Evaluation of Patient-relevant Outcomes of Lymphedema and Lipedema Treatment: Development and Validation of a New Benefit Tool

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WHAT THIS PAPER ADDS
In this study, the first instrument on patient-relevant benefit in the treatment of lymphedema and lipedema is developed. The instrument can be used in both clinical practice and clinical studies to determine patient needs and treatment outcomes.

Objectives: Patient-relevant treatment benefit is traditionally measured with health-related quality of life (HRQoL) instruments. The Patient Benefit Index (PBI) methodology allows for a more direct measurement, with the patients rating both importance and achievement of treatment goals. Here, we developed and validated a PBI version specific for the assessment of benefit in lymphedema and lipedema treatment (PBI-L).
Methods: The development included five steps: (1) open item collection; (2) consensus of items in a multidisciplinary expert panel; (3) application of the German PBI-L in a cross-sectional study ($n = 301$); (4) translation into English; (5) application of the English PBI-L in a randomized clinical trial ($n = 82$). Subscales were developed using factor analysis. Construct validity was analyzed by correlating PBI-L and convergent criteria such as HRQoL and quality of care. To test for responsiveness, the association to change in HRQoL measures was computed.
Results: Floor and ceiling effects were low. There were few missing values. Two well-interpretable subscales were found with Cronbach's alpha >0.8 each. Global and subscale scores correlated with convergent criteria and with change in disease-specific HRQoL, but not with change in generic HRQoL.
Conclusions: The PBI-L is an internally consistent, valid, and responsive instrument for the assessment of patient-relevant benefit of edema treatment.
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INTRODUCTION

Lymphedema and lipedema are chronic conditions that lead to a progressive enlargement of the affected part of the body which is, in most cases, the extremities. There is high uncertainty regarding edema prevalence. Földi[1] estimates that there are as many as 4.5 million people with lymphedema in Germany, corresponding to a prevalence of about 5.5%. Prevalence in the UK was estimated to be much lower at 0.13% of the general population.[2] Up to 42% of patients with breast carcinoma are estimated to develop a secondary lymphedema.[3] Estimations of lipedema prevalence range from 0.06% to 10.00%.[4]

Edema management primarily includes manual lymph drainage, compression therapy, skin care, and physical exercise.[5] Patient-relevant benefit of edema treatment is usually measured using health-related quality of life (HRQoL) instruments:[6] patient benefit is assumed if HRQoL improves in the course of therapy.

In HRQoL questionnaires, benefit is usually evaluated indirectly by computing a pre—post score difference. This makes it susceptible for response shift effects, that is, a biased assessment of treatment effect due to mere changes in the patients' response behavior.[7] In particular, a so-called recalibration response shift[7] can occur with the patients interpreting the response scale differently at two points in time. For example, the same intensity of pain may be rated as "severe" before therapy and as "slight" after therapy. As a consequence, the two assessments may be based on a different metric and may therefore not be comparable anymore. Computing pre—post scores can be misleading in these cases.

The Patient Benefit Index (PBI) methodology allows for a more direct measurement of patient-relevant treatment

benefit.[8] In the first part—the Patient Needs Questionnaire (PNQ)—patients rate the importance of a list of patient-relevant treatment goals on a five-step scale from "not at all" to "very". In the second part—the Patient Benefit Questionnaire (PBQ)—patients rate to what extent the treatment goals have been achieved on the same five-step scale. Alternatively, they can choose "does not apply to me" for each treatment goal in both questionnaires. Thus, the patient directly evaluates treatment benefit instead of rating her/his current HRQoL before and after treatment. A PBI weighted global score ranging from 0 (no benefit) to 4 (maximum benefit) is computed for each patient. The weighting algorithm[8] ensures that the achievement of important treatment goals will have higher impact on the global score than the achievement of less important goals. Disease-specific PBI versions have been developed and validated for a range of different indications, including allergic rhinitis,[9] chronic pruritus,[10] and chronic wounds.[11]

The aim of this study was to develop and validate a PBI version specific for the assessment of patient-relevant benefit in lymphedema and lipedema treatment ("PBI-L").

