emPhasis-10: development of a health-related quality of life measure in pulmonary hypertension

Running title: emPhasis-10

Janelle Yorke (PhD, RGN), 1 Paul Corris, 2 Sean Gaine, 3 Simon S Gibbs, 4,5 David G Kiely, 6 Carl Harries, 7 Val Pollock, 8 Iain Armstrong 6,9

1. School of Nursing, Midwifery and Social Work, University of Manchester, Manchester UK
2. Department of Respiratory Medicine, Freeman Hospital, Newcastle UK
3. Pulmonary Hypertension Unit, Mater Misericordiae University Hospital, Dublin, Ireland
4. National Heart and Lung Institute, Imperial College London UK
5. Pulmonary Hypertension Service, Hammersmith Hospital, London UK
6. Sheffield Pulmonary Vascular Disease Unit, Royal Hallamshire Hospital, Sheffield, UK
7. Pulmonary Hypertension Unit, Royal Brompton and Harefield Foundation NHS Trust, London UK
8. Scottish Vascular Unit, Golden Jubilee National Hospital, Glasgow UK
9. Pulmonary Hypertension Association UK, Sheffield UK

Corresponding author:
Dr Janelle Yorke, Senior Lecturer, School of Nursing, Midwifery & Social Work
University of Manchester, Room 5.320 Jean McFarlane Building, Oxford Road,
Manchester, M13 9PL
Telephone: (+44)161 3067780
Email: Janelle.Yorke@manchester.ac.uk
Summary Point (117 characters)

Summary message: emPHasis-10 is a short, valid tool for routine assessment of health-related quality of life in pulmonary hypertension.
Abstract

To measure the impact of pulmonary hypertension (PH) on health-related quality of life (HRQL), there is a need for a short, validated instrument that can be used in routine clinical practice. Interviews were conducted with 30 patients with PH to derive 32 statements, which were presented as a semantic differential six-point scale (0 – 5), with contrasting adjectives at each end. This item list was completed by patients, attending PH clinics across the UK and Ireland. Rasch analysis was applied to identify items fitting a uni-dimensional model.

226 patients (mean age 55.6±14; 70% female) with PH (82% had pulmonary arterial hypertension (PAH) completed the study questionnaires. Ten of the 32 items demonstrated fit to the Rasch model (chi-square = 16; p>0.05) and generated the EmPHasis-10 questionnaire. Test-retest (ICCC=0.95, n=33) and internal consistency (Chronbach’s alpha=0.9) were strong. EmPHasis-10 scores correlated consistently with other relevant measures and discriminated subgroups of patients stratified by WHO functional class (ANOVA F = 1.73; p <0.001). The EmPHasis-10 is a short, questionnaire for assessing HRQL in PAH. It has excellent measurement properties and sensitive to differences in relevant clinical parameters. It is freely available to use by both the clinical and academic community.

Word count: 196
INTRODUCTION

Pulmonary hypertension (PH) has many causes and is a debilitating and progressive condition that can affect people of any age and shortens life expectancy [1, 2]. It ranges from severe elevations of pressure seen in the context of pulmonary arterial hypertension (PAH) for which drug therapies are available and chronic thromboembolic pulmonary hypertension (CTEPH) which may be cured by surgery to relatively mild elevations of pressure seen in the setting of respiratory and cardiac disease where treatment is principally aimed at the underlying condition [3].

PH is characterised by breathlessness, decreased exercise tolerance, psychological distress, lack of energy and fatigue, resulting in a reduced health-related quality of life (HRQL) [4-7]. As there is no cure except in selected patients with CTEPH, current management strategies aim to prolong survival, alleviate symptoms and improve HRQL. Given the central importance of HRQL as a goal of therapy a tool capable of accurately quantifying this in both the clinical and trial environment would be highly desirable.

The routine collection of valid and reliable HRQL data necessitates the availability of a short, simple patient reported outcome, to measure the impact that PH has on patients’ lives. Available patient reported outcomes frequently used in PH are often multi-dimensional and include the Cambridge Pulmonary Hypertension Outcome Survey (CAMPHOR) [8], Medical Outcome Study 36-Item Short Form (SF-36) [9], Nottingham Health Profile [10], and Minnesota Living with Heart Failure Questionnaire (MLHFQ) [11]. The CAMPHOR is the only currently available PH specific questionnaire and has been validated in many countries to account for
differences in language and culture [12-14]. Whilst these tools have demonstrated validity and reliability for use in a research context [15,16], they have limited clinical utility. In addition the multi-dimensional nature of a number of these tools makes the weighting process more complex in routine clinical practice.

