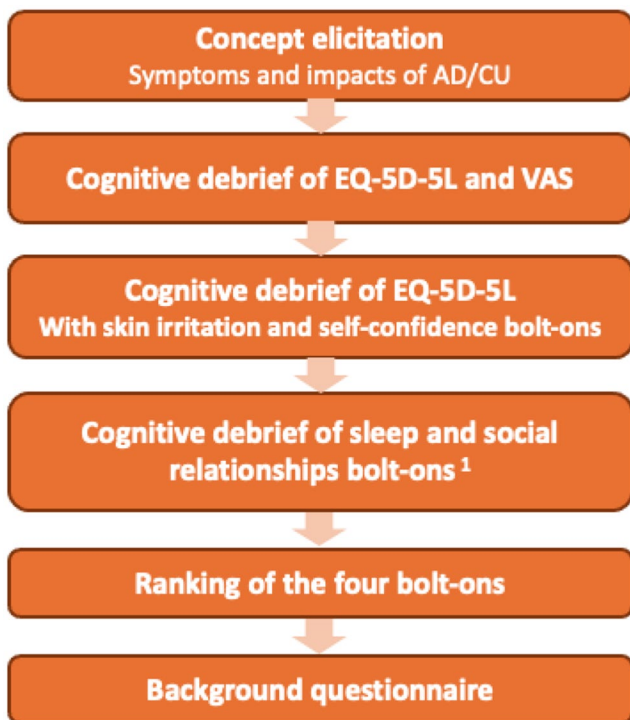


Fig. 1 Overview of interview procedures

was anything they would change about the instruments, such as the recall period. Finally, participants were shown the additional exploratory bolt-ons regarding sleep and social relationships and asked about their relevance.

At the end of the interview participants completed a background questionnaire on socio-demographics, co-morbidities, and current symptoms. Severity of participants' AD and CU was measured using validated self-reported instruments: the Patient-Oriented Eczema Measure (POEM) [37, 38] and the Urticaria Control Test (UCT) [39]. Participants also completed a 10-point (NRS) rating scale to assess their perception of the severity of their condition (from 0: not at all severe to 10: extremely severe).

Analysis

The data from the background questionnaire were summarised using descriptive statistics. Thematic and content analysis was used to analyse interview transcripts to identify common themes and summarise responses to cognitive debriefing questions. Thematic analysis is a method for identifying, analysing and reporting themes in qualitative data [40]. Thematic analysis includes several stages: data familiarisation and coding, grouping of codes, identifying themes and reporting. Software (MAXQDA) was used to aid the qualitative data analysis [41]. An initial framework was developed iteratively based on the concepts that emerged from the interviews. Following the independent coding of a

selection of interview transcripts by two of the interviewers, codes were compared and reconciled wherever differences occurred. Data saturation was monitored throughout analysis using a saturation grid.

Results

Sample characteristics

Interviews were conducted with 15 individuals living with AD and 15 individuals living with CU; most interviews were conducted online ($N=24$; 80%). The sample characteristics of both the AD and CU samples are shown in Table 1 (see more detailed, disease specific clinical characteristics in Supplementary material - Table 1 (AD) and Table 2 (CU)). Participants had a range of sociodemographic backgrounds, with varied age, and employment status, however most had a college/university level of education ($N=27$; 90%) and were female ($N=23$; 77%). Most CU participants had chronic spontaneous urticaria ($N=12$; 80%). The average self-reported severity score on a NRS was similar for both samples, however the responses to the severity measures indicate that most AD participants had only mild or moderate AD at the time of the interview, whereas the majority of the CU sample were not well controlled. On average, the AD sample had been living with AD (mean 19.4, SD 13.5 years) for a lot longer than the CU sample had been living with CU (mean 8.3, SD 8.3 years).

Qualitative results

Concept elicitation: symptoms

Participants spontaneously discussed numerous symptoms of AD and CU (see Fig. 2); example participant quotes are shown in Fig. 3. Among these, itch was the most frequently reported (AD: $N=15$; CU: $n=14$). Most participants in both samples also reported experiencing pain or discomfort (AD: $n=11$; CU: $n=11$). More than half of both samples reported additional symptoms such as hives, swelling and angioedema, bleeding, burning of the skin, soreness, skin redness and dry skin. The majority of symptoms were reported in the first five AD interviews (80%) and first five CU interviews (76%), indicating that data saturation was attained [36].

Concept elicitation: impact on HRQoL

When asked about the impact of living with AD or CU, all the EQ-5D-5L and bolt-on dimensions were spontaneously reported by at least 20% of each sample (see Fig. 2).

Table 1 Sample demographics

Characteristic	Atopic Dermatitis N=15	Chronic Urticaria N=15
Age		
Mean (SD)	36.1 (11.5)	39.6 (12.1)
Range	23, 54	23, 62
Ethnicity		
White N (%)	10 (67%)	11 (73%)
Black N (%)	0 (0%)	1 (7%)
Asian N (%)	4 (27%)	3 (20%)
Other ethnic group N (%)	1 (7%)	0 (0%)
Sex		
Female N (%)	11 (73%)	12 (80%)
Severity		
Mild or moderate AD ¹ / Well controlled CU ²	10 (67%)	4 (27%)
Severe AD ¹ / Not well controlled CU ²	5 (33%)	11 (73%)
Years since diagnosis: Mean (SD)	19.4 (13.5)	8.3 (8.3)
Self-reported severity NRS 0 (not at all) – 10 (extremely severe)		
Mean (SD)	5.3 (2.1)	5.0 (3.1)
Range	2, 9	0, 9
Type of CU		
Chronic spontaneous urticaria (CSU)	-	12 (80%)
Chronic inducible urticaria (CIndU)	-	3 (20%)
Current treatment³		
Over the counter antihistamine	7 (47%)	5 (33%)
Prescribed antihistamine	-	13 (87%)
Over the counter topical therapy (ointment)	12 (80%)	4 (27%)
Prescribed topical therapy (ointment)	9 (60%)	-
Oral corticosteroids	1 (7%)	6 (40%)
Biological therapy	1 (7%)	-
Other	3 (20%)	4 (27%)
None	1 (7%)	-