PATIENTS AND METHODS

The PBI-L was developed and validated following the German guidance on assessing patient reported-outcomes in dermatology[12] and international standards[13,14] in a five-step procedure: (1) open item collection; (2) expert panel and development of the German PBI-L; (3) application of the German PBI-L in a cross-sectional study; (4) translation of the PBI-L into English; (5) application of the English PBI-L in a longitudinal study.

Item collection

Data on patient-relevant treatment goals were collected in an open survey. Patients with lipedema or lymphedema were recruited in four medical practices and two physiotherapy practices, which were members of the "Lymphnetz Hamburg", a network of specialized lymph care providers. Patients were asked to describe their treatment goals and their impairments due to edema in their own words.

German version

The German questionnaire was developed by an expert panel of lymphologists, dermatologists, lymph therapists, representatives of medical stores specialized on edema care, statisticians, experts on HRQoL assessment, and three edema patients. The panel categorized and condensed the patient-relevant topics collected in the open survey. The PBI-L was created by integrating these treatment goals into the standard PBI format.

Cross-sectional study

The PBI-L was implemented in the cross-sectional "LymphEdema Outcomes Study" (LEOS), a survey on the quality of care for edema in Hamburg, Germany. Patients with a medically diagnosed lipedema or lymphedema of any origin affecting the upper or lower limb and persisting for at least 3 months were included. They were recruited via announcements in the local newspapers and by lymph care providers.

The patients were interviewed by MD students in advanced medical education who had been trained by members of "Lymphnetz Hamburg". The PBI-L was included in a patient questionnaire along with the following parameters.

Generic HRQoL. Generic HRQoL was measured with the EQ-5D-3L.[15] A weighted global score ranging from 0 (= lowest HRQoL) to 100 (= highest HRQoL) was computed according to Schulenburg et al.[16] Additionally, a global assessment of generic HRQoL in the preceding week was made by the patients on a visual-numeric analogue scale ranging from 0 (= very bad) to 10 (= very good).

Disease-specific HRQoL. Disease-specific HRQoL was measured with the FLQA-LK, which is a short version of the FLQA-L (Freiburg Life Quality Assessment in Lymphedema).[17] The FLQA-LK global score ranges from 0 (= best HRQoL) to 5 (= worst HRQoL).

Disease-specific health state. A global assessment on disease-specific health state regarding the lymph condition was given by the patients on a visual—numeric analogue scale ranging from 0 (= very bad) to 10 (= very good).

Generic health state. General health state was assessed with the visual analogue scale EQ VAS,[15] ranging from 0 (= worst) to 100 (= best health state).

Quality of care. The quality of care from the patients' point of view was assessed with two items: "How do you rate the treatment of your lymphedema so far?" (quality of care) and "How satisfied are you with health care regarding your condition?" (satisfaction with care). Patients answered on a five-step scale ranging from 0 (= very bad/very unsatisfied) to 4 (= very good/very satisfied).

Clinical severity. Clinical severity (edema stage) was rated based on a clinical assessment with 0 indicating currently no edema symptoms and 3 indicating the worst possible stage, according to the classification of the International Society of Lymphology.[18]

LEOS study results on other topics than the PBI-L have been, or will be, published elsewhere.[19,20]

Translation

The PBI-L was translated into English independently by two professional translators who were English native speakers. The resulting English versions were each back-translated into German independently by two professional translators who were German native speakers. In a conference with the translators into English and one of the questionnaire developers, each item was discussed using all four

Table 1. Mean, SD, number of missing values, and factor loadings of Patient Needs Questionnaire (PNQ) items (cross-sectional study, $n = 301$).

