Hyperhidrosis Quality of Life Index (HidroQoL©): further validation and clinical application in patients with axillary hyperhidrosis using data from a phase III randomized controlled trial

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Summary

Background The Hyperhidrosis Quality of Life Index (HidroQoL©) is a validated patient-reported outcome measure capturing the quality of life of people affected by hyperhidrosis.

Objectives We aimed to extend the validity evidence to physician-confirmed diagnosis of primary axillary hyperhidrosis.

Methods Data from a phase III randomized placebo-controlled clinical trial were used (n = 171). Confirmatory factor analysis was carried out to confirm the a priori two-factor structure of the HidroQoL. Internal consistency was assessed using Cronbach's α. Intraclass correlation coefficients (ICCs) were calculated to evaluate test–retest reliability after days −7 to −4. Convergent validity was assessed using correlations with the Dermatology Life Quality Index (DLQI), the Hyperhidrosis Disease Severity Scale (HDSS) and gravimetric sweat production. Known groups were analysed to evaluate discriminative validity. Responsiveness after 29 days was assessed and minimal important difference (MID) values were calculated using both anchor- and distribution-based approaches. All analyses were carried out for total HidroQoL and its two domains.

Results The two-factor structure of the HidroQoL was confirmed. Internal consistency and test–retest reliability were strong (Cronbach's α 0·81–0·90; ICCs 0·89–0·93). Correlations with other outcome measures were in line with a priori hypotheses. The HidroQoL discriminated between different severity groups (P ≤ 0·001) and showed sensitivity to change towards improvement (P < 0·001). An MID value of 4 is proposed for the total scale.

Conclusions This study supports excellent measurement properties including clinical applicability of the HidroQoL in primary axillary hyperhidrosis and suggests a MID of 4 be applied to clinical trial data.

What is already known about this topic?

- Hyperhidrosis is characterized by excessive sweating that results in substantial daily life and psychosocial impairments for patients.
- The Hyperhidrosis Quality of Life Index (HidroQoL©) is a validated instrument for assessing hyperhidrosis-specific quality of life of people affected by the condition.

- The HidroQoL was developed and tested in a nonclinic population.

What does this study add?

- This study provides further evidence on the strong measurement properties of the HidroQoL based on a phase III trial in a population of patients with hyperhidrosis.
- It establishes optimal psychometric performance of the HidroQoL in patients with physician-confirmed primary axillary hyperhidrosis.
- It confirms the HidroQoL's ability to detect change based on an interventional study.
- It establishes a minimal important difference value of the HidroQoL, estimated at a value of 4.

What are the clinical implications of the work?

- The HidroQoL can be used to evaluate the effects of new treatments for axillary hyperhidrosis in clinical trials from the patients' perspective.
- The HidroQoL is ready to be used in clinical trials in primary axillary hyperhidrosis.

Hyperhidrosis is a disorder of the autonomic nervous system that is characterized by excessive sweating beyond physiological needs. It is classified as either primary, due to a sympathetic dysregulation leading to disproportionate sweating, or secondary, as a result of an underlying medical condition or the use of prescription medications.[1] Primary hyperhidrosis can be generalized or focal, whereby focal hyperhidrosis is typically symmetrically localized to the axillae (axillary hyperhidrosis), hands and feet (palmar and plantar hyperhidrosis), but may also involve other areas of the body, such as the face (craniofacial hyperhidrosis).[2,3] In the USA, a prevalence of 2·8% was reported, of which around half have axillary hyperhidrosis.[4] In another study in Germany, the prevalence was 16·3% including 6·1% of patients with frequent or continuous disturbing sweating.[5] It ranges in severity from being a little bit damp to extreme dripping. Therefore, hyperhidrosis can substantially impair the quality of life (QoL) of affected patients, such as limitations in daily activities, social relationships, study and work, life and emotional well-being.[1,6,7]

To measure QoL, patient-reported outcome measures (PROMs), which means self-completed questionnaires, are used in clinical trials to reflect the patient's perspective.[8] Several PROMs capturing the perspective of patients with hyperhidrosis have been identified in a review,[2] such as the Hyperhidrosis Quality of Life Questionnaire (HQLQ),[9] the Hyperhidrosis Impact Questionnaire (HHIQ),[10] the Hyperhidrosis Questionnaire (HQ)[11] and the Hyperhidrosis Quality of Life Index (HidroQoL©).[12,13] In this review, the HidroQoL was the preferred instrument by a small group of patients with moderate-to-severe hyperhidrosis as it covered everything important and was easy to complete.[2]