The aim of this multi-centre study was to develop and assess the validity of an easily and rapidly administered simple-to-score and interpret, disease-specific questionnaire to assess HRQL in a large population of patients with PH with an aim of developing this as a tool to use in the clinic to assess patients with PAH and CTEPH.

METHODS

The study was approved by the NRES Committee East of England – Hertfordshire (11/EE/0345) and University of Manchester. Patients provided written informed consent prior to study entry. Patients were recruited from nationally designated specialist PH centres in the UK and Ireland, and were approached at the time of their routine clinic visit or identified from the database of the Pulmonary Hypertension Association UK (PHA-UK).

Inclusion criteria required a confirmed diagnosis of PH with a mean pulmonary artery pressure of at least 25 mmHg at cardiac catheterisation and required detailed assessment to allow accurate classification of PH as per international guidelines. [17] Exclusion criteria included age less than 18 years and a history of previous successful pulmonary endarterectomy with normalisation of pulmonary artery pressures.
Time from diagnosis was taken as time from right heart catheter unless the patient had congenital heart disease when the time of diagnosis was when the patient was diagnosed as having PH at the PH referral centre. Targeted pulmonary vascular therapies were recorded at the time of questionnaire completion. The six-minute walk distance (6-MWD) or incremental shuttle walking test (ISWT) and World Health Organisation Functional Class (WHO FC) closest to the time of administration of the questionnaire was recorded.

**Stage 1: Item generation for inclusion in questionnaire**

A qualitative study was conducted with 30 patients to explore the concept of HRQL and their experience of living with PH. Five of these patients also conducted self-videoing for a minimum of 5-10 minutes everyday for a total of seven days. Participants were free to record any aspects of living with PH that was important to them. Following the extraction of a draft item list, cognitive debriefing interviewing was employed [18] with 14 patients and two family members to ensure that all items were clear and easy to understand. Items were presented to patients as a semantic differential six-point scale (0 – 5), anchored at each end by contrasting adjectives. The draft item-list and scaling range was reviewed by clinical experts for clinical relevance.

**Stage 2: Item reduction**

Stage two involved the administration of the draft item list to patients with PH. We also collected participants’ WHO FC, 6-MWD or ISWT, and demographic details at the time of enrolment in the study. All patients were also requested to complete the 32-item list and the following questionnaires;
Minnesota Living with Heart Failure – modified for PH (MLHF-PH): the MLHF-PH is a modified version [19] of the original MLHF questionnaire [11]. The MLHF-PH has been found to be highly reproducible and demonstrated internal consistency reliability, and moderately good validity comparable with the values found with the CAMPHOR [20].

Dyspnoea-12 (D-12): D-12 consists of 12 items that tap the physical perception and emotional effects of dyspnoea [21,22]. The instrument uses simple summation scoring to yield scores from 0-36, with higher scores corresponding to greater impairment.

Hospital Anxiety and Depression scale (HAD): HAD assesses psychological distress (7 items tap anxiety with a score range of 0-21, and 7 items tap depression with a score range of 0-21; higher scores indicate greater emotional distress) [23].

Statistical analyses

Item reduction process

A hierarchical approach to item reduction was used followed by the application of Rasch analysis [24,25]. The aim was to develop a unidimensional instrument that captures a wide range of PH experiences using the least number of items required. The process of identifying items for potential deletion was iterative and included items with >25% missing responses and items that demonstrated significant age or gender bias (p < 0.05). To remove the least discriminative descriptors, items demonstrating floor (>25% endorsement) or ceiling effects (>25% endorsement) were removed. Items were also marked for potential deletion if they demonstrated high item-item correlations (r > 0.7) and low item-total correlations (r < 0.3) [26].
Items that survived hierarchical reduction were scrutinised with Rasch unidimensional model (RUMM2030 software: http://www.rummlab.com). Rasch models provide a template for testing how well each item contributes to the concept being measured [24, 27].

Individual item fit was assessed by examining the residual and Chi squared fit statistic for each item (item residual ±2.5 and chi-square p value > 0.05) [27]. Items with the worst model fit were removed whilst ensuring that the balance of retained items and content validity for the total item-set was retained. The overall fit of the final item-set was determined by examining the person item-trait interaction chi-square statistic where a non significant (p >0.05) indicates fit to the model) [27]. See online supplement for further details.

