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Early View

Research Letter

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Comparability, acceptability and longitudinal adherence with digital emPHasis-10 in pulmonary arterial hypertension

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To the Editor:

Pulmonary hypertension (PH) affects 1% of the global population and significantly impacts health-related quality of life (HRQoL).[1,2] Patient reported outcome measures (PROMs) are standardised tools used in clinical practice and research to assess health outcomes from the patient's perspective. Routine measurement of HRQoL is supported by clinical guidelines, recommending disease-specific PROMs.[1] EmPHasis-10 is a widely used ten-item PROM developed for patients in any World Health Organisation (WHO) PH group.[2,3] Available in numerous languages, it has strengths in both its psychometric properties and feasibility.[2,4] However, it is currently only available in a paper-based format.

Electronic PROMs (ePROMs), such as those delivered on smartphone applications (apps), are recommended by international stakeholders and regulatory bodies.[5-8] Advantages include improved data integrity and accuracy, facilitation and tracking of 'skip' patterns, high acceptability, better compliance, increased power leading to smaller sample sizes, and easier processing.[9] The capacity for patients to use their own devices and the ubiquity of smartphones could reduce trial delivery costs whilst maintaining equitable access. Offering a choice of PROM formats is expected to enhance inclusion and engagement.[8,10,11]

International guidelines recommend evaluation of alternative PROM formats to ensure that measurement properties do not change and only recommend full psychometric validation where certain criteria are met.[8,9] We report the first study evaluating digital and paper emPHasis-10 equivalence, longitudinal adherence and acceptability from the patients' perspective.

As part of a United Kingdom (UK) multi-centre prospective observational study, adult patients with pulmonary arterial hypertension (PAH) consented to participate in Cohort-Digital (IRAS 123349, REC 13/EE/0203) and/or Feasibility of Novel Clinical Trial Infrastructure, Design and Technology for Early Phase Studies in Pulmonary Hypertension (FIT-PH, NCT04078243, REC 19/YH/0354). Participants completed the paper-based emPHasis-10 and the digital format via the Atom5™ app (iOS or Android) as a "bring your own device" study.[12] Participants received fortnightly pre-programmed push notifications (alerts) for a 26-week period asking them to remotely complete the digital emPHasis-10. Passive compliance was audited, with no additional active adherence interventions deployed. Patients could contact the study team for technical assistance if required, and although not audited systematically, this was rare.

A predominantly prevalent and stable PAH population was prioritised. International PROM development guidelines recommend a minimum sample size of fifty for evaluation of measurement error[13]. Stability was determined by a patient-reported neutral score (-1, 0 or +1) on a digital subjective global anchor rating scale (-3 to +3)

asking "*with respect to your pulmonary hypertension, how would you describe yourself NOW compared to when you last completed this questionnaire?*". The UTAUT (Unified Theory of Acceptance and Use of Technology) underpinned a digital survey to evaluate themes of usability and acceptability.[14]

Digital emPHasis-10 was developed and tested with focus groups of patients with PH in collaboration with Pulmonary Hypertension Association UK. Following international recommendations, full psychometric evaluation was not required as the format change from paper to digital was mild to moderate.[9] These 'non-substantive' formatting differences included (a) change in instructions from "placing a tick" (boxes) to "selecting the number" (Likert scale) (b) change from ten items on a single sheet to one item per screen (c) no total score immediately visible on the digital version and (d) automated date and time stamping of digital completion.

Fifty-one patients were enrolled: median age 53 years (IQR 41-62), 71% female, 81% white. Most (41/51; 80%) had a diagnosis of idiopathic PAH and the median time since diagnosis was 5 years (IQR 1-11.5). 82% of patients had a low/intermediate-low COMPERA 2.0 risk score with WHO Functional Class I/II/III/ IV as 7/41/50/ 2%. respectively. The cohort was geographically diverse, with patients enrolled from across the UK.

Fifty-seven pairs of digital/paper PROMs (from multiple clinic visits) were available for evaluation from stable patients. Median time between digital and paper completion was +1 day (IQR 0 to 5) with a range of up to 31 days between formats where patients reported no significant change in their HRQoL as evaluated using the patient-reported anchor score. Paired samples from two participants were excluded after reporting they completed the digital format incorrectly, accidentally inverting the scales. Samples where patients reported a change in HRQoL on the global anchor scale were not included for equivalence comparison.

Mean scores were equal at 20/50 (±14) with standard error of measurement (SEM) of 2. Scores were consistent between paper and digital formats (Spearman's r=0.98, $p<0.0001$, Cronbach's alpha 0.99). Bland Altman analysis (n=57) showed a bias (systematic error) of 0.15 (SD 2.3) with 95% limits of agreement from -4.7 to 4.4 (Figure 1A). All random variation fell below the thresholds estimated to be the MCID (Figure 1A).[15,16]

The overall adherence (Cohort Digital n=49) to completing fortnightly ePROMs was a median of 79% (IQR 29% to 100%) and 29% (14/49) of patients achieved 100% compliance. This included one participant who withdrew from the study before accessing the app. There was a steady drop-off in completion during the first six weeks of the study before reaching a plateau of 61% by 26 weeks (Figure 1B).

Patient-reported acceptability of the app-based emPHasis-10 was high (Figure 1C), consistent with other studies showing preferences for ePROMs[17]. Most participants reported finding it useful, usable, preferable and would use it again in clinical practice or research if available, without major barriers to adoption.

The primary finding from this study is that patients responded consistently between paper and digital formats of emPHasis-10. A further strength is the consistency of PROM scores with patient-reported stability, highlighting the value of anchor-based methodology. Based on the strong association, consistency and acceptability metrics, we suggest that paper or digital formats can be selected in accordance with patient preference, trial design or clinical setting.