The HidroQoL assesses QoL impacts in hyperhidrosis. With 18 items on two domains, it is a short, but comprehensive measure. The first domain with six items refers to daily life activities and the second domain with 12 items covers the psychosocial life of the patients (Figure 1). Each item has three response options (no, not at all = 0; a little = 1; very much = 2), with a total score range from 0 to 36. The recall period is 7 days. It was developed recently by a group of researchers in the UK. Patients with self-reported hyperhidrosis (different types) were involved in the item elicitation.[7] In its initial validation, it showed evidence for excellent measurement properties (structural validity, internal consistency, test–retest reliability, construct validity and responsiveness) and its use in both routine clinical practice and in research for the assessment of QoL impacts in different types of self-reported hyperhidrosis. Furthermore, minimal important difference (MID) values for the total HidroQoL were established.[12,13]

The aims of this study were (i) to evaluate the psychometric properties of the HidroQoL in patients with physician-confirmed primary hyperhidrosis, thus extending the initial validity evidence generated by Kamudoni *et al.*;[13] and (ii) to examine the clinical application as well as establish the MID threshold of the HidroQoL in this population.
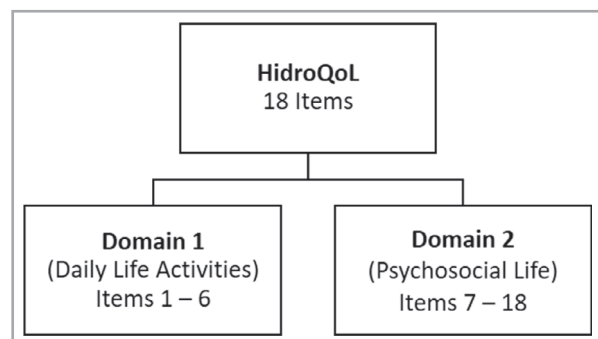

Figure 1 Composition of the Hyperhidrosis Quality of Life Index (HidroQoL).

Patients and Methods

Patients with severe primary axillary hyperhidrosis were asked to complete the HidroQoL four times during the phase III randomized placebo-controlled part of a clinical trial investigating the effects of a topical cream containing 1% glycopyrronium bromide. The safety and efficacy of this topical cream was reported recently.[14] The study was registered (ClinicalTrials.gov identifier: NCT03658616) and ethical approval was given by the corresponding ethics committees of the different countries.

A translation office produced seven linguistically validated versions of the HidroQoL. Cognitive debriefing interviews with a representative sample of the target population revealed that items were easily understood by the participants, which supported conceptual and linguistic equivalence as well as cultural appropriateness.

The phase III trial was multicentre (n = 34) and multicountry (Germany, Austria, Poland, Hungary, UK, Sweden and Denmark). Data were collected using the HidroQoL, the Hyperhidrosis Disease Severity Scale (HDSS) and the Dermatology Life Quality Index (DLQI). The HDSS is a scale for the assessment of disease severity and daily life impairment in patients with hyperhidrosis. It is a single item asking the patient to rate the severity of their hyperhidrosis on a four-point scale.[4,15] The DLQI consists of 10 questions concerning patients' perception of the impact of skin diseases on aspects of their QoL over the last week.[16] It is the most frequently used PROM in randomized controlled trials (RCTs) in dermatology. In addition, gravimetric sweat production was measured in milligrams for a duration of 5 min according to an internal standard operating procedure/manual and as already performed in the previous trial.[14] Data of the HidroQoL and the HDSS were collected at all four timepoints [days −7 to −4 (screening), day 1 (baseline), day 15 and day 29], DLQI data were collected from day 1 to day 29 and gravimetric sweat production was assessed at screening, baseline and day 29 (Figure 2). The study was sponsored by Dr. August Wolff GmbH & Co. KG Arzneimittel.

Data analysis

Psychometric analyses were performed to evaluate structural validity, internal consistency, test–retest reliability, construct validity, responsiveness (ability to detect change over time) and MID values. All statistical analyses were performed using SAS 9·4 and IBM SPSS Statistics 25·0.