**Stage 3: Preliminary reliability and validity of the final item list**

We tested the preliminary reliability and validity of the final item-set using the same data-set as Stage 2. Internal consistency was tested using Cronbach’s alpha (α), for which values from 0.7-0.9 are acceptable [28].

Concurrent validity was assessed by evaluating correlations between the newly developed questionnaire and the MLHF-PH, D-12, HAD and 6-MWD. Patients attending the Sheffield Pulmonary Vascular Disease Unit (n=66) who perform the incremental shuttle walking test did not perform a 6-MWD and were excluded from this part of the analysis. Associations with WHO FC were calculated using one-way analysis of variance (ANOVA).
Test-retest reliability of the finalised item list was tested in a different group of patients, using a postal survey sent to members of PHA UK. Participants were sent two copies of the final item list to complete seven days apart. Each questionnaire set was placed in a separate sealed envelope clearly marked with the Day 0 (date for completion) and Day 7 (date for completion), and participants received written and telephone directions for completion. Test-retest reliability was tested using intra-class correlation co-efficient (ICCC) for which values greater than 0.7 indicate good reliability [29].

RESULTS

Stage 1: Item generation for questionnaire

Thirty patients (table 1) participated in the qualitative interview work that yielded a preliminary list of 32 items. Items covered breathlessness, activity and social limitations, lack of energy, emotional issues, and treatment related issues. Cognitive interviewing with 14 patients and two family carers resulted in only minor adjustments, and participants indicated that the items and response scale used were relevant and easy to understand. PH clinicians confirmed the clinical relevance of the draft instrument.

[insert table 1]

Stage 2: Item reduction

A total of 226 patients with PH (mean age 55±14; 69% female), participated in stage Two (table 2).
See online supplement for a summary of item reduction. The full scaling range (0-5) for all 32 items was used (mean item responses ranged from 2.04 SD±1.5 ‘Being breathlessness never interrupts my conversations’ to 3.88 SD±1.3 ‘when I walk up one flight of stairs I am not breathless’). All items had less than 5% missing responses. Gender bias was significant in two items (one relating to feeling ‘anxious’ and the other to feeling ‘unattractive’ because of PH), and age bias was significant in three items; all five of these biased items were removed. Three items demonstrated a high degree of floor effects, ranging from 25% to 42%, and four items demonstrated a high degree of ceiling effects, ranging from 26% to 30%; all seven of these items were removed. The item ‘walking up a flight of stairs makes me breathless’ demonstrated a ceiling effect (38%), however this item had strong face validity during the item generation stage and was retained to enable further scrutiny with Rasch analysis.

Item-item correlations and Item-total correlations were assessed with the remaining 20 items. Eight items were marked for possible removal due to high item-to-item correlations. Each of these items correlated with more than one other item. Based on the frequency of an item’s high correlation with other items and our previously conducted qualitative work, four of these items were removed at this stage, thus ensuring that a balance between statistical significance and face validity was maintained. One item (‘I feel dizzy or lightheaded’) was removed due to a low item-total correlation.
Following the above tests, 17 items were deleted with the remaining 15 items entered into RUM2030 for Rasch analysis. During the iterative process of analysing the 15 items, five items were removed to achieve an overall fit to the unidimensional Rasch model. This resulted in a 10-item solution demonstrating a good Rasch model fit for individual items (see online supplement) and the 10 items in aggregate (Chi-squared 16.2, \( p = 0.7 \)). There was a good distribution of the item scores across the severity scale (figure 1). The 10 items form the emPHasis-10 with a total score range from 0 to 50 (Figure 2).

**Stage 3: Preliminary reliability and validity**

emPHasis-10 demonstrated excellent internal-reliability (Chronbach’s alpha = 0.9). Thirty-three patients completed the test-retest study – emPHasis-10 demonstrated good stability overtime (ICCC = 0.95).

The emPHasis-10 demonstrated excellent concurrent validity with related patient reported outcome measures including the MLHF-PH \( (r = 0.61) \); HAD total \( (r = 0.77) \); and D-12 \( (r = 0.74) \) (all \( p < 0.001 \)). There was a moderate correlation between the emPHasis-10 and 6MWD \( (r = -0.40; p < 0.001) \). emPHasis-10 scores discriminated subgroups of patients stratified on WHO FC II and III (mean difference = 10.9; \( p <0.001; CI: 7.3 – 14.5 \)) (figure 3). There were insufficient numbers in WHO FC I and IV to draw any conclusive results.