¹POEM is scored out of 28. 0–2 = “clear or almost clear skin”, 3–7 = “mild eczema”, 8–16 = “moderate eczema”, 17–24 = “severe eczema”, 25–28 = “very severe eczema” [37, 38]

²Scores range from 0 (no control) to 16 (complete control); ≥ 12 indicates well controlled urticaria [39]

³Participants reported all of the treatments they were using for their AD/CU at the time of the interview

Mobility was affected for a few participants as a consequence of having a lack of energy, dry skin making moving painful or swelling of the legs and/or feet. Impacts on self-care typically related to washing being painful and causing a flare-up, applying creams, certain clothing types being uncomfortable or causing irritation and covering their skin up due to the visibility of the condition. Usual activities included AD or CU affecting their work, cooking, exercise, social activities, outdoor activities, and swimming. Many participants described how their AD or CU affected levels of anxiety and depression. Other emotional impacts included feelings of anger, frustration, fear, worry

Table 2 Most and least relevant or important bolt-on dimensions

Bolt-on	Most relevant or important ¹		Least relevant or important ²	
	Atopic dermatitis N	Chronic urticaria N	Atopic dermatitis N	Chronic urticaria N
Skin irritation	9	11	-	-
Self-confidence	2	1	-	3
Sleep	2	1	2	3
Social relationships	-	1	7	7

¹Only 14 CU participants and 12 AD participants were asked to rank the bolt-on dimensions as most relevant or important; one participant ranked two as equally relevant or important

²Only 13 CU participants and 9 AD participants were asked to rank the bolt-on dimensions as least relevant or important

and embarrassment. All participants with AD and around half of participants with CU mentioned an impact on their self-confidence. Other concepts reported included feeling self-conscious about appearance, impact on diet, sleep and social relationships. Almost all (95%) impacts on HRQoL were reported in the first five interviews (AD: 90%; CU: 95%), confirming that data saturation was attained [36].

Cognitive debriefing - relevance of the EQ-5D-5L and bolt-ons

All participants found the EQ-5D-5L and skin irritation/self-confidence bolt-ons to be easy to complete. Almost all participants considered the seven dimensions relevant to their condition and agreed that the instrument covered aspects of HRQoL that they consider important: “it’s important to me that you cover all aspects of physical and mental wellbeing and that’s what you’ve included in those” (C005). Several participants thought that the mobility dimension was a less relevant question (AD: $n=5$; CU: $n=6$). Of the other dimensions, self-care (AD $n=3$; CU: $n=1$), usual activities (AD $n=1$) and anxiety or depression (AD: $n=1$; CU: $n=1$) were considered less applicable to a few patients. Example participant quotes about the bolt-ons are shown in Fig. 4.

All participants reported that the EQ-5D-5L with the two bolt-ons better reflected the impact of their condition than the EQ-5D-5L alone. Overall, participants generally interpreted the seven dimensions as intended. Most participants understood mobility in terms of ability to walk, move, run and be active independently. For the self-care dimension, some participants in both samples interpreted this as problems such as applying necessary treatments, skin care, showering at the right temperature, drying their body after washing and choosing the right clothes. Others interpreted problems with self-care as problems doing activities that they enjoy or promote their wellbeing such as gardening, mindfulness, shopping, cooking, and make-up. For usual activities, several participants interpreted the dimension

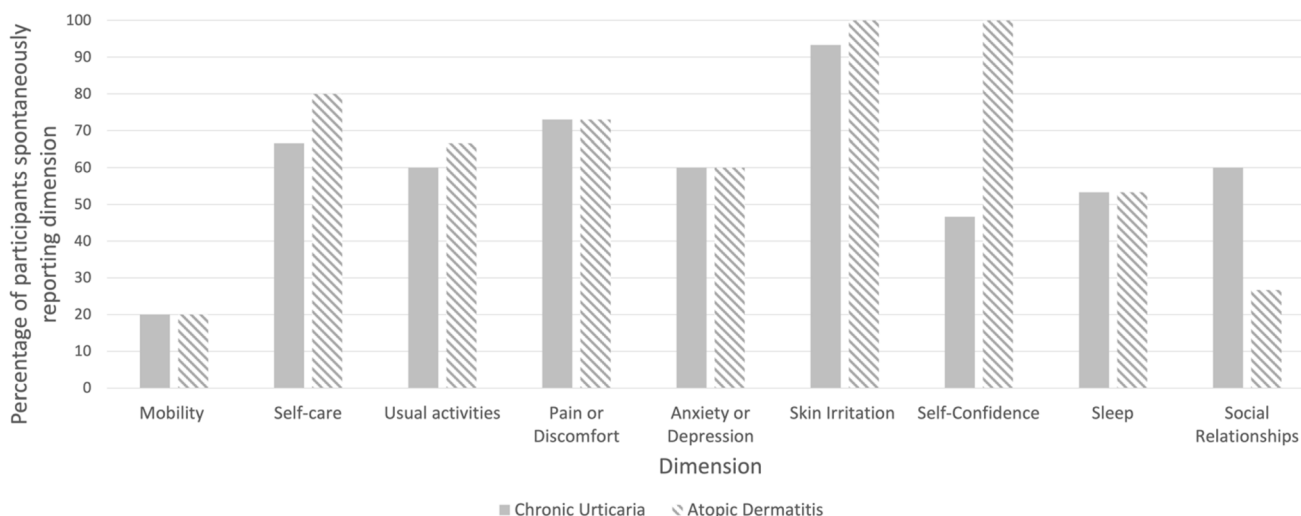


Fig. 2 Proportion of participants spontaneously reporting the EQ-5D-5L and bolt on dimensions during concept elicitation