Structural validity

A confirmatory factor analysis (CFA) was carried out at screening (days −7 to −4) to confirm the two-factor structure of the HidroQoL in the current study population. The following goodness-of-fit indices were used: comparative fit index ≥ 0·95, root mean square error of approximation < 0·08, standardized root mean square residual < 0·08 and Chi square/degrees of freedom ratio (χ^2/df) < 3 (see Table 1).[17–19]

Internal consistency

Cronbach's α was calculated for the HidroQoL total and the two domain scales. Cronbach's α ≥ 0·7 was considered to be appropriate.[19]

Test–retest reliability

Patients were classified as stable when they had no change in their HDSS score. Test–retest reliability was assessed twice, once before the intervention was started (from screening to baseline) and once when the intervention had started (from baseline to day 15). Intraclass correlation coefficients (ICCs) with 95% confidence intervals (CIs) were calculated. An ICC ≥ 0·7 was considered to be acceptable.[19]

Convergent and discriminant validity

We assumed that our PROM validly measures the construct to be measured, which is hyperhidrosis-specific QoL. This was evaluated by estimating the magnitude of correlations with the DLQI, HDSS and the gravimetric sweat production at baseline. We formulated a priori hypotheses and expected Spearman rank correlations with the DLQI ≥ 0·5 because both instruments measure a similar construct, namely health-related QoL. The HDSS measures severity, which is a related, but dissimilar construct to health-related QoL. We expected correlations of between 0·3 and 0·5. The gravimetric sweat
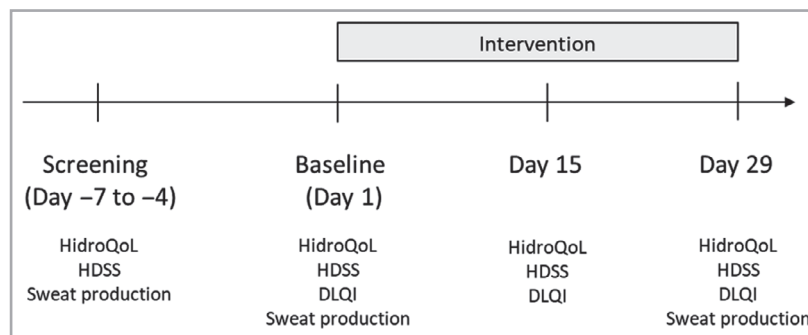

Figure 2 Data collection. DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale; HidroQoL, Hyperhidrosis Quality of Life Index.

Table 1 Goodness-of-fit indices for the HidroQoL (n = 169)

Goodness-of-fit index		Acceptable model fit	HidroQoL
CFI	Comparative fit index	≥ 0.95	0.815
RMSEA	Root mean square error of approximation	< 0.08	0.084 (90% CI 0.071–0.097)
SRMR	Standardized root mean square residual	< 0.08	0.074
χ^2/df	Chi squared/degrees of freedom ratio	< 3	2.179

CI, confidence interval; HidroQoL, Hyperhidrosis Quality of Life Index

production was classified as an objective measure and, therefore, an unrelated construct, and correlations were expected to be low (< 0.3).

Known-groups validity

We assessed whether there were differences in the HidroQoL scores between clinically or demographically distinct groups, i.e. sex, age categories and disease severity, at baseline. We did not expect any differences between male and female patients and between different age categories (18–29, 30–39, 40–49, 50–59, $\geq$ 60 years). However, we expected significant differences between different severity levels according to the HDSS. A Mann–Whitney U-test and Kruskal–Wallis one-way ANOVA were carried out.

Responsiveness

The HidroQoL's responsiveness was assessed using two alternative approaches, including (i) a comparison of scores across patients according to change in HDSS scores before and after the intervention; and (ii) a correlation of the HidroQoL scores against corresponding HDSS and DLQI change scores and change in the gravimetric sweat production.

Firstly, we compared HidroQoL scores before and after the intervention. The HDSS change score after day 29 served as an anchor. In order to see if the anchor could be considered appropriate, the HDSS change score was correlated with the HidroQoL change scores and a correlation > 0.3 was considered to be appropriate.[20] Afterwards, patients were grouped according to the anchor. A Kruskal–Wallis test over all HDSS change score groups was carried out and we expected those groups to significantly differ from each other in their HidroQoL scores. Furthermore, scores before and after the intervention were compared using nonparametric Wilcoxon matched-pair tests (because the data were not normally distributed). A significant improvement in QoL scores for the improving conditions (where HDSS improved) was expected. Finally, effect sizes were calculated to define the magnitude of those effects

(r = Z/$\sqrt{N}$; with r < 0.3: small, 0.3 < r < 0.5: moderate, r > 0.5: large effect).