PNQ items (importance of treatment goals)	n	Missing values (% of 299 patients who filled in the PNQ)	"Does not apply to me" (% of 299 patients who filled in the PNQ)	Mean[a]	SD[a]	Factor loading factor 1[b]	Factor loading, factor 2[b]
1. To be free of pain	297	0.7	19.4	3.7	0.7	(−.10)	.55
2. To experience less swelling and tension	297	0.7	2.3	3.8	0.5	(.15)	.21
3. To have no dry or sore skin	294	1.7	29.8	3.4	1.0	(.03)	.51
4. To experience no skin discomfort	292	2.4	18.1	3.4	0.9	(.17)	.45
5. To cope better with heat	294	1.7	16.4	3.2	1.1	.32	(.14)
6 To be less restricted in your ability to move around	295	1.4	14.0	3.6	0.8	(.05)	.72
7. To be able to stand or sit for longer periods	295	1.4	17.4	3.5	0.9	(.05)	.64
8. To avoid complications	288	3.8	11.4	3.7	0.7	(−.10)	.69
9. To have no fear that the disease will become worse	293	2.1	6.7	3.6	0.9	(.27)	.40
10. To be more productive in everyday life	296	1.0	10.7	3.5	0.9	(.09)	.73
11. To be able to exercise unhindered	294	1.7	13.7	3.3	1.0	.26	(.23)
12. To be less limited in your choice of clothing	295	1.4	15.7	3.3	1.1	.56	(−.07)
13. To receive optimal hosiery (e.g., color, fit, prescription quantity)	295	1.4	8.4	3.7	0.7	.24	(.02)
14. To gain more self-assurance and self-esteem	294	1.7	23.4	3.0	1.3	.77	(.03)
15. To feel more attractive	294	1.7	17.4	3.1	1.2	.84	(−.16)
16. To be able to better accept the condition	294	1.7	16.4	3.0	1.2	.76	(−.04)
17. To improve your emotional sense of wellbeing	292	2.4	20.1	3.0	1.3	.67	(.09)
18. To be able to have more contact with other people	295	1.4	39.5	2.3	1.5	.57	(.10)
19. To be asked less often about lymphedema	293	2.1	32.4	2.1	1.5	.63	(−.01)
20. To need less time for treatment	291	2.8	13.0	2.7	1.4	.63	(−.04)
21. To have fewer out-of-pocket treatment expenses	293	2.1	12.7	2.9	1.3	.52	(−.02)
22. To find a clear diagnosis and therapy	295	1.4	11.0	3.6	1.0	.43	(.09)
23. To get prescriptions for treatments more easily	294	1.7	14.0	3.2	1.3	.34	(.13)

[a] Scale: 0 = "not at all" to 4 = "very"; "does not apply to me" was also coded as 0 for computation of mean and SD.
[b] Factor loadings in brackets indicate that the item was not assigned the respective subscale.

versions (two translations and two back translations) and the original version; a consensus on the final translation was reached.

Longitudinal study

The English PBI-L was implemented in a randomized clinical trial on patients in the UK and USA suffering from primary or secondary lymphedema located in arms or legs. Both groups were subdivided into four groups receiving different sorts of compression therapy and additional manual lymphatic drainage and skin care. The English versions of PBI-L, FLQA-LK (on edema-specific HRQoL), and EQ-5D-3L (on generic HRQoL) were assessed at treatment onset and 19 days later. The clinical results of the study[21] were not an objective of this investigation.

Validation procedures

The terminology used in this article to describe validation procedures is in conformity with the COSMIN checklist for studies evaluating measurement properties of health-related patient-reported outcomes (www.cosmin.nl).[22]

The following analyses were performed to evaluate the PBI-L in the cross-sectional study.

To determine subscales of the PBI-L (and thereby structural validity) an explorative principal axes factor analysis with oblique rotation on the needs items (PNQ) was performed. For this analysis, the response "does not apply to me" was coded as 0. Thereby, it was put on a level with the response "not at all" important because both answers imply that the respective goal was not relevant for the patient. Only factors with an eigenvalue of 1 or higher (i.e., those that explained more than the variance of a single item) were extracted. Afterwards, all items were assigned to the factor they loaded highest on, thereby grouping the items to subscales. The respective subscale values for each patient were computed by applying the weighting algorithm described above, that is, weighting the benefits within the respective domain by their importance to the individual patient.