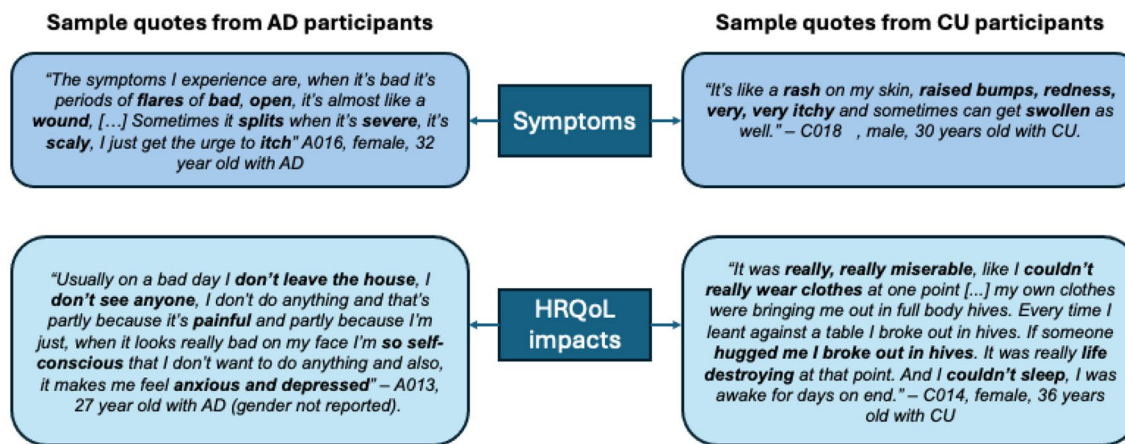


Fig. 3 Example quotes from participants

as how daily activities, such as swimming or exercising, cause skin irritation. Others interpreted it in terms of avoiding the gym at certain times, or avoiding applying for jobs that require an office presence. Pain and discomfort was understood by many as general pain and being “uncomfortable” (n=8), however some participants also understood the dimension in relation to their CU or AD, such as itchiness, swelling, burning, dry skin and the physical feeling of flare-ups and appearance of hives. Additionally, three AD and two CU participants defined pain and discomfort in terms of how it restricts their ability to sleep and do usual activities and four AD participants referred to mental pain and emotional discomfort. For anxiety and depression, most participants interpreted the dimension in the context of their skin condition, for instance, anxiety around triggers, people judging their appearance, feeling self-conscious, sleeping, exposure to sunlight, planning, treatment, uncertainty,

having anxiety and depression during flare-ups and dying due to their condition.

Skin irritation

All participants in both samples reported that the skin irritation bolt-on question is relevant and important to understanding their condition. All participants expressed a preference for the skin irritation dimension to be added to the EQ-5D-5L (n=15 in each sample). Participants mostly interpreted the bolt-on dimensions as intended. Skin irritation was described as itching, redness, raised skin, pain from skin, hives, burning and ability to refrain from scratching.

Self-confidence

All participants in both samples described self-confidence as relevant and important to understanding their condition

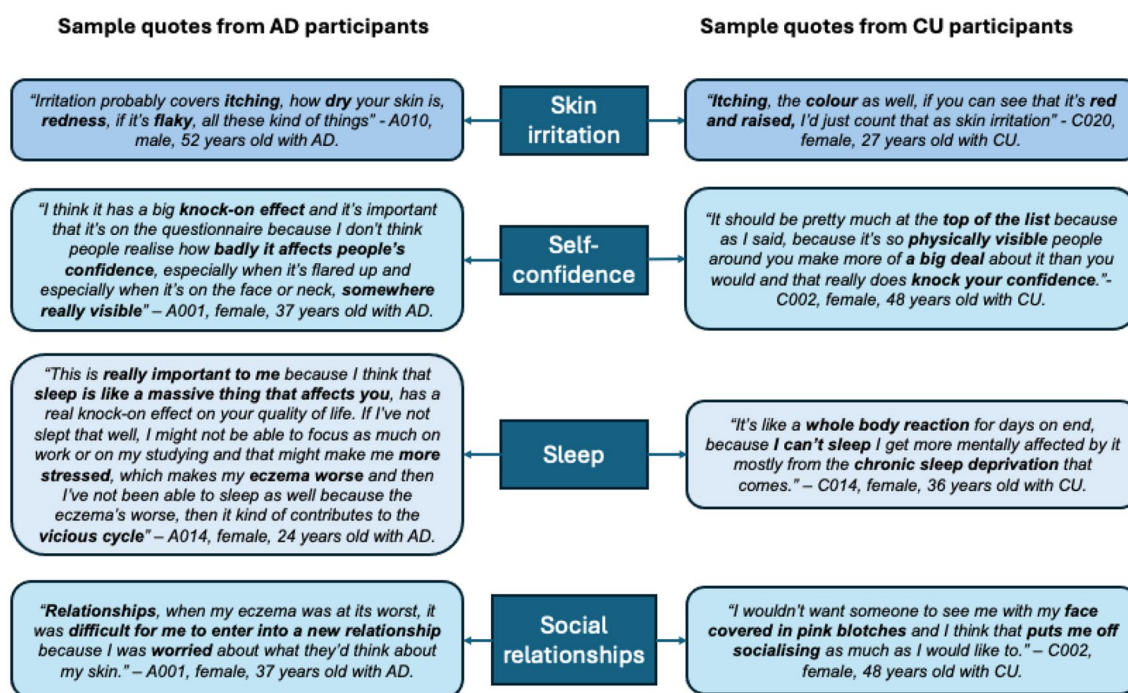


Fig. 4 Example quotes from the bolt-on cognitive debriefing

and an important addition to the EQ-5D-5L. Most of those prompted expressed a preference for the self-confidence dimension to be added to the EQ-5D-5L ($n=9$ in each sample) while a few stated it does not need to be added.

Self-confidence was understood by participants as feeling confident in themselves and their own skin and ability to interact with others and do usual activities without the fear of being judged. Some participants interpreted issues with self-confidence in terms of their condition, for instance fear of judgement and impact of visibility of hives. Participants also discussed how self-confidence is negatively impacted when experiencing flare-ups, particularly in visible body parts.

Sleep

Over half reported the sleep bolt-on to be relevant and important to understanding their condition (AD: $n=10$; CU: $n=11$). Most of those asked felt that the sleep dimension should be added to the EQ-5D-5L (AD: $n=9$; CU: $n=10$), although one stated that the wording should refer to itch/scratching during sleep. Six participants ($n=3$ in each sample) did not think sleep should be added to the EQ-5D-5L.