Secondly, the HidroQoL change scores were compared with other outcome measurement instruments. The HidroQoL change scores were correlated with other outcome measure change scores (again HDSS, DLQI and gravimetric sweat production) using the Spearman rank correlation coefficient. The following a priori hypotheses were tested:

- Correlations with changes in instruments measuring similar constructs (DLQI) should be $\geq$ 0.5.
- Correlations with changes in instruments measuring related, but dissimilar constructs (HDSS) should be lower (between 0.5 and 0.3).
- Correlations with changes in instruments measuring unrelated constructs (gravimetric sweat production) should be < 0.3.

Estimation of minimal important difference

MID is the smallest difference in scores that patients perceive as beneficial.[21] It can be seen as a threshold and any change greater than this threshold can be interpreted to be clinically meaningful.[22] We used three approaches to define MID values: an anchor-based approach, a distribution-based approach and an integration of both.

Using the anchor-based approach, the HDSS and the DLQI served as anchors because their change scores had shown an acceptable correlation with the HidroQoL change scores (> 0.3). Using the HDSS as an anchor, patients were grouped according to their HDSS change scores. Because the DLQI is a multi-item tool, two different methods were used when defining what is minimally improved in order to group the patients according to the anchor. Firstly, an established banding was applied to the DLQI.[23] A one-category change towards improvement was considered to be slightly improved and patients were grouped according to their DLQI category change scores. Secondly, given MID values for the DLQI in patients with hyperhidrosis (2.2–5.0)[24] were used to form five different groups. For all approaches, the mean score change in the slightly improving group provided the MID estimate.[12,25] The mean change method is also one of the most commonly found in the literature.

The distribution-based approach is based on the statistical characteristics of the baseline sample. Two methods have been proven to provide valid MID values, the half SD[26] and the standard error of measurement [SEM = $\sigma_x\sqrt{(1-rel)}$], where σ_x = SD of the scale or subscale and *rel* = reliability of the scale or subscale (internal consistency).[27]

The integrated approach integrates the anchor-based and distribution-based methods using the upper bound of a one-tail 95% CI for the mean score change in the 'no change' group. The following formula was used: mean score change in the patient group that did not change + 1.645 × standard error (SE).[12,28] Patients were equally grouped as when using the classical anchor-based approach.

Results

Demographic characteristics of the study participants

The sample consisted of 171 patients with severe primary axillary hyperhidrosis. Eighty-seven (50·9%) patients were male and 84 (49·1%) were female. The patients had a mean ± SD age of 37·57 ± 12·09 and a median of 36 (range 18–65) years.

Distribution of response categories

The distribution of responses was assessed. The items showed a negative skew reflecting some ceiling effects. This was not surprising as only patients with severe primary axillary hyperhidrosis were included in the study. The highest response category was chosen by 26–91% of the patients.

Structural validity

Goodness-of-fit indices for the HidroQoL indicated an acceptable model fit as two indices were below the a priori stated cut-off values (Table 1). Regarding the first three indices, at least one criterion should be met for a sufficient structural validity rating,[19] which was fulfilled by the HidroQoL. Standardized factor loadings for the corresponding factors were high (> 0·3), except for item 1 where the SE was the highest (Table 2).

Internal consistency

We found a Cronbach's α of 0·90 for the HidroQoL total scale, 0·81 for the first domain (daily life activities) and a

Cronbach's α of 0·87 for the second domain (psychosocial life) (n = 169). The findings were consistent with those of Kamudoni *et al.*[13]

Test–retest reliability

The ICCs from screening to baseline without any intervention were strong and almost identical with the findings of Kamudoni *et al.*[13] (Table 3). From screening to baseline, 95 patients were stable in their HDSS; from baseline to day 15, 144 patients were stable. From baseline to day 15, ICCs were lower because the intervention had started and the time interval was longer, although patients reported no change in their HDSS score (Figure 3).

Convergent and discriminant validity

All correlations between HidroQoL scores and other subjective/objective measures were in line with our hypotheses (Table 4).

Known-groups validity

We were able to confirm all our expectations. There were no significant differences in the HidroQoL total and the two domain scores between sexes (P ≥ 0·216) and different age categories (P ≥ 0·485). However, differences between different severity groups (HDSS = 2, 3, 4) were significant for the total and the two domain scores (n = 169, P < 0·001). This is in line with the findings of Kamudoni *et al.*[13] The HidroQoL is capable of distinguishing between patients experiencing different levels of self-reported disease severity (based on the HDSS scores).