To determine internal consistency within the different subscales, Cronbach's alpha was computed for the respective PNQ items of each subscale. The response "does not apply to me" was, again, coded as 0.

The strict focus of item development on the results of the open item collection and the participation of edema patients in the expert panel should ensure that the items were relevant for the population of edema patients (content validity). As an indicator of irrelevant item content, the percentage of patients choosing "does not apply to me" in the PNQ was computed for all items. Additionally, the amount of missing values was computed, because many missing observations were assumed to indicate that an item was incomprehensible or irrelevant for the patients.

To test for construct validity, we made hypotheses about the associations of PBI-L global and subscale scores with different convergent criteria such as HRQoL and current health state in advance. These hypotheses are described in detail in the "Results" section.

To test for responsiveness, we hypothesized associations of the PBI-L with change in HRQoL in the longitudinal study in advance (see "Results" section) and tested them by correlating post-treatment values of PBI-L and HRQoL measures, controlling for baseline HRQoL values (partial correlations).

RESULTS

Item collection and pilot version

Of the 120 item collection questionnaires distributed to patients, 65 (54.2%) were filled in and returned. Of these patients, 72.3% had leg edema, 15.4% arm edema, and 12.3% both leg and arm edema; 10.8% had primary edema, 30.8% secondary edema, and 40.0% had lipedema or lipolymphedema (18.5% missing). Based on the impairments and treatment goals described by these patients, 23 non-redundant items on patient-relevant treatment goals could be formulated by the expert panel (Table 1).

Patients

Thirty-three centres recruited patients for the cross-sectional LEOS study, including 15 physiotherapists, seven general practitioners, four hospitals, three medical supply stores, three lymphologists, and one dermatologist. 348 patients were interviewed, of whom 301 also returned the patient questionnaire; the analyses reported in this article are based on these 301 patients.

Of these 301 patients, 91.7% ($n = 276$) were women. Mean age was 57.4 ± 14.3 years (range, 24—89 years). In 19.6% ($n = 59$), the edema was located in the arm(s), in 63.5% ($n = 191$) in the leg(s), and 16.9% ($n = 51$) had combined leg and arm edema. 21.9% ($n = 66$) had primary lymphedema, 43.5% ($n = 131$) secondary lymphedema, and 1.0% ($n = 3$) had both; 33.6% ($n = 101$) had lipedema or lipolymphedema.

Eighty-two patients were included in the longitudinal study; 93.9% ($n = 77$) were women. 48.8% ($n = 40$) had leg edema and 51.2% ($n = 42$) had arm edema. Average age was 60.2 ± 13.9 years (range, 24—87 years). The four treatment groups comprised between 18 and 22 patients.

Structural validity

In the explorative factor analysis, 265 patients without missing values in the PNQ were included. Six factors with an eigenvalue >1 were found, explaining 61.6% of overall variance. A subsequent factor analysis was conducted restricting the number of factors to two for two reasons: (1) the scree plot suggested that only two factors represented more than measurement error because a bend was visible between factor 2 and 3; (2) after rotation, only two of the factors remained with an eigenvalue >1. These two factors explained 35.4% of overall variance.

The first subscale was interpreted as "normal everyday-life and psychological wellbeing" and comprised 14 items (Table 1). The second subscale comprised the remaining nine items and was interpreted as "physical wellbeing and capability".

Distribution of PBI-L scores

The treatment goal rated most important by the patients in the cross-sectional study was "to experience less swelling and tension" (mean: 3.8 on the scale of 0—4; Table 1). The goal rated least important was "to be asked less often about lymphedema" (mean: 2.1). Less swelling and tension was also the goal rated as best achieved by the patients for whom it was applicable (mean benefit of 2.8; Table 2). The lowest treatment benefit was achieved regarding the goals "less time for treatment" and "fewer out-of-pocket treatment expenses", with an average value of 1.0 each.

