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The Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR): A measure of health-related quality of life and quality of life for patients with pulmonary hypertension

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Abstract

Objective: No outcome measures specific to pulmonary hypertension (PH) currently exist. The aim of the study was to develop health-related quality of life (symptoms and functioning) scales and a quality of life scale that would allow comprehensive, accurate and valid patient-reported outcome assessment in clinical studies. *Methods*: The content of the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) was derived from qualitative interviews conducted with 35 patients. Item reduction was based on the analysis of responses to a postal survey (n = 75) and patient interviews (n = 15) designed to determine face and content validity. A final postal validation study (n = 91) was performed to determine reproducibility and construct validity. *Results*: The questionnaire was well received by participants who found it to be relevant, comprehensible and quick and easy to complete. Rasch and factor analyses were conducted to ensure unidimensionality of the final CAMPHOR scales; Overall symptoms (made up of Energy, Breathlessness and Mood subscales), Functioning and Quality of life. The CAMPHOR scales had good internal consistency ($\alpha = 0.90$–0.92) and reproducibility (test–retest correlations = 0.86–0.92). They also exhibited convergent, divergent and known groups validity. *Conclusions*: The CAMPHOR is a valuable new instrument for assessing patient-reported outcome in PH clinical trials and routine practice.

Key words: Functioning, Health status indicators, Pulmonary hypertension, Quality of life, Symptoms

Abbreviations: CAMPHOR – Cambridge Pulmonary Hypertension Outcome Review; CTEPH – Chronic Thrombotic and/or Embolic Disease; EQ-5D – EuroQoL; HRQL – health-related quality of life; NHP – Nottingham Health Profile; NSCAG – National Specialist Commissioning Advisory Group; NYHA – New York Heart Association classification; PH – Pulmonary Hypertension; PVDU – Pulmonary Vascular Disease Unit; QoL – Quality of Life; RUMM – Rasch Unidimensional Measurement Model; VAS – visual analogue scale

Introduction

Pulmonary hypertension (PH) is a disease characterized by a progressive rise in pulmonary artery pressure and pulmonary vascular resistance, ultimately resulting in right heart failure and death [1]. PH can affect persons of all races and ages and if untreated the disease carries a high mortality rate [2]. Symptoms include breathlessness, fatigue, palpitations, ankle oedema, chest pain, and syncope. The condition is often not diagnosed until late in the disease progression due to subtle and non-specific symptoms in the early stages. Licensed treatments for PH range from oral tablet

medication with endothelin receptor antagonists through to intermittent nebulized, continuous intravenous or subcutaneous infusions of prostaglandin or prostaglandin analogues [3]. Many of these treatments impose a significant burden on patients and families in terms of inconvenience and side-effects. For example, intravenous Prostacyclin [4] is associated with diarrhoea, systemic vasodilation-related flushing, headaches, jaw pain and hypotension. There are also complications inherent in the delivery system, including skin rash, pain, line sepsis and rebound PH from accidental interruption to the infusion [5]. Current treatments for PH, with the exception of pulmonary endarterectomy for thromboembolic PH, do not cure the disease. The present aim of treatment is to lengthen survival time, to ameliorate symptoms and to improve quality of life (QoL).

Patient-reported outcome in PH

No PH-specific instruments have been developed to assess outcome in clinical studies or for assessing progress of individual patients in clinical practice. Methods currently employed include the 6 min walking test [6], the New York Heart Association (NYHA) classification, and the Borg Dyspnea Index [7]. These measures represent rather basic estimates of impairment (symptoms) and disability (functioning) and cannot capture the full impact of PH on the patient.

Generic health-related quality of life (HRQL) measures employed in PH populations such as the Nottingham Health Profile (NHP) [8], EuroQol [9] and SF-36 [10] have proved to be of limited value in the assessment of PH [11–13]. As the measures are not specific to PH their relevance to patients is limited. Furthermore, they have poor sensitivity [see for example: 8, 14–16] and, consequently, are unlikely to detect real changes in health status over time – a crucial attribute of instruments that are to be employed in clinical trials. Measures specific to other conditions deemed to be similar to PH, such as the Minnesota Living with Heart Failure Questionnaire [17], have also been used inappropriately [12]. Given the current instruments available for outcome assessment in PH, there is a clear need for a high-quality disease-specific measurement tool for this condition.

Measurement models for the new measure

A decision was taken to develop the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR). The CAMPHOR was intended to consist of both a HRQL measure assessing impairment (symptoms) and disability (functioning) and a separate QoL measure.

The HRQL section of the measure consists of two scales. The first assesses impairment (any loss or abnormality of psychological, physiological or anatomical structure or function, equating to symptoms) and the second disability (any restriction or lack of ability to perform an activity in the manner or within the range considered normal for a human being, also termed functioning). Impairment and disability, both consequences of disease, are major influences on QoL [18].

The theoretical basis adopted for the CAMPHOR QoL scale is the needs-based model of QoL [19]. This states that life gains its quality from the ability and capacity of the individual to satisfy their needs, that QoL is highest when most needs are met and that disease influences QoL only insofar as it limits need fulfillment. This model has been employed successfully in the development of several disease-specific QoL instruments [19–28].

The CAMPHOR was required to be specific to PH, practical and to consist of unidimensional subscales that are reproducible and valid.

Methods

Ethics

The study was granted local research ethics committee approval and all participants gave their written informed consent.

Patient samples

Patients were considered for study inclusion if; they were aged over 18 years and had a diagnosis of PH according to the World Health Organization Diagnostic Classification. Exclusion criteria were; younger than 18 years, having undergone the surgical procedure of Pulmonary Thromboendarterectomy and if in the opinion of the investigator, they would be unable to understand

what was required of them or if their circumstances meant that they might suffer unacceptable distress during interview. Patients who met the inclusion criteria were identified using the Pulmonary Vascular Disease Unit (PVDU) Database at Papworth Hospital, Cambridge, UK.