Responsiveness

Using the first approach, the HidroQoL total change score had a correlation of 0·53, domain 1 (daily life activities) had a correlation of 0·56, and domain 2 (psychosocial life) had a correlation of 0·48 with the HDSS change score (n = 162). The anchor was therefore considered as appropriate and patients were grouped according to their HDSS change scores. The Kruskal–Wallis tests disclosed that patients with different HDSS change scores differed significantly in their HidroQoL scores (n = 162; P < 0·001). There was a significant difference (P < 0·001) in the HidroQoL total change and the two domain change scores in those reporting a change (HDSS change score ≤ −1) vs. those reporting no change (HDSS change score = 0). Single Wilcoxon U-tests were calculated for the 'no change' group (HDSS change score = 0), the 'slightly better' group (HDSS change score = −1) and the 'somewhat better' group (HDSS change score = −2). For the 'slightly worse' group (HDSS change score = 1) and the 'a good deal better' group (HDSS change score = −3) only descriptive statistics are presented because the sample size was small (Table 5). Even patients experiencing no change according to

Table 2 Standardized factor loadings and standard errors (SE)

	Factor 1		Factor 2	
	Estimate	SE	Estimate	SE
Item 1	0·1668	0·0831	–	–
Item 2	0·6923	0·0512	–	–
Item 3	0·7609	0·0455	–	–
Item 4	0·4556	0·0699	–	–
Item 5	0·5300	0·0646	–	–
Item 6	0·6599	0·0540	–	–
Item 7	–	–	0·4851	0·0652
Item 8	–	–	0·5296	0·0618
Item 9	–	–	0·5449	0·0606
Item 10	–	–	0·5351	0·0614
Item 11	–	–	0·3692	0·0726
Item 12	–	–	0·5617	0·0592
Item 13	–	–	0·5851	0·0572
Item 14	–	–	0·4378	0·0685
Item 15	–	–	0·6303	0·0532
Item 16	–	–	0·5642	0·0590
Item 17	–	–	0·6371	0·0525
Item 18	–	–	0·7060	0·0459

Table 3 Intraclass correlation coefficients for the Hyperhidrosis Quality of Life Index total and the two domain scores before and with intervention

	Intraclass correlation coefficient (95% CIs)		
	Before intervention: from screening to baseline (days −7 to −4)	With intervention: from baseline to day 15 (14 days)	Kamudoni *et al.*[13]
Total score	**0·93** (0·897–0·954)	0·61 (0·280–0·771)	0·93 (0·89–0·95)
Domain 1	**0·89** (0·841–0·929)	0·53 (0·173–0·710)	0·88 (0·83–0·92)
Domain 2	**0·92** (0·879–0·947)	0·66 (0·383–0·800)	0·91 (0·87–0·94)

CI, confidence interval. **bold** indicates values are sufficient (P > 0·7), not significant
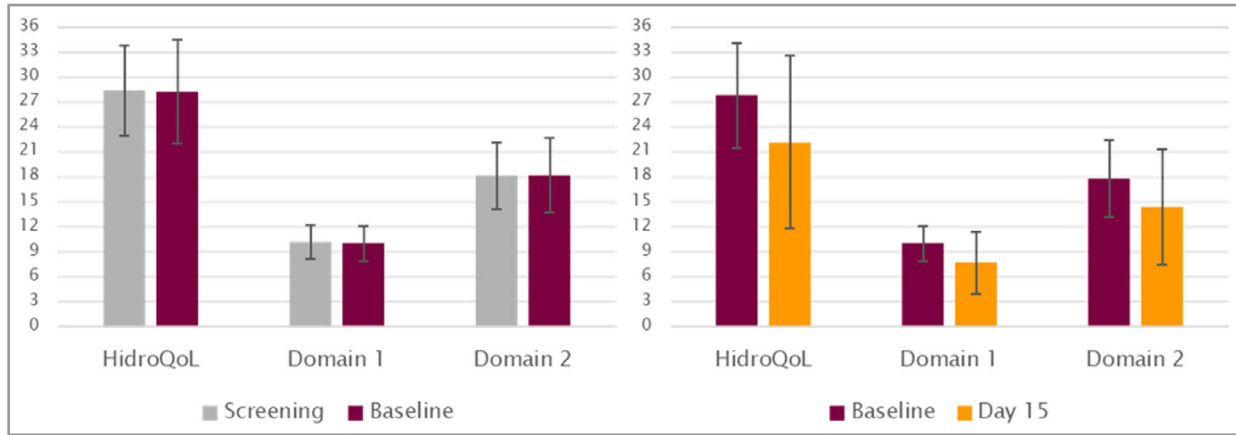

Figure 3 Hyperhidrosis Quality of Life Index (HidroQoL) mean scores for stable patients from screening to baseline (n = 95, left diagram) and from baseline to day 15 (n = 144, right diagram).