One patient (0.4%, in $n = 285$) had the lowest possible PBI-L score of 0.0; 15 patients (5.3%) had the highest

Table 2. Mean, SD, and number of missing values in Patient Benefit Questionnaire (PBQ) items (cross-sectional study, n = 301).

PBQ items (achievement of treatment goals)	n	Missing values (% of 289 patients who filled in the PBQ)	Mean[a] (of patients who did not tick "does not apply")	SD[a] (of patients who did not tick "does not apply")
1. To be free of pain	285	1.4	2.5	1.1
2. To experience less swelling and tension	287	0.7	2.8	1.1
3. To have no dry or sore skin	284	1.7	2.1	1.4
4. To experience no skin discomfort	283	2.1	2.3	1.2
5. To cope better with heat	285	1.4	1.6	1.4
6. To be less restricted in my ability to move around	285	1.4	2.4	1.3
7. To be able to stand or sit for longer periods	285	1.4	2.2	1.3
8. To avoid complications	283	2.1	2.7	1.3
9. To have no fear that the disease will become worse	284	1.7	2.2	1.4
10. To be more productive in everyday life	288	0.3	2.1	1.3
11. To be able to exercise unhindered	287	0.7	1.9	1.4
12. To be less limited in my choice of clothing	286	1.0	1.5	1.5
13. To receive optimal hosiery (e.g., color, fit, prescription quantity)	284	1.7	2.6	1.4
14. To gain more self-assurance and self-esteem	284	1.7	1.9	1.4
15. To feel more attractive	286	1.0	1.7	1.4
16. To be able to better accept the condition	283	2.1	2.2	1.4
17. To improve your emotional sense of wellbeing	286	1.0	1.9	1.4
18. To be able to have more contact with other people	287	0.7	1.3	1.3
19. To be asked less often about lymphedema	285	1.4	1.2	1.4
20. To need less time for treatment	283	2.1	1.0	1.3
21. To have fewer out-of-pocket treatment expenses	284	1.7	1.0	1.5
22. To find a clear diagnosis and therapy	285	1.4	2.4	1.5
23. To get prescriptions for treatments more easily	287	0.7	2.1	1.6

[a] Scale: 0 = "not at all" to 4 = "very"; "does not apply to me" was *not* coded as 0 here.

possible score of 4.0. The average PBI-L global score was 2.2 ± 1.0 (median 2.1).

The mean score of subscale 1 (normal everyday-life and psychological wellbeing) was 1.8 ± 1.1 (median 1.6). Two patients (0.7%, n = 281) had the lowest possible score; ten patients (3.6%) had the highest possible score. The mean score of subscale two (physical wellbeing and capability) was 2.2 ± 1.0 (median 2.2), indicating a higher treatment benefit in this area as compared with subscale one. Two patients (0.7%, n = 284) had the lowest possible score; 17 patients (6.0%) had the highest possible score.

Internal consistency

Cronbach's alpha for the PNQ items of subscale 1 was 0.87 (n = 281). Corrected item–scale correlations ranged

between 0.24 ("to receive optimal hosiery") and 0.71 ("to gain more self-assurance and self-esteem").

Cronbach's alpha for the PNQ items of subscale two was 0.82 (n = 276). Corrected item-scale-correlations ranged between 0.29 ("to experience less swelling and tension") and 0.66 ("be more productive in everyday life").

Content validity

The percentage of patients choosing "does not apply to me" in the PNQ ranged between 2.3% for the goal "less swelling and tension" and 39.5% for "more contact with other people" (Table 2). Thus, each item was applicable to more than 60% of the patients.

All 301 patients who returned the patient questionnaire filled in the PBI, at least partially. 299 (99.3%) filled in the PNQ

Table 3. Hypothesis testing: correlation of Patient Benefit Index—lymphedema and lipedema (PBI-L) global score and subscales with convergent criteria.