The sleep dimension was interpreted by most in the context of their skin condition, for instance, itching at night either uncontrollably and unconsciously or discomfort at night restricting ability to sleep or getting woken up by extreme irritation.

Social relationships

Many participants described the dimension as relevant and important to understanding their condition (AD: $n=8$; CU: $n=10$). Some participants in each sample felt that the social relationships dimension should be added to the EQ-5D-5L (AD: $n=7$; CU: $n=6$), however a few in each sample reported they would not add the dimension to the EQ-5D-5L (AD: $n=3$; CU: $n=2$). The relationships inferred from the social relationships dimension included friends, families, colleagues, teachers, and romantic relationships. Two CU participants interpreted problems with social relationships as CU causing issues with their partner and others being insensitive about their condition.

Ranking of bolt-on dimensions

When asked to rank the four bolt-on dimensions in terms of relevance or importance, the majority of participants considered skin irritation as the most relevant or important (AD: $n=9$; CU: $n=11$) while the remaining dimensions were all ranked most relevant or important by just one or two participants each (Table 2). Self-confidence (AD: $n=3$; CU: $n=5$) and sleep (AD: $n=4$; CU: $n=5$) were most commonly ranked as second most important. Social relationships was most frequently mentioned as the least relevant or important bolt-on ($n=7$ from each sample). Self-confidence was more often reported as least important to participants with CU ($n=3$) compared to those with AD ($n=0$).

Conceptual overlaps between the dimensions

When completing the EQ-5D-5L, half of both samples ($n=7$ AD and $n=7$ CU participants) spontaneously reported aspects of skin irritation when answering the pain or discomfort dimension, indicating a possible conceptual overlap. Also, when asked specifically if any dimensions overlap, ten AD and six CU participants referred to these two dimensions. However, it was generally agreed that the dimensions are sufficiently different and should remain as separate dimensions. When completing the EQ-5D-5L, several AD ($n=5$) participants discussed concepts such as self-consciousness and fear of judgement when answering the anxiety or depression dimension, these concepts were also discussed in relation to the self-confidence bolt-on indicating a potential overlap. Additionally, when asked to consider dimension overlap, most AD ($n=11$) and five CU participants identified an overlap between self-confidence and anxiety/depression. However, most agreed that the two dimensions capture different things and therefore should remain as separate dimensions. Social relationships and self-confidence bolt-ons were also considered inter-related or overlapping by seven participants (AD $n=5$, CU $n=2$).

Suggested changes

Many participants suggested changes to one or more of the seven dimensions (Table 3). Participants suggested the content of certain dimensions should be elaborated on, added to, or some recommended splitting the composite dimension of anxiety or depression into two questions. However, several participants suggested they would make no changes to the instrument (AD: $n=4$; CU: $n=6$).

Most participants were satisfied with the recall period with some reporting there would be no change in their responses if the recall period changed to the past week (AD: $n=7$; CU: $n=5$). However, seven participants from each sample reported that they would provide different responses if they were to refer to their health over the past week. Two CU participants reported asking about any one day is not reflective of their whole experience of CU due to the daily fluctuations in their disease symptoms. A few participants also made suggested changes to the recall period (Table 3).

Discussion

This study used qualitative interviews with individuals living with AD and CU to assess the content validity of the EQ-5D-5L and four different bolt-ons in two chronic skin conditions, AD and CU. Our findings provide support for the inclusion of the skin irritation bolt-on for

HRQoL measurement in both AD and CU as skin irritation was experienced by all participants and all felt this dimension was important. There is some evidence that the pain and discomfort caused by skin irritation is captured within the pain or discomfort dimension. In the original development of the skin irritation and self-confidence bolt-ons in psoriasis, psychometric analyses indicated that the bolt-ons measured additional variance [10]. Both bolt-ons also significantly impacted UK general public participants' strength of preferences when valuing health states, indicating that the bolt-ons were considered distinct from EQ-5D dimensions [10]. Further research into potential conceptual overlap between pain/discomfort and skin irritation dimensions in dermatology is recommended to avoid over-estimating the HRQoL impact.

The current study also supports the relevance of the self-confidence dimension in AD and CU. All AD participants spontaneously mentioned a negative impact on their self-confidence, whilst half of the CU sample did, although all felt it was important and relevant. Very few in either sample ranked this dimension as most relevant or important out of the four bolt-ons, although for several it was ranked second. The study also provides preliminary support for the inclusion of a sleep bolt-on for AD and CU, but the evidence for the addition of a social relationships bolt-on is less strong. Although participants did frequently state that all four bolt-ons discussed should be added to the EQ-5D-5L for HRQoL measurement in both AD and CU.

The current study's findings are supported by recent work on content validity of the EQ-5D-5L with skin irritation and self-confidence bolt-ons for patients with AD in Hungary [15]. One key difference between the two studies is that the Hungarian sample consisted of a higher proportion of participants on systemic treatments, indicating that the sample had more severe AD than the current study. Despite this difference, the results were in line with the current study. In the Hungarian study, participants with AD reported that the EQ-5D-5L with two bolt-ons was easy to complete, comprehensive, and covered the most important aspects of HRQoL for their condition. The Hungarian AD participants also reported that itch was the main impact and most frequently ranked it as the most important dimension out of all original EQ-5D dimensions and the two bolt-ons. Self-confidence was relevant to the AD sample but less so than skin irritation. Conceptual overlaps between dimensions similar to the current study were also discussed in the Hungarian study [15].