The small SEM (score of 2) of digital emPHasis-10 during a period of self-reported stability suggests that a threshold of >2 could be significant. Low scoring variability suggests that emPHasis-10 may be sensitive to changes below the registry-estimated MCIDs of 6 to 8[15,16]. Evaluation of responsiveness of digital emPHasis-10 is underway through on-going therapeutic trials.[18,19]

Most patients regularly used the ePROM. The observed drop-off over six months is a recognised phenomenon.[17] The modest initial disengagement could be mitigated by making the tool seemingly more interactive or useful, such as diarising ePROM scores over time - a function we have subsequently co-developed with patients. This tracker function also aims to reassure patients that data is not lost, a concern expressed on the UTAUT survey. An “investigator in the loop” design, rather than solely notification-driven reminders, is recommended to maximise completion rates, address technical issues and prevent drop-off, as supported by our usability data and the literature[20]. Strategies to optimise longitudinal adherence are ongoing through the Cohort-Digital randomised study.

In conclusion, this is the first equivalence evaluation of a digital format of emPHasis-10. Established using a patient-reported anchor question, this methodology follows international recommendations and strengthens the field in HRQoL outcome measurement, with broad applicability. This ePROM is highly acceptable to patients with PAH and has reasonable adherence longer-term. The digital format will allow for more frequent, convenient and remote collection of meaningful HRQoL data in both clinical practice and trials.

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Declarations of interest

Professor DG Kiely and Dr I Armstrong were involved in the derivation of EmPHasis-10. EHD is an employee of Aparito Ltd. These authors contributed to reviewing the manuscript, but statistical analysis was performed independently by JN/FV. Other authors have no conflicts of interest.

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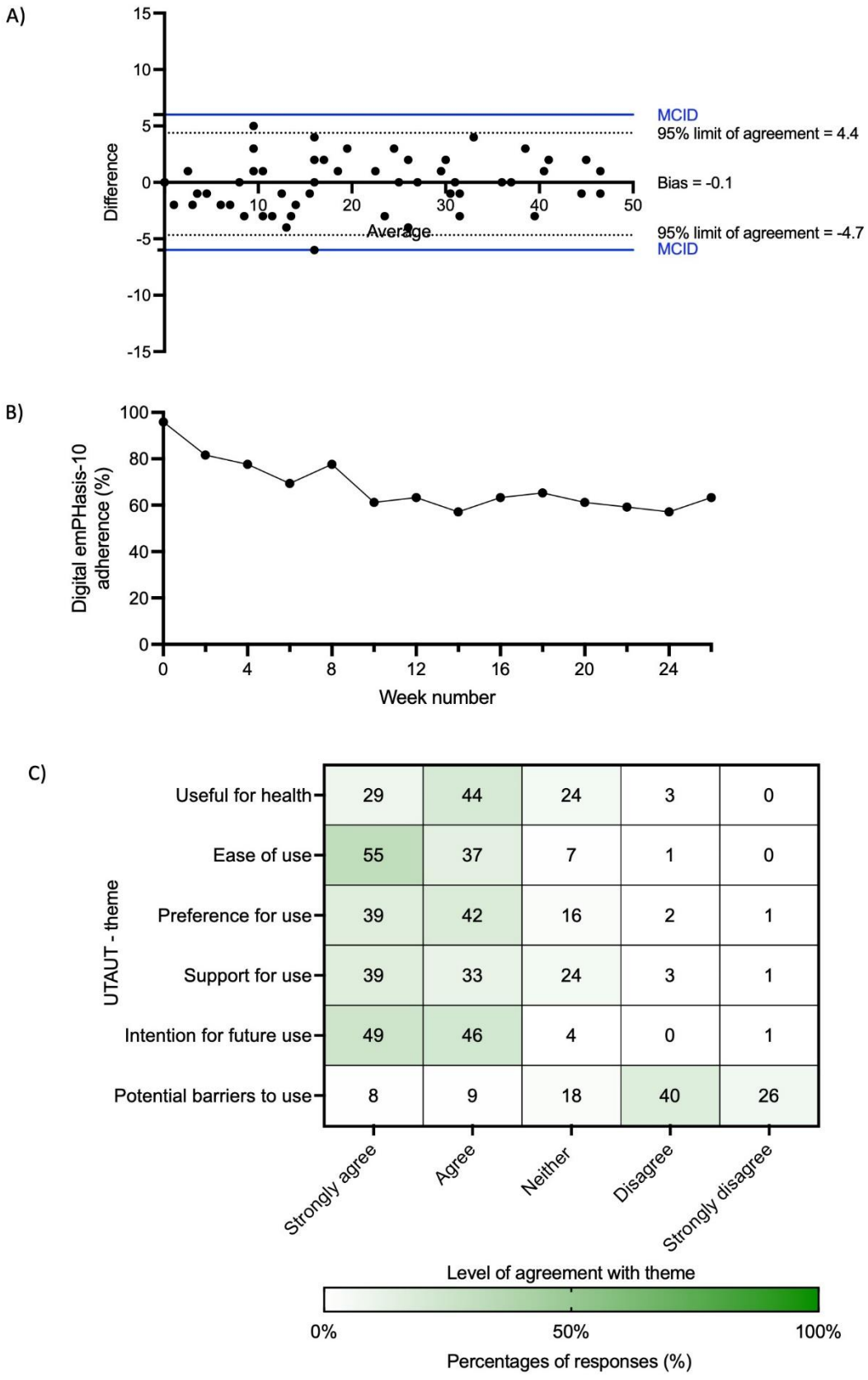

Figure 1