Convergent criterion	PBI-L global score			PBI-L subscale 1 (normal everyday-life and psychological wellbeing)			PBI-L subscale 2 (physical wellbeing and capability)		
	n	r	p	n	r	p	n	r	p
Cross-sectional study									
Generic HRQoL: EQ-5D-3L	283	.21	<.001	279	.15	.012	282	.15	.013
Generic HRQoL: global assessment	279	.29	<.001	275	.23	<.001	278	.18	.002
Disease-specific HRQoL: FLQA-LK[a]	279	−.31	<.001	275	−.27	<.001	278	−.19	.002
Generic health state: EQ-5D-VAS	282	.25	<.001	278	.22	<.001	281	.18	.002
Disease-specific health state: global assessment	279	.50	<.001	275	.44	<.001	278	.36	<.001
Patient assessment of quality of care	283	.52	<.001	279	.45	<.001	282	.45	<.001
Patient satisfaction with care	283	.47	<.001	279	.42	<.001	282	.37	<.001
Clinical severity: edema stage[b]	282	−.14	.017	278	−.13	.028	281	−.15	.013
Longitudinal study									
Generic HRQoL: EQ-5D-3L after treatment, controlled for baseline values	62	−.09	.478	61	−.06	.629	61	−.01	.923
Disease-specific HRQoL: FLQA-LK after treatment, controlled for baseline values	74	−.34	.003	73	−.34	.050	73	−.34	.004

Note. HRQoL = health-related quality of life; FLQA-LK = short version of Freiburg Life Quality Assessment in Lymphedema (FLQA-L); VAS = visual analogue scale.
[a] In the FLQA-LK, lower values represent better quality of life.
[b] Correlations with edema stage were analyzed with non-parametric Spearman correlations. All other correlations were Pearson correlations.

and 289(96.0%) filled in the PBQ. Among the 12 patients who did not fill in the PBQ, four stated that they currently received no treatment at all (free text in the PBQ questionnaire), seven gave no information on current treatment, and one wrote that he currently received lymph therapy.

Among those patients who filled in the PNQ, between 0.7% and 3.8% had missing values, depending on the item (average: 1.8%; Table 1). The PNQ items with the highest number of missing values were "to avoid complications" (3.8%) and "to need less time for treatment" (2.8%).

In the PBQ, there were between 0.3% and 2.1% missing values in those 289 patients who completed the questionnaire (average: 1.4%; Table 2). The PBQ items with the highest rate of missing values were "to experience less swelling and tension" (2.8%) and, as in the PNQ, "to avoid complications" (2.7%).

Construct validity

We had hypothesized a positive correlation of PBI-L with HRQoL, with the highest correlation regarding the disease-specific instrument FLQA-LK. PBI-L global score and subscales correlated with all three measures of HRQoL (Table 3). The effect was of low-to-medium size (absolute r = .15—.31). Correlations with the disease-specific

instrument FLQA-LK were higher than with the generic instruments, but only slightly so.

We had hypothesized a positive correlation of PBI-L with patient assessment of current health state (EQ-VAS on health state in general; global assessment of health state regarding the edema) with a higher correlation with the edema-specific measurement. As predicted, the correlations with the edema-specific measure were markedly higher (r = .36—.50) than with the generic measure (r = .18—.25).

A positive correlation of PBI-L with patients' assessment of quality of care and satisfaction with care was found, as hypothesized (medium-to-high effect sizes of r = .37—.52). The hypothesis that the correlation with satisfaction would be higher than with quality of care could not be confirmed.

The hypothesized negative correlation of PBI-L global score and subscales with edema stage was also found, implying that patients with a lower clinical severity rated treatment benefit as higher. However, correlations were low (r = −.13 to −.15).

Responsiveness

We had hypothesized that PBI-L global score and subscales correlate positively with change in HRQoL, and that the

correlation with the disease-specific instrument FLQA-LK would be higher. A positive correlation was found with change in disease-specific HRQoL (FLQA-LK). The effect was of medium size (r = −.34) and significant. The correlations with generic HRQoL (EQ-5D-3L) were very low (r = −.01 to −.09) and not significant.