This study expands on recent work on the application of bolt-ons in dermatology [10, 12, 15] by exploring two additional bolt-ons: social relationships and sleep [34]. In qualitative literature people with chronic skin conditions frequently report impacts on social activities and

Table 3 Participant reported suggested changes to the EQ-5D-5L and bolt-ons

Themes	Chronic Urticaria, N(%)	Atopic Dermatitis, N(%)	Example quote
Response options			
• Only one of the following response options are needed: 'extreme' or 'severe' for all dimensions.	0 (0%)	1 (7%)	A001: The question about the severe and the extreme, that might be difficult for some people to understand ... to differentiate between those two.
Recall			
• Describing health over a week, month, or specific time of year such as winter, would be more informative.	0 (0%)	3(20%)	A002: A month? It's just a time thing, like day to day there isn't much change but two to three weeks in a month, it could be all clear or absolutely awful. So I think a month.
Mobility			
• Reword	0 (0%)	2 (13%)	A004: If it said, "I have slight irritation when walking about", "I have moderate irritation and feelings when walking about", I think I would tick the "I have moderate irritation when walking around", so it could be clearer.
Self-care			
• Distinguish whether mental or physical problems impacting self-care	0 (0%)	1 (7%)	A013: I think when I was thinking about self-care and usual activities, I was wondering whether you meant, do I have problems mentally or do I have problems physically?
• Split in to 2 questions	0 (0%)	1 (7%)	A015: with washing and dressing, I think they're quite different, you know, with eczema you do have problems with washing just naturally with soap and if your skin has open wounds from eczema then it would sting them. But that wouldn't affect dressing at all.
• Add further examples to self-care	2 (13%)	0 (0%)	C008: I think maybe on self-care, it can come down to are you able to feed yourself, are you able to make that shopping trip to get some food
Usual activities			
• Further define usual activities	1 (7%)	1 (7%)	C013: you could add in there indoors and outdoors, so it elaborates a bit more, if that makes sense. Because like I said to you just now, I'm not restricted within my household when I'm at home, it's when I'm out, that's where the restriction comes in.
• Distinguish whether mental or physical problems impacting usual activities	0 (0%)	1 (7%)	A013: I think when I was thinking about self-care and usual activities, I was wondering whether you meant, do I have problems mentally or do I have problems physically?
• Add "socialising"	1 (7%)	0 (0%)	C002: Perhaps in usual activities add in socialising
Pain and discomfort			
• Distinguish between the mental and physical aspects within pain and discomfort	0 (0%)	1 (7%)	A013: I would distinguish between physical pain and discomfort and mental pain and discomfort
• Replace 'discomfort' with 'uncomfortable'	0 (0%)	1 (7%)	A002: I would use the word "uncomfortable" more than "discomfort" personally
Anxiety and depression			
• Split in to 2 questions	1 (7%)	3 (20%)	C012: I would say anxiety and depression being put together actually could be separated, because they're quite different states. Whereas pain and discomfort might be considered to be part of the same continuum, I think anxiety and depression are not. That would probably capture more if it was separated.
• Replace 'anxiety' with 'worry'	0 (0%)	1 (7%)	A002: Maybe worried instead of anxious because again anxiety for me speaks more for mental health, chronic thing whereas I can be worried about eczema
Skin irritation			
• Replace response options of 'itching' to 'skin irritation'	2 (13%)	1 (7%)	A006: the other options are just about itching not about skin irritation, but it should be, "I have no skin irritation, I have slight skin irritation." It reads to me that it's all about itching.
• Add other variations of skin irritation	1 (7%)	0 (0%)	C013: you might want to add other words to describe variations on skin irritation that people can experience. Sensitivity is another thing, or skin specific pain, or tingling is another sensation that I sometimes have with it, or burning.

Additional results relating to missing concepts are included in the Supplementary materials

relationships due to their condition [21, 26, 42–44]. Additionally, commonly used validated dermatology-specific HRQoL measures, such as the DLQI [45] and Skindex [46], contain items that capture problems with social relationships. Impact on social relationships was also raised as a missing concept from the EQ-5D for capturing disease burden of psoriasis during the development of the skin irritation and self-confidence bolt-ons for psoriasis [10]. However, factor analyses assessing the dimensional structure of the EQ-5D and potential bolt-ons for psoriasis indicated that skin irritation and self-confidence were more important predictors of the measure variance. Hence, impact on social relationships was dropped as a bolt-on dimension for psoriasis [10]. In the previously mentioned qualitative study with the skin irritation and self-confidence bolt-ons in Hungary, five participants with AD reported impact on social relationships missing as a dimension [15]. The current study provides further evidence of the impact of chronic dermatological conditions on social relationships. However, this dimension was considered less relevant in AD and CU than the other bolt-ons, and therefore, its use does not seem justified in these patient populations.

Impacted sleep was relevant and important to both AD and CU samples in this study, suggesting a potential benefit of including a sleep bolt-on in HRQoL evaluation in these populations. Sleep was also identified as a missing concept from the EQ-5D with skin irritation and self-confidence bolt-ons for AD participants in Hungary [15]. Other recent literature showed a co-existence of insomnia in 82% of AD patients [47] and a negative influence of itch on sleep quality in AD patients [48]. The higher frequency of problems with insomnia and sleep quality for people with AD [45] and sleep impairment for people with CU [47]) compared to those with psoriasis could explain why impaired sleep was not selected during development of bolt-ons for psoriasis, but was relevant to the current study's samples. Further exploration of the psychometric properties and added value of the sleep bolt-on is recommended both in AD and CU.

A strength of this study is the inclusion of two relevant diagnoses with clinically and demographically heterogeneous samples. A further strength of the study is the utilization of not only the psoriasis bolt-ons but also two other relevant bolt-ons. The interview design to include concept elicitation before the 'think-aloud' cognitive debriefing of the HRQoL dimensions, was a further strength of the study, allowing participants to report their symptoms and impact of their chronic health condition spontaneously before being prompted, reducing bias in the HRQoL impacts discussed. A final strength of this

study is the possible generalizability of the findings to other English-speaking countries.