Item generation

Items for the CAMPHOR were derived from in-depth qualitative, unstructured interviews with PH patients. The interviewees were all from a single specialist centre, designated by the National Specialist Commissioning Advisory Group (NSCAG) for the treatment of PH in the UK. The interviews took place at the clinic or in the patient's own home. The interviewees were encouraged to talk at length about their experience of PH and to describe the physical and psychological impact of the condition.

With the permission of the interviewees the interviews were audio-recorded and transcribed; this was done with the assurance of interviewee anonymity. The interview transcripts were content analysed by three independent researchers to provide potential items for each (QoL and HRQL) outcome measure.

The results of these analyses were synthesized and draft items selected for the symptom and functioning item pools if they represented commonly occurring themes or were deemed by PH specialists to be areas of importance. They were selected for the QoL item pool if they reflected needs that were affected by PH. Duplicate and idiosyncratic items were removed. As far as possible, the original words of the interviewees were used to make the items more personal and immediate to future respondents. A draft item pool for each scale was produced.

Items were then selected on the basis of the following criteria:

- they reflected symptoms of PH or reflected needs or functions, that were affected by PH,
- they were applicable to all potential respondents,
- they were expressed in the first person,
- they reflected a single idea,
- they were unambiguous, and
- they were short and simple.

Following item selection a draft CAMPHOR measure was created.

Scaling postal survey

As the initial forms of the scales were too long to be field-tested, a pre-field-test postal survey was included in the study design. This enabled the reduction of the draft scales so that they would be less of a burden for the patients participating in the field-testing stage. One hundred patients from the PDVU database were selected who met the inclusion criterion. Patients were sent the initial draft questionnaires for completion by post. Rasch analysis was performed on the data from the returned questionnaires to identify misfitting items for removal. The CAMPHOR was redrafted after item reduction.

Field-test interviews

The second draft of the CAMPHOR was field-tested with a new sample of 15 PH patients via one-to-one semi-structured interviews, to examine the practicality, face and content validity of the scales. Patients completed the questionnaire in the presence of an interviewer who observed any problems experienced and following completion of the questionnaire asked the respondent to explain the problems. A series of further questions tested comprehension, relevance and perceived redundancy. Changes in wording and format suggested by more than one respondent were tested in further interviews and, if judged preferable, were retained in a third draft version of the CAMPHOR.

Postal validation study

The third draft of the measure was posted to a sample of 120 PH patients together with the NHP and then again 2 weeks later with the EuroQol (EQ-5D). Both the NHP and EuroQol are widely used patient reported outcomes measures in Europe. The NHP is a measure of perceived distress that consists of six sections covering; Energy level, Pain, Physical mobility, Sleep, Emotional reactions and Social isolation. The EuroQol is a measure of health status that consists of two parts.

The EQ-5D contains five items covering; mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Part 2 is a numerical analogue scale (the EQ-VAS) which provides an alternative method for respondents to indicate their health status. Utility values have been derived for responses to the EQ-5D. The completed and returned questionnaires were then subjected to Rasch analysis [29] ('rating scale' model) for final item reduction using the Rasch Unidimensional Measurement Model (RUMM) [30]. The fit of the individual items was evaluated through individual item χ^2 fit statistics. A statistically significant χ^2 is taken to indicate inadequate fit to the model. $p < 0.01$ was considered to indicate significant misfit while $p = 0.01$–0.05 was considered to indicate borderline misfit. Scales in the final version of the CAMPHOR were assessed for unidimensionality (fit to the Rasch model). Adequacy of fit of the CAMPHOR scales was evaluated through a total χ^2 fit statistic. In addition, factor analysis was employed to evaluate the dimensionality of the scales. The following psychometric properties were also assessed:

Internal consistency. Cronbach's α coefficients were calculated with values below 0.70 taken as indicating that individual items are providing an inadequate contribution to the overall scale [31].

Test–retest reliability (reproducibility). Spearman's rank correlations were used to assess the association between scores at the two administrations. A high correlation (0.85 or above) was taken as being indicative that the scale is suitable for use in clinical trials [32].

Construct validity. This property was established by assessing the degree (estimated using Spearman's correlation coefficients) to which scores on the CAMPHOR scales were associated with those on the comparator instruments, which measured related and unrelated constructs (convergent and divergent validity). Known groups validity was assessed by comparing scores on the CAMPHOR scales obtained by subgroups of patients based on their self-perceived general health, symptom level and NYHA classification. Mann–Whitney *U* Tests were used where two groups were compared and Kruskal–Wallis One-way Analysis of Variance where there were three or more groups.

Table 1. Study sample characteristics

	Interview sample	Scaling postal survey	Field-test interviews	Validation postal survey
Packages administered		100		120
Sample size	35	75	15	91
Number (%) males	9 (25.7)	20 (26.7)	5 (33.3)	27 (29.7)
Number (%) females	26 (74.3)	55 (73.3)	10 (66.7)	64 (70.3)
Mean (SD) age; years	50.5 (16.5)	52.2 (15.3)	52.3 (16.8)	52.6 (16.0)
Age range (years)	20–81	19–81	25–72	18–81
Number of (%) married/co-habiting	27 (77.1)	53 (70.7)	11 (78.6)	58 (64.4)
Number of (%) living alone	8 (22.9)	22 (29.3)	3 (21.4)	32 (35.6)
Number of (%) employed	3 (8.6)	12 (16.7)	2 (13.3)	11 (12.2)
Number of (%) not employed	32 (91.4)	60 (83.3)	13 (86.6)	79 (87.8)
Time (SD) since diagnosis	4.0 (4.6)	5.7 (6.9)	3.9 (4.0)	4.8 (6.0)
Perceived general health:				
Very good		3 (4.0)	1 (6.7)	7 (7.7)
Good		24 (32.0)	7 (46.7)	30 (33.0)
Fair		37 (49.3)	7 (46.7)	38 (41.8)
Poor		11 (14.7)	0	16 (17.8)
Diagnosis:				
Primary PH (%)	15 (42.9)	25 (33.3)	3 (20.0)	33 (36.3)
Chronic thromboembolic (%)	11 (31.4)	28 (37.3)	6 (40.0)	30 (33.0)
$2^{nd}$to congential heart disease (%)	4 (11.4)	16 (21.3)	3 (20.0)	21 (23.1)
$2^{nd}$to connective tissue disease (%)	5 (14.3)	6 (8.0)	1 (6.7)	6 (6.6)
Other PH (%)	0	0	2 (13.3)	1 (1.1)