DISCUSSION

The aim of this study was to develop and validate the PBI-L, a questionnaire for the assessment of patient-relevant benefit in lymphedema and lipedema treatment.

With the PBI-L, patients rate the extent to which their treatment goals have been achieved. By doing so, they both rate the improvement since treatment onset and judge whether the improvement is caused by treatment. In contrast to HRQoL questionnaires where pre—post differences are usually interpreted as treatment effects, patients can exclude changes not caused by treatment from their benefit assessment in the PBI-L. Furthermore, treatment benefit is assessed retrospectively. In contrast, HRQoL questionnaires are usually used prospectively, which means that benefit is evaluated by computing pre—post HRQoL differences. The PBI-L also comprises a pre-treatment assessment with the PNQ, but this only concerns goal importance; the benefit assessment with the PBQ is conducted after treatment only. This retrospective assessment prevents response shift effects. However, it involves the risk of recall bias if patients do not correctly recall the extent of their impairment before therapy and therefore make a biased benefit assessment. The question of whether a recall bias occurs in the PBI is currently being investigated in a longitudinal study.

We wanted to be certain that the PBI-L covers all treatment goals that are relevant to edema patients. Therefore, we conducted an open item collection regarding goals and impairments in patients with different types of edema (primary, secondary, lip- and lymphedema, localized at arms or legs), and we involved patients in the discussion of, and decision on, the final items.

In the quantitative analysis of the cross-sectional and the longitudinal study, well-interpretable PBI-L subscales providing more detailed information on patient benefit in addition to the PBI global score were found. Floor and ceiling effects were small, all items were applicable to the majority of the patients, and the amount of missing values was low.

To examine construct validity in this study, hypotheses were defined a priori, which could largely be confirmed. Both PBI-L global score and subscales correlated with the convergent criteria, and the association was higher regarding disease-specific measures of HRQoL and current health state as compared to measures of non-edema-specific aspects of health. A high correlation was found with patients' assessment of quality of care and satisfaction with care. This is plausible because both measures represent retrospective assessments just as the PBI-L does, as opposed to the HRQoL and health state measures, which

only assess the current state. In contrast to our assumption that satisfaction with care was more similar to the construct of treatment benefit, the association of patient assessment of quality of care with PBI-L was slightly higher. The low association of treatment benefit and edema stage might be explained by the fact that disease severity is influenced by many factors beyond quality of treatment, for example by disease duration.

Good responsiveness was found regarding change in disease-specific HRQoL, which correlated markedly with treatment benefit. However, we could not confirm the hypothesized association with change in generic HRQoL. A possible explanation might be that the very specific benefit of edema treatment is difficult to display with a generic instrument like the EQ-5D.

With the available data, reliability of the PBI-L could only be assessed with regard to internal consistency. Further longitudinal studies will investigate retest reliability.

We conclude that the PBI-L is an internally consistent, valid, and responsive instrument for the assessment of patient-relevant benefit of edema treatment suitable for use in clinical studies and quality of care studies or in clinical routine.

FUNDING

CONFLICT OF INTEREST

REFERENCES

1 Földi M. The neglected vascular system. *MMW-Fortschr Med* 2004;**146**(3—4):23—4 [in German].

2 Moffatt CJ, Franks PJ, Doherty DC, Williams AF, Badger C, Jeffs E, et al. Lymphoedema: an underestimated health problem. *QJM* 2003;**96**(10):731—8.

3 Norman SA, Localio AR, Potashnik SL, Simoes Torpey HA, Kallan MJ, Weber AL, et al. Lymphedema in breast cancer survivors: incidence, degree, time course, treatment, and symptoms. *J Clin Oncol* 2009;**27**(3):390—7.