There are a few limitations of this study to consider. The severity question used as a screening question for quotas was simplified (mild/moderate/severe) and self-reported, meaning it often did not align with the severity of experience discussed in the interviews or measures of severity scores derived from validated tools. Diagnoses of AD and CU were self-reported, risking people participating who did not have a formal diagnosis of either condition. This risk was mitigated by not naming the conditions of interest or the compensation amount in the recruitment advert, participants were required to select their condition from a list of chronic skin conditions. Potential participants were also screened such that those reporting chronic skin conditions other than AD and CU, or reporting both AD and CU were excluded from participating. The CU sample was imbalanced in the type of CU which participants were diagnosed with, three (20%) had chronic inducible urticaria, while twelve had chronic spontaneous urticaria. However, these frequencies align with their incidence frequency within the population [50]. Future research could explore the bolt-ons in different geographical or cultural contexts to broaden the application of this study's results.

Conclusions

This study is the first to explore the use of EQ-5D-5L bolt-ons in CU and supports the findings of recent work on the skin irritation and self-confidence bolt-ons in AD. The study supports the relevance of the skin irritation and self-confidence bolt-ons in both samples. There is also preliminary support for the addition of the sleep bolt-on, however the evidence for the social relationships bolt-on is less clear. Further quantitative research on the impact of the bolt-ons to the valuation of health states and exploring the psychometric properties of the bolt-ons would be beneficial to this field to potentially further enhance the measurement performance of the instrument in AD and CU populations.

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Data availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate The study was performed in line with the principles of the Declaration of Helsinki and was reviewed and approved by the University of Portsmouth ethics review committee (reference: 23/ETHICS/002).

Consent for publication N/A.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Competing interests AKS, MG, AL and KG are employees of Acaster Lloyd Consulting. AL and FR are members of the EuroQol group (a non-profit organization responsible for the development of EQ-5D). Views expressed by the authors in the publication do not necessarily reflect the views of the EuroQol Foundation.

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References

- Herdman, M., Gudex, C., Lloyd, A., Janssen, M. F., Kind, P., Parkin, D., Bonsel, G., & Badia, X. (2011). Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research*, 20(10), 1727–1736. <https://doi.org/10.1007/s11136-011-9903-x>
- Whitehead, S. J., & Ali, S. (2010). Health outcomes in economic evaluation: The QALY and utilities. *British Medical Bulletin*, 96(1), 5–21. <https://doi.org/10.1093/bmb/ldq033>
- Barton, G. R., Bankart, J., Davis, A. C., & Summerfield, Q. A. (2004). Comparing Utility scores before and after hearing-aid provision. *Applied Health Economics and Health Policy*, 3(2), 103–105. <https://doi.org/10.2165/00148365-200403020-00006>
- Brazier, J. (2010). Is the EQ-5D fit for purpose in mental health? *British Journal of Psychiatry*, 197(5), 348–349. <https://doi.org/10.1192/bjp.bp.110.082453>
- Espallargues, M., Czoski-Murray, C. J., Bansback, N. J., Carlton, J., Lewis, G. M., Hughes, L. A., Brand, C. S., & Brazier, J. E. (2005). The Impact of Age-Related Macular Degeneration on Health Status Utility values. *Investigative Ophthalmology & Visual Science*, 46(11), 4016. <https://doi.org/10.1167/iovs.05-0072>
- Haywood, K. L., Garratt, A. M., Lall, R., Smith, J. F., & Lamb, S. E. (2008). EuroQol EQ-5D and condition-specific measures of health outcome in women with urinary incontinence: Reliability, validity and responsiveness. *Quality of Life Research*, 17(3), 475–483. <https://doi.org/10.1007/s11136-008-9311-z>
- Zhou, T., Guan, H., Wang, L., Zhang, Y., Rui, M., & Ma, A. (2021). Health-related quality of life in patients with different diseases measured with the EQ-5D-5L: A systematic review. *Frontiers in Public Health*, 9. <https://doi.org/10.3389/fpubh.2021.675523>
- Geraerds, A. J. L. M., Bonsel, G. J., Janssen, M. F., Finch, A. P., Polinder, S., & Haagsma, J. A. (2021). Methods used to identify, test, and assess impact on preferences of Bolt-Ons: A systematic review. *Value in Health*, 24(6), 901–916. <https://doi.org/10.1016/j.jval.2020.12.011>
- Institute for Quality and Efficiency in Health Care (IQWiG) (2022). General Methods - Version 6.1. www.iqwig.de
- Swinburn, P., Lloyd, A., Boye, K. S., Edson-Heredia, E., Bowman, L., & Janssen, B. (2013). Development of a Disease-Specific Version of the EQ-5D-5L for use in patients suffering from Psoriasis: Lessons learned from a feasibility study in the UK. *Value in Health*, 16(8), 1156–1162. <https://doi.org/10.1016/j.jval.2013.10.003>
- Pickard, A. S., Gooderham, M., Hartz, S., & Nicolay, C. (2017). EQ-5D health utilities: Exploring ways to improve upon responsiveness in psoriasis. *Journal of Medical Economics*, 20(1), 19–27. <https://doi.org/10.1080/13696998.2016.1219359>
- Rencz, F., Mukuria, C., Bató, A., Poór, A. K., & Finch, A. P. (2022). A qualitative investigation of the relevance of skin irritation and self-confidence bolt-ons and their conceptual overlap with the EQ-5D in patients with psoriasis. *Quality of Life Research*, 31(10), 3049–3060. <https://doi.org/10.1007/s11136-022-03141-y>
- Dewilde, S., Philips, G., Paci, S., Beauchamp, J., Chirolì, S., Quinn, C., Day, L., Larkin, M., Palace, J., Berrih-Aknin, S., Claeys, K. G., Muppidi, S., Mantegazza, R., Saccà, F., Meisel, A., Bassez, G., Murai, H., & Janssen, M. F. (2023). Patient-reported burden of myasthenia gravis: Baseline results of the international prospective, observational, longitudinal real-world digital study MyRealWorld-MG. *British Medical Journal Open*, 13(1), e066445. <https://doi.org/10.1136/bmjopen-2022-066445>
- Fotheringham, J., Guest, J., Latus, J., Lerma, E., Morin, I., Schaufler, T. Impact of Difelikefalin on the Health-Related Quality of Life of Haemodialysis Patients with Moderate-to-Severe Chronic Kidney Disease-Associated Pruritus: A Single-Arm Intervention Trial. Patient [Internet]. 2024 Mar 1 [cited 2024 Mar 28];17(2):203–13. <https://link.springer.com/article/https://doi.org/10.1007/s40271-023-00668-1>
- Szlávicz, E., Szabó, Á., Kinyó, Á., Szeiffert, A., Bancsók, T., Brodszky, V., Gyulai, R., & Rencz, F. (2023). Content validity of the EQ-5D-5L with skin irritation and self-confidence bolt-ons in patients with atopic dermatitis: A qualitative think-aloud study. *Quality of Life Research*. <https://doi.org/10.1007/s11136-023-03519-6>
- David Boothe, W., Tarbox, J. A., & Tarbox, M. B. (2017). Atopic Dermatitis: Pathophysiology. In pp. 21–37.
- Girolomoni, G., & Busà, V. M. (2022). Flare management in atopic dermatitis: From definition to treatment. *Therapeutic Advances in Chronic Disease*, 13, 204062232110667. <https://doi.org/10.1177/20406223211066728>
- Augustin, M., Misery, L., von Kobyletzki, L., Armario-Hita, J. C., Mealing, S., & Redding, M. (2022). Unveiling the true costs and societal impacts of moderate-to-severe atopic dermatitis in Europe. *Journal of the European Academy of Dermatology and Venereology*, 36(S7), 3–16. <https://doi.org/10.1111/jdv.18168>