Table 4 Correlations of the HidroQoL total and the two domain scores with the HDSS, DLQI and the gravimetric sweat production (GSP)

	HidroQoL total	Domain 1	Domain 2	HDSS	DLQI	GSP
HidroQoL total	1	0·81	0·97	**0·45**	**0·69**	**0·08**
Domain 1		1	0·67	**0·47**	**0·62**	**0·07**
Domain 2			1	**0·40**	**0·65**	**0·09**
HDSS				1	0·35	0·15
DLQI					1	0·07
GSP						1
	n = 170	n = 170	n = 170	n = 169	n = 170	n = 166

bold indicates hypotheses confirmed. DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale; HidroQoL, Hyperhidrosis Quality of Life Index.

their HDSS, significantly improved in their HidroQoL scores after day 29. Effect sizes were moderate to high.

Using the second approach, correlations with other outcome measure change scores were mostly in line with our hypotheses (Table 6).

Estimation of minimal important difference values

Using different approaches, several MID values were calculated and are presented in Table 7. Kamudoni[12] proposed a MID of 3 for the HidroQoL total score. We found MID values for the total score from 1·9 to 6·8 and tend to suggest a

MID of 4 which is 1 point above the MID proposed by Kamudoni.[12]

Discussion

All results were consistent with the initial validation of Kamudoni *et al.*[12,13] and confirmed the psychometric properties of the HidroQoL.

We could confirm the two-factor structure of the HidroQoL with an acceptable model fit. The scale and the two subscales showed strong internal consistency, and test–retest reliability between screening and baseline was excellent. The results

Table 5 HidroQoL responsiveness using HDSS change scores[a]

Anchor				Change scores				
HDSS cs	Patient group	n	Scale	Mean baseline ± SD	Mean day 29 ± SD	Z	P-value[b]	ES
0	No change	90	HidroQoL total	27·71 ± 5·95	24·79 ± 8·78	−5·035	< 0·001	−0·531
			Domain 1	9·978 ± 2·08	8·75 ± 3·27	−4·742	< 0·001	−0·500
			Domain 2	17·73 ± 4·34	16·04 ± 5·93	−4·221	< 0·001	−0·445
−1	Slightly better	38	HidroQoL total	27·47 ± 6·06	20·68 ± 8·07	−5·059	< 0·001	−0·821
			Domain 1	10·05 ± 1·93	7·11 ± 2·82	−5·101	< 0·001	−0·828
			Domain 2	17·42 ± 4·48	13·58 ± 5·58	−4·522	< 0·001	−0·734
−2	Somewhat better	23	HidroQoL total	28·30 ± 7·65	10·91 ± 9·20	−4·107	< 0·001	−0·856
			Domain 1	10·30 ± 2·62	3·57 ± 2·83	−4·113	< 0·001	−0·858
			Domain 2	18·04 ± 5·58	7·39 ± 6·63	−4·019	< 0·001	−0·838

cs, change score; ES, effect size; HDSS, Hyperhidrosis Disease Severity Scale; HidroQoL, Hyperhidrosis Quality of Life Index. [a]n < 10 for the patient groups 'slightly worse' (HDSS change score = 1) and 'a good deal better' (HDSS change score = −3); [b]Wilcoxon matched-pair test.

Table 6 Correlations of the Hyperhidrosis Quality of Life Index (HidroQoL) total change score and the two domains with the HDSS change score, DLQI change score and change in the gravimetric sweat production (GSP)

	HidroQoL total cs	Domain 1 cs	Domain 2 cs	HDSS cs	DLQI cs	Change in GSP
HidroQoL total cs	1	0·88	0·95	**0·53**	**0·55**	**0·18**
Domain 1 cs		1	0·72	**0·56**	**0·52**	**0·11**
Domain 2 cs			1	**0·48**	**0·53**	**0·22**
HDSS cs				1	0·37	0·11
DLQI cs					1	0·21
Change in GSP						1
	n = 163	n = 163	n = 163	n = 162	n = 163	n = 152

bold indicates hypotheses (almost) confirmed. cs, change score; DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale.