[insert table 3]
DISCUSSION

We have developed emPHasis-10, a rapidly administered simple-to-score disease-specific questionnaire to assess HRQL in PH. The final 10-items are formatted as a semantic six-point differential scale, a format that has previously proven to be easy to administer and easy for patients to complete in the clinical setting [30]. We have demonstrated that emPHasis-10 scores correlate strongly with measures of HRQL, dyspnoea and psychological distress. Although the emPHasis-10 has primarily been developed for evaluative purposes, this study shows that the emPHasis-10 also has strong discriminative measurement properties according to WHO FC - emphasis-10 scores increased significantly as functional class declined. The performance characteristics of emPHasis-10, supports the validity of this tool for assessing the impact of PH on the lives of patients with PAH.

Important components of the impact of PH are covered in emPHasis-10, including, breathlessness, fatigue and lack of energy, social restrictions and concerns regarding effects on significant others [4-7]. Despite this, the emPHasis-10 fits a unidimensional model where each question carries a similar weighting. Many existing HRQL instruments are multidimensional, comprising separately scored sub-domains that are often lengthy with complex scoring algorithms. A concern with many multidimensional instruments is the reporting a total HRQL score when the totality of its parts might not necessarily provide a valid overall score of HRQL [26]. Our primary objective was to develop an overall measure of PH HRQL with a simple scoring system that does not require complex analysis and interpretation.
In developing this instrument, we used Rasch modeling to facilitate the development of a questionnaire that provides measurement of HRQL using a parsimonious collection of items that form a unidimensional measure. HRQL is generally acknowledged to be a multidimensional construct. The emPHasis-10 is compatible with this view since it contains items that cover a range of experiences (e.g. energy, breathlessness, social confidence and independence). The 10 items contribute reliably to the measurement of HRQL in PH. To do this, we required all items to fit a unidimensional model whereby the underlying trait (i.e. HRQL) has a single dimension on which all of the test items rely. This process may have excluded items that may have behaved differently, with different measurement properties. Our approach created a pragmatic instrument with clinical utility.

There are a number of limitations in this study. The population studied have various forms of PH and are representative of the typical patients under chronic follow up in a UK pulmonary hypertension centre. The vast majority had PAH where we feel this questionnaire is likely to have most value. Further studies need to be performed in other important forms of PH such as CTEPH given the relatively small numbers in this group. The questionnaire is not currently recommended for use in other forms of PH such as PH owing to left heart disease or respiratory disease, given the small number of patients included in this study. The patients who were interviewed were at different points on the illness trajectory with many having relatively long standing disease and it is likely that the duration of disease will impact on HRQL. The current study presents cross-sectional data; a prospective longitudinal study would be required to test the sensitivity of the instrument to change over time. We used data from the item reduction stage (stage 2) to test concurrent validity of the emPHasis-10
with other relevant outcomes. These preliminary results require subsequent validation in a separate study. We have compared emPHasis-10 to a number of other questionnaires but not to CAMPHOR, unfortunately at the time that this study was conducted, permission to use in this study was declined. Currently emPHasis-10 is only available in English but the PHA-UK is in the process of making this available in a number of different languages.

In conclusion, the emPHasis-10 is a short, simple questionnaire for assessing HRQL in PH. It has excellent measurement properties and construct validity, and is sensitive to differences in clinical parameters. Further work is required to evaluate its value in routine clinical practice and to assess the impact of treatment interventions in various form of PH. A number of HRQL questionnaires are not freely available and various copyright laws preclude their use by both the clinical and academic community. The PHA-UK (The UK Patients Association) has funded this study with the specific intention of making it free to use by both the clinical and academic communities.
SUPPORT STATEMENT

This study was funded by the Pulmonary Hypertension Association UK

STATEMENT OF INTEREST

No authors have any conflicts of interest to declare.

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References

1. Yi L, Johnson M, Kiely DG, et al. Changing demographics and epidemiology of incident idiopathic pulmonary arterial hypertension. *Am J Resp Crit Care Med* 2012; 186: 790-796.

2. Hurdman J, Condliffe R, Elliot CA, et al. ASPIRE Registry: assessing the spectrum of pulmonary hypertension identified at a referral centre. *Eur Respir J* 2012; 39: 945-955.

3. Kiely DG, Elliot CA, Sabroe I, Condliffe R. Pulmonary hypertension: diagnosis and management. *BMJ* 2013; 346: f2028.

4. Armstrong I, Harries C, Rochnia N, Yorke J. The trajectory to diagnosis with pulmonary hypertension: a qualitative study. *BMJ Open* 2012; eScholarID:000806 doi:10.1136/bmjopen-2011-000806.