19. Ban, G. Y., & Ye, Y. M. (2023). Real-world Disease Burden of Chronic Urticaria and Vaccine Hesitancy. *Allergy Asthma & Immunology Research*, 15(1), 1–3. <https://doi.org/10.4168/aa.2023.15.1.1>
20. Radonjic-Hoesli, S., Hofmeier, K. S., Micaletto, S., Schmid-Grendelmeier, P., Bircher, A., & Simon, D. (2018). Urticaria and Angioedema: An update on classification and Pathogenesis. *Clinical Reviews in Allergy & Immunology*, 54(1), 88–101. <https://doi.org/10.1007/s12016-017-8628-1>
21. Cappuccio, A., Limonta, T., Parodi, A., Cristaudo, A., Bugliaro, F., Cannavò, S., Rossi, O., Gurioli, C., Vignoli, A., Parente, R., Iemoli, E., Caldarola, G., Pità, O., Nuzzo, S., Cancian, M., Potenza, C., Caminati, M., Stingeni, L., Saraceno, R., & Marini, M. (2017). Living with chronic spontaneous urticaria in Italy: A Narrative Medicine Project to improve the pathway of Patient Care. *Acta Dermato Venereologica*, 97(1), 81–85. <https://doi.org/10.2340/00015555-2478>
22. Dias, G. A. C., Pires, G. V., Valle, S. O. R., do, Dortas, S. D., Levy, S., França, A. T., Baiardini, I., & Canonica, W. G. (2016). Impact of chronic urticaria on the quality of life of patients followed up at a university hospital. *Anais Brasileiros De Dermatologia*, 91(6), 754–759. <https://doi.org/10.1590/abd1806-4841.20165071>
23. Hashizume, H., & Takigawa, M. (2006). Anxiety in allergy and atopic dermatitis. *Current Opinion in Allergy & Clinical Immunology*, 6(5), 335–339. <https://doi.org/10.1097/01.all.0000244793.03239.40>
24. Kelsay, K., Klinnert, M., & Bender, B. (2010). Addressing Psychosocial aspects of atopic dermatitis. *Immunology and Allergy Clinics of North America*, 30(3), 385–396. <https://doi.org/10.1016/j.iac.2010.05.003>
25. Peters, E. M. J., Michenko, A., Kupfer, J., Kummer, W., Wiegand, S., Niemeier, V., Potekaev, N., Lvov, A., & Gieler, U. (2014). Mental stress in atopic dermatitis – neuronal plasticity and the Cholinergic System are affected in atopic dermatitis and in response to Acute Experimental Mental stress in a Randomized Controlled Pilot Study. *Plos One*, 9(12), e113552. <https://doi.org/10.1371/journal.pone.0113552>
26. Ameen, M., Meller, S., Pinter, A., Shear, N. H., & Soria, A. (2021). Perception and experience of Biologic Therapy in atopic dermatitis: A Qualitative Focus Group Study of Physicians and patients in Europe and Canada. *Dermatology and Therapy*, 11(6), 2159–2177. <https://doi.org/10.1007/s13555-021-00631-8>
27. Berrino, A. M., Voltolini, S., Fiaschi, D., Pellegrini, S., Bignardi, D., Minale, P., Troise, C., & Maura, E. (2006). Chronic urticaria: Importance of a medical-psychological approach. *European Annals of Allergy and Clinical Immunology*, 38(5), 149–152.
28. Marron, S. E., Cebrian-Rodriguez, J., Alcalde-Herrero, V. M., Garcia-Latasa de Aranibar, F. J., & Tomas-Aragones, L. (2020). Impacto Psicosocial en adultos con dermatitis atópica: Estudio cualitativo. *Actas Dermo-Sifiliográficas*, 111(6), 513–517. <https://doi.org/10.1016/j.ad.2019.03.018>
29. Pierce, E. J., Boytsov, N. N., Vasey, J. J., Sudaria, T. C., Liu, X., Lavelle, K. W., Bogdanov, A. N., & Goldblum, O. M. (2021). A qualitative analysis of Provider notes of atopic dermatitis-related visits using Natural Language Processing methods. *Dermatology and Therapy*, 11(4), 1305–1318. <https://doi.org/10.1007/s13555-021-00553-5>
30. Ring, J., Zink, A., Arents, B. W. M., Seitz, I. A., Mensing, U., Schielein, M. C., Wettemann, N., Carlo, G., & Fink-Wagner, A. (2019). Atopic eczema: Burden of disease and individual suffering – results from a large <scp>EU study in adults. *Journal of the European Academy of Dermatology and Venereology*, 33(7), 1331–1340. <https://doi.org/10.1111/jdv.15634>
31. Staubach, P., Eckhardt-Henn, A., Dechene, M., Vonend, A., Metz, M., Magerl, M., Breuer, P., & Maurer, M. (2006). Quality of life in patients with chronic urticaria is differentially impaired and determined by psychiatric comorbidity. *British Journal of Dermatology*, 154(2), 294–298. <https://doi.org/10.1111/j.1365-2133.2005.06976.x>
32. Silverberg, J. I., Garg, N. K., Paller, A. S., Fishbein, A. B., & Zee, P. C. (2015). Sleep disturbances in adults with Eczema Are Associated with impaired overall health: A US Population-based study. *Journal of Investigative Dermatology*, 135(1), 56–66. <https://doi.org/10.1038/jid.2014.325>
33. Zuberbier, T., Orlov, S. J., Paller, A. S., Taïeb, A., Allen, R., Hernandez-Hermosa, J. M., Ocampo-Candiani, J., Cox, M., Langeraar, J., & Simon, J. C. (2006). Patient perspectives on the management of atopic dermatitis. *Journal of Allergy and Clinical Immunology*, 118(1), 226–232. <https://doi.org/10.1016/j.jaci.2006.02.031>
34. Haagsma, J. (n.d.). *POPCORN: longitudinal effects of the COVID-19 pandemic on individual's health-related quality of life (EQ project 238-RA)*.
35. O'Brien, B. C., Harris, I. B., Beckman, T. J., Reed, D. A., & Cook, D. A. (2014). Standards for reporting qualitative research. *Academic Medicine*, 89(9), 1245–1251. <https://doi.org/10.1097/ACM.0000000000000388>
36. Guest, G., Bunce, A., & Johnson, L. (2006). How many interviews are enough? An experiment with data saturation and variability. *Field Methods*, 18(1), 59–82. <https://doi.org/10.1177/1525822X05279903>
37. Charman, C. R., Venn, A. J., Ravenscroft, J. C., & Williams, H. C. (2013). Translating patient-oriented Eczema measure (POEM) scores into clinical practice by suggesting severity strata derived using anchor-based methods. *British Journal of Dermatology*, 169(6), 1326–1332. <https://doi.org/10.1111/bjd.12590>
38. Charman, C. R., Venn, A. J., & Williams, H. C. (2004). The patient-oriented Eczema measure: Development and initial validation of a New Tool for measuring atopic Eczema Severity from the patients' perspective. *Archives of Dermatology*, 140(12). <https://doi.org/10.1001/archderm.140.12.1513>
39. Weller, K., Groffik, A., Church, M. K., Hawro, T., Krause, K., Metz, M., Martus, P., Casale, T. B., Staubach, P., & Maurer, M. (2014). Development and validation of the Urticaria Control Test: A patient-reported outcome instrument for assessing urticaria control. *Journal of Allergy and Clinical Immunology*, 133(5), 1365–1372. <https://doi.org/10.1016/j.jaci.2013.12.1076>
40. Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, 3(2), 77–101. <https://doi.org/10.1191/1478088706qp0630a>
41. VERBI Software (n.d.). MAXQDA 2022. Berlin: Maxqda. Com.; 2021..
42. Howells, L., Lancaster, N., McPhee, M., Bundy, C., Ingram, J. R., Leighton, P., Henaghan-Sykes, K., & Thomas, K. S. (2021). Thematic synthesis of the experiences of people with hidradenitis suppurativa: A systematic review*. *British Journal of Dermatology*, 185(5), 921–934. <https://doi.org/10.1111/bjd.20523>
43. Johnston, S. A., Krasuska, M., Millings, A., Lavda, A. C., & Thompson, A. R. (2018). Experiences of rosacea and its treatment: An interpretative phenomenological analysis. *British Journal of Dermatology*, 178(1), 154–160. <https://doi.org/10.1111/bjd.15780>
44. Meneguín, S., de Godoy, N. A., Pollo, C. F., Miot, H. A., & de Oliveira, C. (2020). Quality of life of patients living with psoriasis: A qualitative study. *BMC Dermatology*, 20(1), 22. <https://doi.org/10.1186/s12895-020-00116-9>
45. Finley, A. Y., & Khan, G. K. (1994). Dermatology Life Quality Index (DLQI)-a simple practical measure for routine clinical use. *Clinical and Experimental Dermatology*, 19(3), 210–216. <https://doi.org/10.1111/j.1365-2230.1994.tb01167.x>
46. Chren, M. M., Lasek, R. J., Quinn, L. M., Mostow, E. N., & Zyzanski, S. J. (1996). Skindex, a quality-of-life measure for patients with skin disease: Reliability, validity, and responsiveness.