Results

Unstructured interviews

Three patients declined to take part in the study as they lived more than 60 miles from the centre. Unstructured qualitative interviews were conducted with 35 adults with PH; (mean age 50 [range 20–81] years. Twenty six (74%) of the interviewees were female and 9 (26%) were male. The diagnostic classes of the 35 patients who participated in the semi-structured interviews are shown in Table 1.

Analysis of the interview transcripts identified statements concerning symptoms, physical functioning and QoL. The content of the first two of these types of outcome were considered by clinical members of the research team. They added items covering pain, cough, oedema and syncope to the symptom scale. Few items in these areas were generated directly from patients. This resulted in a scale containing 51 items that primarily covered energy level, breathlessness, mood, pain and oedema. The draft Functioning scale consisted of 18 items.

Quality of life statements were related to patients' ability to fulfill needs. PH-specific needs highlighted included;

- Need for socializing/interaction with others.
- The loss of a role in life.
- The need to be understood, accepted and valued – PH is not well recognized by the general public, with patients feeling that the validity of their experience was doubted by significant people in their lives.
- Self-esteem needs.
- Need for independence – financial as well as physical.
- Need for security – fears of being left alone and a general fear of the future.

A 47-item QoL scale was drafted from the relevant statements identified.

Scaling postal survey

The initial set of PH outcome measures were fully completed and returned by 75 PH patients. The returned questionnaires were entered into factor and Rasch analyses to facilitate item reduction. Sample details are included in Table 1.

Rasch analyses indicated that 12 symptom items should be deleted from the draft CAMPHOR due to misfit. One further item was amended and two added from the original interview transcripts. Following these changes, Rasch and factor analyses confirmed the four subscales of the Symptom measure; Energy level, Oedema, Breathlessness and Mood. Items in these scales were combined with others (covering such issues as syncope and chest pain) to form an Overall Symptoms scale that also fitted the Rasch model. This new scale consisted of 41 items.

Rasch analyses also indicated that one item in the Functioning scale and 11 in the QoL scale misfit and these were removed. This left 17 items in the Functioning scale and 36 in the QoL scale.

Field-test interviews

Fifteen PH patients were interviewed to test the face and content validity of the new drafts of the scales (see Table 1).

The questionnaires were, on the whole, well received by the participants who found them relevant, comprehensible, easy and quick to complete. All the scales (forming the draft CAMPHOR) were completed in a mean time of 10 (SD = 4) minutes.

No changes were made to the Overall symptoms or QoL scales as a result of the field-test interviews. Some interviewees who used oxygen constantly found difficulty in responding to the Functioning scale and the questionnaire instructions were amended accordingly. One item was amended to clarify its meaning.

Validation postal survey

The amended CAMPHOR was posted on two occasions together with comparator questionnaires, 2-weeks apart to PH patients. Table 1 shows details of the respondents. The mean time between completion of the two packages was 17.1 (SD = 4.9) days.

Following Rasch analyses of the responses to the survey, the final versions of the CAMPHOR scales were as follows:

- A 25-item overall symptoms scale scored 0–25, with a higher score indicating the presence of more symptoms. This scale was made up of three subscales:

– An Energy symptom subscale consisting of 10 items
– A Breathlessness symptom subscale consisting of 8 items
– A 7 item Mood subscale
• A 15 item Functioning scale scored 0–30, where a low score indicates good functioning.
• A 25-item QoL scale scored 0–25, with a high score indicating poor QoL.

The Symptom and QoL scales have dichotomous ('True'/'Not true') response options while the Functioning scale has three-point ('Able to do on own **without** difficulty'/'Able to do on own **with** difficulty'/'Unable to do on own') response options. Example items are shown in Appendix 1.

The greatest changes were made to the symptom scales, with the Oedema subscale removed completely. The oedema items did not form a scale and, individually, caused the total symptom scale to misfit substantially.

All CAMPHOR scales showed good fit to the Rasch model (as shown by the Rasch item statistics included in Appendix 2) indicating that the scales are unidimensional. Rasch person-item distribution maps for the overall symptoms, Functioning and QoL scales are shown in Figures 1–3. The figures show the location of both items and respondents in terms of their score on the scales. It can be seen that items are well distributed across the measurement range for the three scales. It also shows that most respondents can be given valid scores. However, some patients had very low scores on the QoL scale indicating very good QoL. The unidimensionality of the scales was confirmed by the factor analyses applied to the dataset.

CAMPHOR summary statistics for the two time-points are shown in Table 2.

Test–retest reliability (reproducibility) and internal consistency

The test–retest reliability and internal consistency of the CAMPHOR scale are shown in Table 3. All scales obtained adequate α coefficients indicating acceptable internal consistency. The test–retest Spearman rank correlation coefficients for all CAMPHOR scales and subscales reach the minimum required (0.85), indicating that the measure has good reliability, producing low levels of random measurement error.