5. McDonough A, Matura LA, Carroll DL. Symptom experience of pulmonary arterial hypertension patients. *Clinical Nursing Research* 2011; 20: 120-134.

6. Lowe B, Grafe K, Ufer C, et al. Anxiety and depression in patients with pulmonary hypertension. *Psychosomatic Medicine* 2004; 66: 831-836.

7. Flattery MP, Pinson JM, Savage L, Salyer J. Living with pulmonary arterial hypertension: patient’s experiences. *Heart Lung* 2005; 34:99e107.

8. McKenna SP, Doughty N, Meads DM, et al. The Cambridge pulmonary hypertension outcome review (CAMPHOR): a measure of health-related quality of life and quality of life for patients with pulmonary hypertension. *Quality of Life Research* 2006; 15:103-115.

9. Ware J, Kosinski M, Dewey JE. How to score version 2 of the SF-36 health survey. Lincoln, RI: *QualityMetric Incorporated* 2000.
10. Hunt SM, McEwan J. The development of a subjective health indicator. *Sociology of Health and Illness* 1980; 2: 231-246.

11. Rector TS, Kubo SH, Cohn JN. Patients’ self-assessment of their congestive heart failure. Part 2: Content, reliability and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. *Heart Failure* 1987; 198-209.

12. Gomberg-Maitlan M, Thenaappan T, Rizvi K, et al. United States Validation of the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR). *JHLT* 2008; 27: 124–130.

13. Coffin D, Duval K, Martel S, et al. Adaptation of the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) into French-Canadian and English-Canadian. *Can Respir. J* 2008; 15:77–83.

14. Ganderton L, Jenkins S, McKenna SP, et al. Validation of the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) for the Australian and New Zealand population. *Respirology* 2011; 16: 1235-1240.

15. Taichman DB, Shin J, Hud J, et al. Health-related quality of life in patients with pulmonary arterial hypertension. *Respir Res* 2005; 6:92.

16. Suntharalingam J, Treacy CM, Doughty NJ, et al. Long-term use of Sildenafil in Inoperable Chronic Thromboembolic Pulmonary Hypertension. *Chest* 2008; 229-236.

17. Galie N, Hoeper MM, Humbert M, et al. Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heat J* 2009; 30: 2493-2537.

18. Drennan J. Cognitive interviewing: verbal data in the design and pretesting of questionnaires. *JAN* 2003; 42: 57-63.

19. Cenedese E, Speich R, Dorschner S, et al. Measurement of quality of life in pulmonary hypertension and its significance. *Eur Resp J* 2006; 28: 808-815.
20. Zlupko M, Harhay MO, Gallop R, et al. Evaluation of disease-specific health-related quality of life in patients with pulmonary arterial hypertension. Respir Med. 2008;102:1431-8.

21. Yorke J, Moosavi SH, Shuldham C, et al. Quantification of breathlessness using descriptors: development and initial testing of Dyspnoea-12. Thorax 2010; 65:21-26.

22. Yorke J, Swigris J, Russell AM, et al. Dyspnoea-12 is a valid and reliable measure of breathlessness in patients with interstitial lung disease. Chest 2011; 139: 159-164.

23. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scandinavica 1983; 67:361-370.

24. Yorke J, Horton M, Jones PW. A critique of Rasch analysis using the Dyspnoea-12 as an illustrative example. Journal of Advanced Nursing 2011; 68:191-98.

25. O'Leary CJ, Jones PW. The influence of decisions made by developers on health status questionnaire content. Quality of Life Research 1998; 7:545-50.

26. Rattray J, Jones MC. Essential elements of questionnaire design and development. JCN 2007; 16: 234-243.

27. Pallant JF, Tennant A. An introduction to the Rasch measurement model: an example using the Hospital Anxiety and Depression Scale (HADS). British Journal of Clinical Psychology 2007; 46: 1–18.