- Journal of Investigative Dermatology*, 107(5), 707–713. <https://doi.org/10.1111/1523-1747.ep12365600>
47. Kaaz, K., Szepietowski, J., & Matusiak (2019). Influence of Itch and Pain on Sleep Quality in atopic dermatitis and psoriasis. *Acta Dermato Venereologica*, 99(2), 175–180. <https://doi.org/10.2340/00015555-3065>
48. Chang, Y. S., Chou, Y. T., Lee, J. H., Lee, P. L., Dai, Y. S., Sun, C., Lin, Y. T., Wang, L. C., Yu, H. H., Yang, Y. H., Chen, C. A., Wan, K. S., & Chiang, B. L. (2014). Atopic dermatitis, melatonin, and Sleep Disturbance. *Pediatrics*, 134(2), e397–e405. <https://doi.org/10.1542/peds.2014-0376>
49. Mendelson, M. H., Bernstein, J. A., Gabriel, S., Balp, M. M., Tian, H., Vietri, J., & Lebwohl, M. (2017). Patient-reported impact of chronic urticaria compared with psoriasis in the United States. *Journal of Dermatological Treatment*, 28(3), 229–236. <https://doi.org/10.1080/09546634.2016.1227421>
50. Kolkhir, P., Giménez-Arnau, A. M., Kulthanan, K., Peter, J., Metz, M., & Maurer, M. (2022). Urticaria. *Nature Reviews Disease Primers* 2022, 8:1(1), 1–22. <https://doi.org/10.1038/s41572-022-00389-z>. 8.

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