Construct validity

Levels of association among the CAMPHOR scales on the first administration are shown in Table 4.

Convergent and divergent validity

Table 5 shows Spearman correlation coefficients indicating the level of association among the CAMPHOR scales and the comparator scales. The levels of association are as expected with more closely related scales having higher levels of association (NHP Energy level with CAMPHOR Energy = 0.84; NHP Emotional reactions and CAMPHOR Mood = 0.84 and NHP Physical

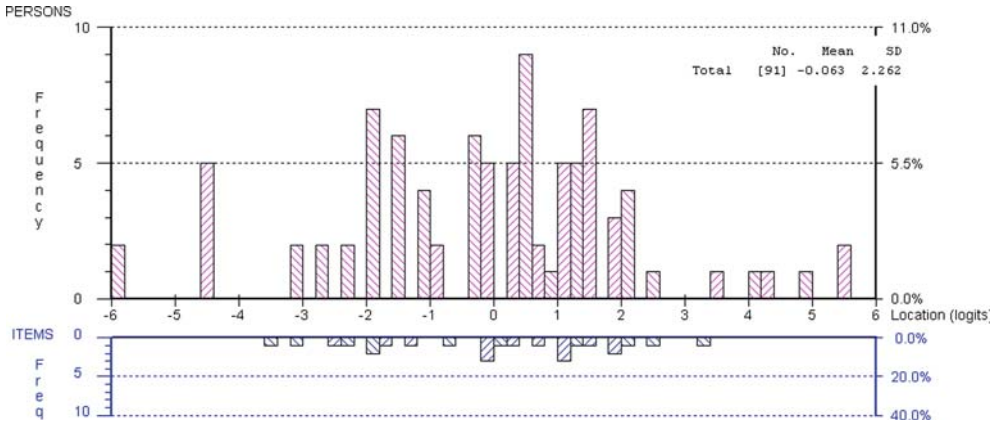

Figure 1. Person–item distribution maps for the Overall Symptoms scale. The rising bars represent the number of respondents at each position on the scale. The falling bars represent the location of the individual items in the scale. Negative values represent the mild end of the scale.

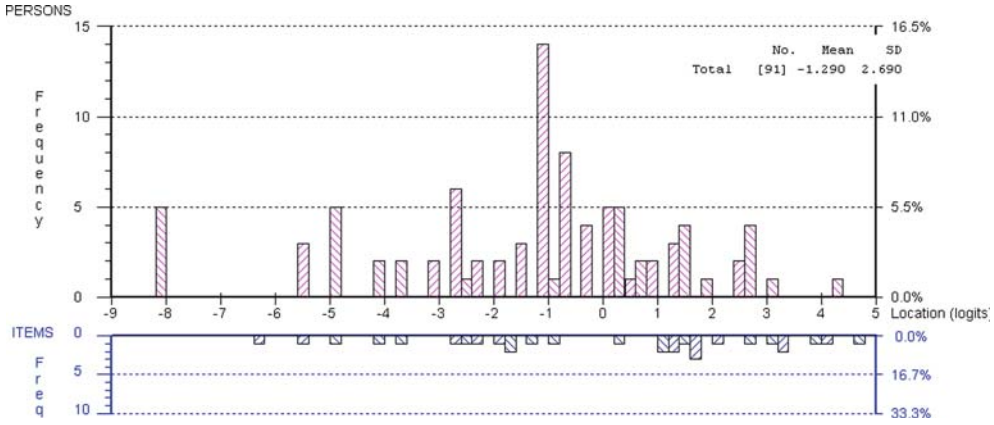

Figure 2. Person–item distribution maps for the overall Functioning scale. The rising bars represent the number of respondents at each position on the scale. The falling bars represent the location of the individual items in the scale. Negative values represent the mild end of the scale.

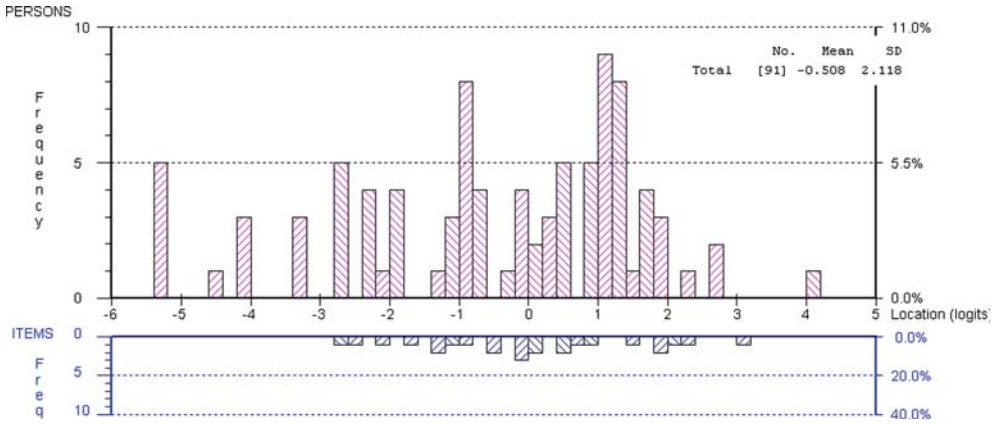

Figure 3. Person–item distribution maps for the QoL scale. The rising bars represent the number of respondents at each position on the scale. The falling bars represent the location of the individual items in the scale. Negative values represent the mild end of the scale.

mobility and CAMPHOR Functioning = 0.85). This provides evidence of the construct validity of the CAMPHOR.

The EQ-5D correlated most closely with CAMPHOR Functioning (0.74). This was anticipated as three of the five EQ-5D items relate to functioning (mobility, self-care, usual activities). In contrast the EQ-VAS correlated most closely (0.71) with CAMPHOR Energy and total symptoms.