28. Cronbach L. Coefficient alpha and the internal structure of tests. Psychometrika 1951; 22:293e6.

29. Bland J, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307e10.

30. Jones PW, Harding G, Berry P, et al. Development and first validation of the COPD Assessment test. Eur Respir J 2009; 34: 648–654.
Table 1: Participant characteristics - Qualitative phase

|                             | Number of patients (N = 30) |
|-----------------------------|-----------------------------|
| Sex (female: male)          | 18:12                       |
| Age (mean years (SD; range) | 56.3 (38; 26-80)            |
| Aetiology of pulmonary hypertension |                             |
| Group 1: Pulmonary arterial hypertension |             |
| Idiopathic                  | 12                          |
| Connective tissue disease   | 7                           |
| Congenital heart disease    | 5                           |
| Heritable                   | 1                           |
| Portal hypertension         | 1                           |
| Drugs/toxins                | 1                           |
| Group 3: Owing to Respiratory Disease | 1          |
| Group 4: Chronic thromboembolic PH | 2           |
| Time since PAH diagnosis    |                             |
| < 1 year                    | 2                           |
| 1 - < 3 years               | 2                           |
| 3 - < 5 years               | 7                           |
| 5 - < 10 years              | 12                          |
| > 10 years                  | 7                           |
| WHO Functional Class        |                             |
| I                           | 0                           |
| II                          | 9                           |
| III                         | 19                          |
| IV                          | 2                           |
Table 2: Participant characteristics – Item reduction phase

| Participant characteristics                              | n (%) except as indicated |
|----------------------------------------------------------|---------------------------|
| Patients, N                                              | 226                       |
| Female                                                   | 157 (70)                  |
| Age, years (mean ±SD)                                    | Mean 55.6 ± 14            |
| **Aetiology of pulmonary hypertension**                  |                           |
| Group 1: Pulmonary arterial hypertension                 |                           |
|   Idiopathic                                             | 89 (40)                   |
|   Congenital heart disease                               | 50 (22)                   |
|   Connective tissue disease                              | 43 (19)                   |
|   Heritable                                              | 3 (1)                     |
|   Portal hypertension                                    | 1 (0.5)                   |
| Group 2: PH-Left heart disease                           | 1 (0.5)                   |
| Group 3: PH-Lung                                         | 1 (0.5)                   |
| Group 4: Chronic thromboembolic PH                       | 36 (16)                   |
| Group 5 (neurofibromatosis & sarcoidosis)                | 2 (1)                     |
| **PH therapy**                                           |                           |
| Mono-therapy                                             | 125 (55)                  |
| Dual-therapy                                             | 78 (35)                   |
| Triple-therapy                                           | 11 (5)                    |
| Not recorded                                             | 12 (5)                    |
| **Route**                                                |                           |
|   Inhaled iloprost                                       |                           |
|     Intravenous iloprost                                 | 20 (9)                    |
|     Intravenous treprostinil                             | 8 (4)                     |
| - Intravenous epoprostenol | 5 (2) |
|---------------------------|-------|
|                           | 4 (2) |

**Oxygen use (continuous or as needed)** 87 (38)

**6-MWD, metres (mean ± SD) (n = 98)** *

336 ± 130

**Employment status**

|               |       |
|---------------|-------|
| Fulltime work | 25 (11) |
| Part-time work | 31 (14) |
| Student       | 2 (1)  |
| Unemployed/retired | 168 (74) |

**WHO FC**

|   |       |
|---|-------|
| I | 3 (1) |
| II | 73 (32) |
| III | 115 (51) |
| IV | 34 (15) |

**MLHF-mPH (mean ± SD)** 47.8 ± 25

**HADS**

|               |       |
|---------------|-------|
| Total         | 13.3 ± 7.5 |
| Anxiety       | 6.9 ± 4.4 |
| Depression    | 6.3 ± 3.9 |

**D-12**

|               |       |
|---------------|-------|
| Total         | 12.8 ± 9.8 |
| Physical      | 8.5 ± 5.8 |
| Affective     | 4.4 ± 4.6 |
PH: pulmonary hypertension; 6MWD: six-minute walk distance; FC: World Health Organisation Functional Class; MLHFQ-PH: Minnesota Living with Heart Failure Questionnaire – modified pulmonary hypertension; HADS: Hospital anxiety and depressions scale; D-12: Dyspnoea-12 questionnaire

*Patients attending the Sheffield Pulmonary Vascular Disease Unit (n= 66) underwent exercise testing with the incremental shuttle walking test and did not perform the 6-MWD
Figure 1: Distribution of patients and items based on Rasch logit locations. This figure shows the distributions of patient HRQL severity and item severity (locations) along the same linear scale measured in logits. Patients are on the upper part of the graph and item locations on the lower part. Most items are located between -2 and +2 logits.
Figure 2: The final emPHasis-10. The PHA-UK (The UK Patients Association) has funded this study with the specific intention of making it free to use by both the clinical and academic communities. It can be downloaded free of charge from the PHA-UK website and reproduced without cost for clinical and academic use. Various different language versions will be made available in due course.
Figure 3: Mean emPHasis-10 scores for each WHO functional class