4 Fife CE, Maus EA, Carter MJ. Lipedema: a frequently misdiagnosed and misunderstood fatty deposition syndrome. *Adv Skin Wound Care* 2010;**23**(2):81—92.

5 Mayrovitz HN. The standard of care for lymphedema: current concepts and physiological considerations. *Lymphat Res Biol* 2009;**7**(2):101—8.

6 Franks PJ, Moffatt CJ, Doherty DC, Williams AF, Jeffs E, Mortimer PS. Assessment of health-related quality of life in patients with lymphedema of the lower limb. *Wound Repair Regen* 2006;**14**(2):110—8.

7 Schwartz CE, Bode R, Repucci N, Becker J, Sprangers MA, Fayers PM. The clinical significance of adaptation to changing

health: a meta-analysis of response shift. *Qual Life Res* 2006;**15**(9):1533—50.

8 Augustin M, Radtke MA, Zschocke I, Blome C, Behechtnejad J, Schäfer I, et al. The patient benefit index: a novel approach in patient-defined outcomes measurement for skin diseases. *Arch Dermatol Res* 2009;**301**(8):561—71.

9 Franzke N, Schäfer I, Jost K, Blome C, Rustenbach SJ, Reich K, et al. A new instrument for the assessment of patient-defined benefit in the treatment of allergic rhinitis. *Allergy* 2011;**66**(5):665—70.

10 Blome C, Augustin M, Siepmann D, Phan NQ, Rustenbach SJ, Ständer S. Measuring patient-relevant benefits in pruritus treatment: development and validation of a specific outcomes tool. *Br J Dermatol* 2009;**161**(5):1143—8.

11 Augustin M, Blome C, Zschocke I, Schäfer I, Koenig S, Rustenbach SJ, et al. Benefit evaluation in the therapy of chronic wounds from the patients' perspective — development and validation of a new method. *Wound Repair Regen* 2012;**20**(1):8—14.

12 Augustin M, Amon U, Braathen L, Bullinger M, Gieler U, Klein GF, et al. Assessment of quality of life in dermatology. *J Dtsch Dermatol Ges* 2004;**2**(9):802—6 [in German].

13 Scientific Advisory Committee of the Medical Outcomes Trust. Assessing health status and quality-of-life instruments: attributes and review criteria. *Qual Life Res* 2002;**11**(3):193—205.

14 Mokkink LB, Terwee CB, Knol DL, Stratford PW, Alonso J, Patrick DL, et al. The COSMIN checklist for evaluating the methodological quality of studies on measurement properties: a clarification of its content. *BMC Med Res Methodol* 2010;**10**:22.

15 The EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy* 1990;**16**(3):199—208.

16 Schulenburg JMvd, Claes C, Greiner W, Uber A. German version of the EuroQol questionnaire. *Z Gesundh Wiss* 1998;**11**(1):3—20 [in German].

17 Augustin M, Bross F, Földi E, Vanscheidt W, Zschocke I. Development, validation and clinical use of the FLQA-I, a disease-specific quality of life questionnaire for patients with lymphedema. *Vasa* 2005;**34**(1):31—5.

18 International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema. 2009 Consensus Document of the International Society of Lymphology. *Lymphology* 2009;**42**(2):51—60.

19 Herberger K, Blome C, Sandner A, Altheide F, Heyer K, Münter KC, et al. Quality of care of patients with chronic lymphoedema in Germany. *Dermatology* 2013;**226**(3):238—46.

20 Herberger K, Heyer AK, Blome C, Sandner A, Altheide F, Lader-Holtorf M, et al. Development and use of guideline-derived quality indicators for community lymphoedema. *J Eur Acad Dermatol Venereol* 2013;**27**(2):227—34.

21 Moffatt CJ, Franks PJ, Hardy D, Lewis M, Parker V, Feldman JL. A preliminary randomized controlled study to determine the application frequency of a new lymphoedema bandaging system. *Br J Dermatol* 2012;**166**(3):624—32.

22 Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol* 2010;**63**(7):737—45.