Known groups validity

Correlations among the CAMPHOR scales and NYHA classification (Table 5) were generally moderate but highest with the Functioning scale (0.62) – unsurprising given that the classification is based largely on functional capacity. Table 6 shows that (with the exception of the Mood Symptom scale) all CAMPHOR scales were capable of discriminating among patients based on their NYHA classification.

Table 6 also shows the Functioning and QoL scores for patients based on their symptom scores (an alternative indicator of disease severity). The sample was divided into quartiles based on their Symptom scale scores. At both time-points the CAMPHOR Functioning and QoL scales distinguished between the different subgroups. As symptom score increases, those on the Functioning and QoL scales increase significantly.

Table 2. CAMPHOR summary scores for first administration of the validation postal survey

	n	Mean (SD)	Score range	% Scoring minimum	% Scoring maximum
Energy	89	5.2 (3.1)	0–10	10.1	11.2
Breathlessness	88	4.0 (1.9)	0–8	8.0	4.5
Mood	88	2.8 (2.3)	0–7	19.3	5.7
Overall symptoms	88	12.0 (6.2)	0–25	2.3	2.3
Functioning	89	11.5 (6.3)	0–27	5.6	0.0
QoL	88	11.4 (6.7)	0–24	5.7	0.0

Table 3. CAMPHOR Internal consistency and test–retest reliability (reproducibility)

Scale	Internal consistency Time 1	Internal consistency Time 2	Test–retest reliability coefficient
Energy	0.87	0.89	0.87
Breathlessness	0.76	0.79	0.85
Mood	0.80	0.87	0.92
Overall symptoms	0.90	0.93	0.92
Functioning	0.92	0.92	0.86
QoL	0.92	0.94	0.92

Table 4. Correlations among CAMPHOR scales at first administration of the validation postal survey

	Energy level	Breathlessness	Mood	Overall symptoms	Functioning
Energy	–				
Breathlessness	0.68	–			
Mood	0.60	0.52	–		
Overall Symptoms	0.92	0.81	0.81	–	
Functioning	0.64	0.66	0.36	0.64	–
QoL	0.66	0.59	0.74	0.78	0.55

Table 5. Correlations between CAMPHOR, comparator scales and NYHA

	Energy level	Breathlessness	Mood	Overall symptoms	Functioning	QoL
Time 1						
NHP energy level	0.84	0.60	0.53	0.81	0.63	0.69
NHP pain	0.49	0.41	0.43	0.53	0.61	0.46
NHP emotional reactions	0.56	0.46	0.84	0.73	0.35	0.81
NHP sleep	0.38	0.35	0.37	0.44	0.40	0.47
NHP social isolation	0.47	0.28	0.68	0.57	0.27	0.64
NHP physical mobility	0.66	0.68	0.40	0.69	0.85	0.60
NHP distress	0.69	0.54	0.81	0.83	0.48	0.84
NYHA	0.47	0.55	0.30	0.51	0.62	0.47
Time 2						
EQ-VAS	−0.71	−0.59	−0.56	−0.71	−0.60	−0.66
EQ-5D	−0.58	−0.68	−0.52	−0.65	−0.74	−0.61

Table 6. CAMPHOR scales cores by NYHA classification and CAMPHOR symptom score

NYHA class	n	Energy	Breathlessness	Mood	Overall symptoms	Functioning	QoL
1 Mean (SD)	3	1.3 (2.3)	1.0 (1.7)	0.7 (0.6)	3.0 (4.4)	2.7 (3.1)	3.7 (4.7)
2 Mean (SD)	27	3.6 (3.1)	2.7 (1.6)	2.0 (2.0)	8.3 (5.6)	7.9 (5.6)	7.2 (5.9)
2.5 Mean (SD)	9	4.2 (2.7)	3.9 (1.8)	3.6 (2.8)	11.6 (6.3)	7.6 (4.7)	12.2 (8.2)
3 Mean (SD)	42	6.5 (2.2)	4.7 (1.6)	3.2 (2.1)	14.4 (4.8)	14.6 (5.1)	13.4 (5.1)
4 Mean (SD)	6	6.2 (4.0)	5.7 (1.6)	3.3 (2.7)	15.3 (7.7)	17.2 (4.8)	15.6 (7.7)
p		<0.001	<0.001	0.08	<0.001	<0.001	0.001
CAMPHOR symptom score							
0–6 Mean (SD)	20					5.3 (4.8)	3.4 (2.9)
7–12 Mean (SD)	23					11.1 (5.8)	9.8 (4.9)
13–16 Mean (SD)	22					12.5 (3.8)	13.2 (5.3)
17–25 Mean (SD)	23					16.2 (5.8)	17.8 (3.4)
p						<0.001	<0.001

Figure 4 illustrates mean CAMPHOR scale scores associated with perceived general health. CAMPHOR scores differed statistically significantly ($p \leq 0.001$) among groups of patients who rated their health as 'Very good/Good', 'Fair' and 'Poor'.

Discussion

Pulmonary hypertension is a syndrome that presents with a variety of signs and symptoms ranging from mild breathlessness on exertion through to severe breathlessness at rest with associated symptoms of right heart failure resulting in severe functional impairment. Treatments can be time consuming, painful, inconvenient and anxiety generating, placing a responsibility on the clinician to both take the patient's lifestyle and wishes into account when choosing a treatment modality and to assess the effects of treatment on QoL in addition to the usual clinical indicators.

The Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR), a new PH-specific

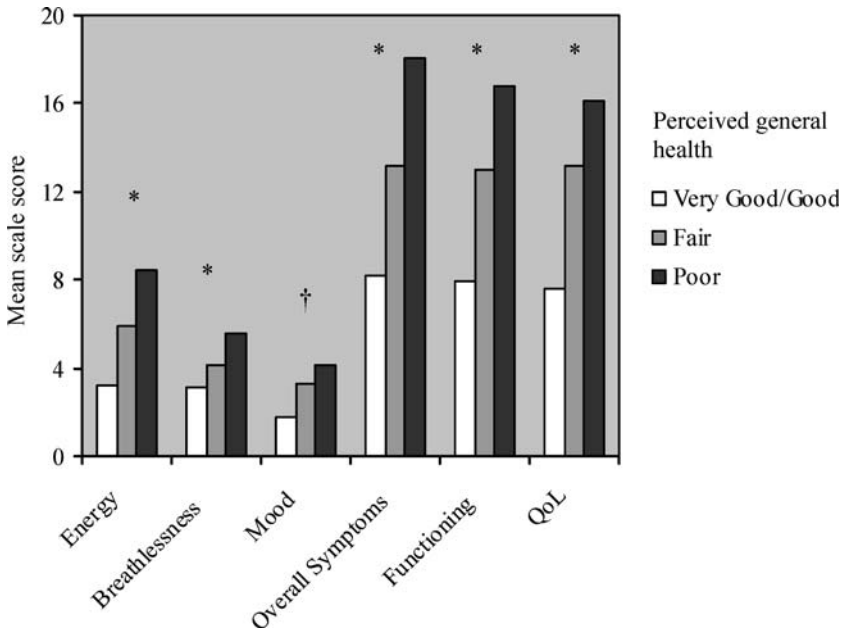

Figure 4. Mean Time 1 CAMPHOR scale scores by perceived general health (validation survey, Time 1) *$p < 0.001$; †$p = 0.001$.

instrument, has been developed and validated to facilitate the measurement of HRQL (symptoms and functioning) and QoL in this patient group. The QoL scale adopts the needs-based model [19, 33, 34, 35]. In this model, impairments (symptoms) and functioning (disability) are seen as influences on QoL rather than being indicators of QoL *per se*. Functional ability is only important insofar as it enables needs to be fulfilled. The model also allows non-health influences to be taken into account – such as environment and available resources – as these interact with health status to influence QoL. Thus, for example, we would expect the QoL scores to reflect the resources (social, financial etc.) available to the patients and their individual personalities. Scores on the QoL scale in the CAMPHOR indicate the extent to which PH patients are able to meet their needs. The relevant needs were derived from qualitative patient interviews and so are specific to this disease. However, similar needs may be prevented from being fulfilled by other diseases. Assuming disease-specific unidimensional QoL scales are developed for a range of diseases, this opens the opportunity for item banking. By co-calibrating the scales across diseases, potentially valid comparisons can be made between the QoL impact of different diseases.

The CAMPHOR scales are based on a coherent measurement model, are unidimensional, their content was generated primarily from patients and they have very good psychometric properties, ensuring that they measure what is intended with relatively low levels of measurement error. In addition, the CAMPHOR has been shown to be relevant, comprehensible and quick and easy for PH patients to complete.

It is interesting to note that the oedema items failed to fit with the other symptom items. A similar finding has subsequently been made by another research group looking into symptomatology in PH (personal communication to ND; March 2004). It seems that these items are influenced by more than just the presence of PH. In particular they may be more closely related to the specific treatment patients are receiving. Such items, if included in the scale, would be expected to exhibit differential item functioning and invalidate comparisons of the impact of differing treatments in a clinical trial. As an additional check a further analysis was made of the frequency with which oedema was mentioned by respondents in the initial patient interviews. This found that of over 1400 potential items derived only eight referred to oedema compared, for example, with 166 potential items related to energy problems. This confirms that oedema is a relatively minor problem for this patient group. No respondents to the validation survey made comments about the absence of items on oedema. It should also be noted that the total symptoms scale is not intended to be a diagnostic instrument but a patient-reported outcome measure. Items in the scale represent different severities of impairment – it is not necessary to include all potentially relevant items. Indeed including all potentially relevant items would produce an unwieldy measure.

It is likely that use of the CAMPHOR will facilitate communication between clinicians and patients by opening up areas for discussion that may not usually be addressed during a clinical encounter [36]. Issues covered by the measure such as ability to socialize or to maintain independence, and feelings of vulnerability may be of great importance to the patient. Improving communication is important because research suggests that there can be wide discrepancies between clinicians' and patients' views on the best treatments and what constitutes a desirable outcome [37].

The scaling and psychometric qualities of the CAMPHOR are such that it may be used on an individual basis in routine clinical practice and as an outcome measure in clinical trials assessing the impact of new interventions on symptoms, physical impairment and quality of life.

Study design limitations

Study participants all came from a single tertiary referral centre and it is possible that this may have biased the interviews and postal validation studies. Consequently, there may be some question about the validity of the CAMPHOR when generalized to patients who are not managed in specialist centres.

No information is available on how representative the samples employed were in terms of educational achievement. However, given the lack of demographic information about patients with pulmonary hypertension it is not possible to say whether this has biased the research. A high proportion of all such patients in the UK were

included in the study and the relatively high responses to the postal surveys suggests that any potential bias will be limited.

The items in the CAMPHOR were all derived from patients' statements about the impact of their illness. It is possible that there is a cultural bias in our study population as, through an accident of geography, they were all white. This could limit the CAMPHOR's generalizability to non-white populations and indicates the need for careful assessment of the relevance of the instrument's content or cultural adaptation in order not to reduce the sensitivity of the measure when using it with other ethnic/national groups.