Table 7 Minimal important difference (MID) values using different approaches

	Anchor-based approach			Distribution-based approach		Integrated approach		
	HDSS	DLQI[a]	DLQI[b]	½ SD	SEM baseline	HDSS	DLQI[a]	DLQI[b]
HidroQoL total	6·8	4·5	3·4	3·09	1·93	3·79	3·43	3·79
Domain 1	2·9	1·9	1·5	1·05	0·91	1·57	1·57	1·64
Domain 2	3·8	2·6	1·9	2·27	1·65	2·29	1·96	2·25

DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale; HidroQoL, Hyperhidrosis Quality of Life Index; SEM, standard error of measurement. [a]category change, [b]MID change.

regarding construct validity were in line with all our hypotheses. We showed that the HidroQoL is capable of discriminating between patients experiencing different levels of change, and single Wilcoxon U-tests demonstrated that all patients whose HDSS score improved had significantly better HidroQoL scores at day 29. Even when the patients did not report any change in their HDSS score, HidroQoL scores significantly improved. This shows that the HidroQoL is a more sensitive tool towards change than the HDSS and allows us to assess responsiveness to improvement. In order to interpret change scores and to make them useful for routine clinical practice, we calculated cut-off scores, namely MID values. Using different approaches and two anchors (HDSS and DLQI), several MID values were found.

We synthesized our findings and agreed on a MID value of 4 for the HidroQoL total score (Kamudoni[12] proposed a MID value of 3 for the HidroQoL). This can be justified by the fact that this validation study used data from an RCT with physician-diagnosed primary axillary hyperhidrosis with a more homogeneous sample than the sample used by Kamudoni et al.,[12,13] who included patients with self-reported hyperhidrosis, encompassing patients with different manifestations of their hyperhidrosis (not just axillary hyperhidrosis, but also palmoplantar and generalized hyperhidrosis). For these reasons, it is not surprising that a 'higher' change score of 4 compared with the proposed 3 is needed to be perceived as beneficial by the patients.

Regarding PROMs in hyperhidrosis, recent advances included the development of the Axillary Sweating Daily Diary[29] or the Hyperhidrosis Disease Severity Measure-Axillary.[30] Those two instruments were developed and validated to assess axillary sweating severity. Health-related QoL is a different, more complex construct than severity and, therefore, a multi-item, multidomain PROM is needed. For this reason, the HidroQoL is a true QoL instrument and its use is following the most appropriate scientific approach.

A strength of this study is the clinical confirmation of the patient's diagnosis. Because the study was conducted in the context of an RCT that was compliant with good clinical practice guidelines, almost all patients from baseline completed the consecutive follow-up assessments. The sample size of 171 patients was adequate. A larger sample size (> 300) would have allowed for the application of item response (modern test) theory approaches to provide additional evidence for validity as Kamudoni et al.[13] have carried out. Furthermore, SAS codes were quality-controlled to reduce susceptibility to errors. As a limitation of this study, the use of the HDSS and the DLQI as anchors can be mentioned. The HDSS for example is a single item combining two concepts in one question. Even the DLQI has several serious issues, e.g. double-barrelled and redundant items and evidence for insufficient measurement properties.[31,32] In this study, data were collected across multiple countries using different language versions of the Hidro-QoL. Validating a PROM across different countries is challenging as cultural differences might bias the data. However, prior to use in this study, the original HidroQoL developed in English (UK) was linguistically validated to support different language versions. The results of the cognitive interviews in the context of the linguistic validation also provide a bridge from the original content validation in hyperhidrosis in general to axillary hyperhidrosis. Another limitation is the fact that only patients with moderate-to-severe hyperhidrosis with a HDSS of 3 or 4 were included in the study population. Patients with mild hyperhidrosis were not represented in the sample.

Data from an ongoing phase IIIb study will be used to extend the evidence presented by further psychometric analyses.

In conclusion, this study showed good measurement properties of the HidroQoL in terms of validity reliability and responsiveness to change. Findings from our analyses are consistent with the validity evidence generated in the original development and validation of the HidroQoL. It can be used in RCTs for the assessment of QoL impacts in primary axillary hyperhidrosis.

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