It remains necessary to establish the responsiveness of the scales (their ability to determine real change in outcome related to changes in disease severity). This is the additional information necessary to conclude that the instrument will prove effective in a clinical trial. Information is also required on the meaningfulness of such changes in score, in order to aid interpretation of changes in health status and QoL. As part of this process larger datasets are being collected to explore how the CAMPHOR scales relate to NYHA classification.

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Appendix

Appendix 1. Example CAMPHOR items

Symptoms (25 items)	
Energy (10 items)	My stamina levels are low
	I get tired very quickly
	I feel very weak
Breathlessness (8 items)	When I walk I get out of breath
	I get breathless going up one step
	I get breathless without doing anything
Mood (7 items)	I get very down
	I've forgotten what it's like to enjoy myself
	I often feel anxious
Functioning (15 items)	
	Get dressed
	Walk short distances on level ground
	Stand for a short time
	Lift heavy items
Quality of life (25 items)	
	My condition puts a strain on my close relationships
	I can't do things on the spur of the moment
	It feels like my body has let me down
	I feel as if I am a burden to people
	I'm unable to join in activities with my family and friends

Anyone interested in receiving a copy of the CAMPHOR should contact Dr McKenna at the address shown above.

Appendix 2. Rasch item statistics for the Symptom, Functioning, and Quality of life scales

Item	Location	SE	FitResid	χ^2	Prob
Symptoms					
1	−1.86	0.32	−0.83	1.24	0.54
2	−1.71	0.31	0.60	7.13	0.03
3	0.07	0.27	−1.41	5.79	0.06
4	−1.95	0.33	−0.72	2.49	0.29
5	1.25	0.28	−0.30	0.49	0.78
6	1.01	0.28	−0.51	0.26	0.88
7	1.96	0.32	0.10	0.71	0.70
8	1.07	0.28	−0.29	2.37	0.31
9	−2.43	0.35	−1.27	0.78	0.68
10	−0.07	0.27	−0.92	1.34	0.51
11	2.07	0.33	−0.32	1.53	0.47
12	0.79	0.27	0.52	5.16	0.08
13	−2.28	0.34	−0.54	0.87	0.65
14	−0.74	0.28	1.84	0.91	0.63
15	2.56	0.36	−0.58	4.39	0.11
16	−3.12	0.41	−0.21	0.33	0.85
17	3.21	0.44	−0.46	2.22	0.33
18	−3.54	0.45	−0.79	1.06	0.59
19	−0.06	0.27	3.58	2.58	0.28
20	−0.01	0.27	0.27	0.48	0.79
21	1.93	0.31	−0.44	2.02	0.36
22	1.14	0.28	−0.31	6.64	0.04
23	1.56	0.30	−0.43	4.78	0.09
24	−1.24	0.30	0.95	0.48	0.79
25	0.39	0.27	2.39	0.48	0.79

Appendix 2. Continued

Item	Location	SE	FitResid	χ^2	Prob
Functioning					
1	0.22	0.22	1.24	4.44	0.11
2	1.69	0.25	−0.15	0.52	0.77
3	2.67	0.29	−0.53	0.64	0.73
4	2.54	0.29	−0.70	0.64	0.73
5	2.56	0.29	−0.12	0.56	0.76
6	−0.62	0.24	−0.43	1.48	0.48
7	−0.44	0.32	−0.83	2.20	0.33
8	−1.20	0.25	0.79	0.58	0.75
9	0.51	0.24	1.96	1.34	0.51
10	3.11	0.32	−0.65	2.45	0.29
11	−0.29	0.24	1.25	0.26	0.88
12	−3.26	0.25	1.71	2.45	0.29
13	−4.06	0.27	−1.02	1.51	0.47
14	0.52	0.23	−0.38	1.42	0.49
15	−3.96	0.28	−1.06	2.26	0.32
Quality of life					
1	2.22	0.33	−0.17	0.68	0.71
2	1.96	0.32	−0.42	0.34	0.84
3	0.11	0.28	−1.05	0.59	0.75
4	−1.73	0.32	0.68	0.45	0.80
5	0.84	0.28	−0.35	0.57	0.75
6	−0.09	0.28	0.29	0.13	0.94
7	−1.17	0.30	−0.13	0.24	0.89
8	0.47	0.27	0.24	2.47	0.29
9	3.07	0.42	−0.33	1.46	0.48
10	−0.51	0.28	−1.80	4.86	0.09
11	1.41	0.29	−0.17	1.91	0.38
12	−2.43	0.34	−0.18	0.37	0.83
13	−1.25	0.30	0.58	2.60	0.27
14	2.09	0.32	1.53	0.70	0.71
15	0.42	0.27	−0.60	1.25	0.54
16	0.66	0.27	−0.45	0.80	0.67
17	0.00	0.28	−1.39	2.60	0.27
18	−0.57	0.28	−0.38	0.61	0.74
19	−1.23	0.30	−0.69	2.89	0.24
20	−1.00	0.30	−0.41	0.53	0.77
21	−0.10	0.28	1.48	0.25	0.88
22	−2.17	0.34	0.01	0.66	0.72
23	−2.78	0.37	−0.30	0.39	0.82
24	−0.11	0.28	−0.66	4.77	0.09
25	1.88	0.31	−0.72	1.03	0.60

References

1. Rubin LJ. Primary pulmonary hypertension. N Engl J Med 1997; 336: 111–117.
2. D'Alonzo GE, Barst RJ, Ayres SM, et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. Ann Int Med 1991; 115: 343–349.
3. Gibbs JSR, Higgenbottam TW. Recommendations on the management of pulmonary hypertension in clinical practice. Heart 2001; 86(Suppl): i1–i13.
4. Galie N, Manes A, Branzi A. Prostanoids for pulmonary arterial hypertension. Am J Respir Med 2003; 2(2): 123–137.
5. Myers SA, Ahearn GS, Angelica Selim M, Tapson VF. Cutaneous findings in patients with pulmonary arterial hypertension receiving long-term epoprostenol therapy. J Am Acad Dermatol 2004; 51(1): 98–102.
6. Kadikar A, Maurer J, Kesten S. The six-minute walk test: A guide to assessment for lung transplantation. J Heart Lung Transplant 1997; 16(3): 313–319.
7. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982; 14(5): 377–381.
8. Hunt SM, McEwen J, McKenna SP. Measuring Health Status. London: Croom Helm, 1986.
9. EuroQoL Group. EuroQoL: A new facility for the measurement of health-related quality of life. Health Policy 1990; 16: 199–208.
10. Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 Health Survey: Manual and Interpretation Guide. Boston, MA: The Health Institute, New England Medical Centre, 1993.
11. Galie N, Humbert M, Vachiery JL, et al. Effects of beraprost sodium, an oral prostacyclin analogue, in patients with pulmonary arterial hypertension: A randomized double-blind, placebo-controlled trial. J Am Coll Cardiol 2002; 39(9): 1496–1502.
12. Simonneau G, Barst RJ, Galie N, et al. Treprostinil Study Group. Continuous subcutaneous infusion of treprostinil, a prostacyclin analogue, in patients with pulmonary arterial hypertension: A double-blind, randomized, placebo-controlled trial. Am J Respir Crit Care Med 2002; 165(6): 800–804.
13. Olschewski H, Simonneau G, Galie N, et al. Inhaled iloprost for severe pulmonary hypertension. N Engl J Med 2002; 347(5): 322–329.
14. Dixon P, Heaton J, Long A, Warburton A. Reviewing and applying the SF-36. Outcomes Briefing August 1994; 4: 3–25.
15. Ziebland S. The short form 36 health status questionnaire: Clues from the Oxford region's normative data about its usefulness in measuring health gain in population surveys. J Epidemiol Community Health 1995; 49: 102–105.
16. Wolfe F, Hawley DJ. Measurement of the quality of life in rheumatic disorders using the EuroQol. Br J Rheumatol 1997; 36: 786–793.
17. Rector RS, Kubo SH, Cohn JN. Patients' self-assessment of their congestive heart failure. Heart Fail 1987; 1: 198–209.
18. World Health Organization. International Classification of Functioning, Disability and Health. Geneva: WHO Publication, 2001.
19. Hunt SM, McKenna SP. The QLDS: A scale for the measurement of quality of life in depression. Health Policy 1992; 22: 307–319.
20. Holmes SJ, McKenna SP, Doward LC, Shalet SM. Development of a questionnaire to assess the quality of

life of adults with growth hormone deficiency. Endocrinol Metab 1995; 2: 63–69.
21. Wagner TH, Patrick DL, McKenna SP, Froese MA. Cross-cultural development of a quality of life measure for men with erection difficulties. Qual Life Res 1996; 5: 443–449.
22. de Jong Z, van der Heijde D, McKenna SP, Whalley D. The reliability and construct validity of the RAQoL: A rheumatoid arthritis-specific quality of life instrument. Br J Rheumatol 1997; 36: 878–883.
23. McKenna SP, Doward LC, Mackenzie Davey K. The development and psychometric properties of the MSQOL; a migraine-specific quality-of-life instrument. Clin Drug Invest 1998; 15: 413–423.
24. Doward LC, McKenna SP, Kohlmann T, et al. The international development of the RGHQoL: A quality of life measure for recurrent genital herpes. Qual Life Res 1998; 7: 143–153.
25. McKenna SP, Whalley D, Dewar AL, Erdman RA, Kohlman T, Niero M, et al. International development of the Parents' Index of Quality of life in Atopic Dermatitis (PIQoL-AD). Qual Life Res 2005; 14: 231–241.
26. McKenna SP, Cook SA, Whalley D, et al. Development of the PSORIQoL, a psoriasis-specific measure of quality of life designed for use in clinical practice and trials. Br J Dermatol 2003; 149(2): 323–331.
27. Doward LC, Spoorenberg A, Cook SA, et al. Development of the ASQoL: A quality of life instrument specific to ankylosing spondylitis. Ann Rheum Dis 2003; 62: 20–26.
28. McKenna SP, Doward LC, Whalley D, Tennant A, Emery P, Veale DJ. Development of the PsAQoL: A quality of life instrument specific to psoriatic arthritis. Ann Rheum Dis 2004; 63(2): 162–169.
29. Rasch G. Probabilistic Models for some Intelligence and Attainment Tests. Chicago: University of Chicago Press, 1980.
30. Andrich D. Rasch Models for Measurement. London: Sage Publications, 1988.
31. Weiner EA, Stewart BJ. Assessing Individuals. Boston: Little Brown, 1984.
32. Streiner D, Norman G. Health Measurement Scales. Oxford: Oxford University Press, 1989.
33. McKenna SP, Whalley D, Doward LC. Which outcomes are important in schizophrenia trials? Int J Methods Psychiatr Res 2000; 9(1) Suppl: S58–S67.
34. McKenna SP, Doward LC. The Needs-Based Approach to Quality of Life Assessment. Value Health 2004; 7(s1): S1–S3.
35. Tennant A, McKenna SP, Hagell P. Application of Rasch analysis in the development and application of quality of life instruments. Value Health 2004; 7(s1): S22–S26.
36. Detmar SB, Muller MJ, Schornagel JH, et al. Health-related quality of life assessments and patient–physician communication: A randomized controlled trial. JAMA 2002; 288: 3027–3034.
37. Doward LC, McKenna SP. Evolution of quality of life assessment. In: Rajagopalan R, Sheretz EF, Anderson RT (eds.), Care Management of Skin Diseases: Life Quality and Economic Impact. New York: Marcel Dekker, 1997: 9–33.

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