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RESEARCH ARTICLE

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Remote exercise testing in pulmonary hypertension (PHRET)

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Abstract

Remote exercise tests for patients with pulmonary hypertension (PH) would improve the telemedicine strategies in this disease. The PHRET study assessed the validity and feasibility of four remote exercise tests performed by PH patients at home. Participants undergoing diagnostic assessment for PH were included. At baseline, patients completed a 6MWT followed by a range of study tests including a Timed Up and Go (TUG) test, a Sit-to-Stand (STS), a Step Test (ST), and a tele-6MWT (T6MWT) performed outside using a GPS-enabled smartphone. Patients performed these tests at home following discharge and at first follow-up. Analysis focused on comparing the results of study tests to the standard 6MWT. The discontinuation rate was 15%. Ninety-seven percent of patients were able to complete a TUG, 92% a STS, 73% a ST, and 49% a T6MWT. At baseline, correlation between the standard 6MWT and study tests, respectively, was T6MWT 0.93, ST 0.78, STS 0.71, and TUG −0.76 ($p < 0.001$). Direction of change in the study test agreed with the standard 6MWT in 68% of the follow-up ST, 68% of the STS, 71% of the TUG, and 79% of the T6MWT. Patients were able to complete the tests at home, there were no adverse incidents and ≥92% of patients were happy to continue performing home tests. Remote exercise testing is feasible. The T6MWT was a valid remote measure of exercise capacity, but could only be performed by a limited number of patients. The high discontinuation rate may impact the utility of remote tests.

KEYWORDS
6-min walk test, risk assessment, risk stratification, telehealth, telemedicine

INTRODUCTION

Exercise intolerance is a hallmark feature of pulmonary hypertension (PH).[1] The 6-min walk test (6MWT) is a validated tool in PH and the 6-min walk distance (6MWD) is incorporated into risk assessment tools at baseline and follow-up.[2,3] While the 6MWT is low cost, standardized, simple, and easily interpretable, it requires a technician to administer the test, a corridor of sufficient length and patients to travel to a healthcare facility for assessment and supervision.[4] Furthermore, a proportion of patients with PH will be unable to undertake a 6MWT due to disease severity, frailty or other mobility issues, such as joint pain. During the 2019 coronavirus pandemic, face-to-face contact between healthcare providers and PH patients was limited and while PH centers responded rapidly and many outpatient services continued in a teleclinic setting, these were not informed by the results of functional capacity testing.[5–8]

Studies, predominantly over the last decade, have investigated the feasibility and benefits of remote assessment of exercise capacity and alternative capacity tests among patients with PH.[9–15] However, few studies have assessed the ongoing feasibility of performing such tests at home, or whether change in study test results are concordant with other measures of risk stratification. Alternative and remote tests may allow a greater proportion of patients to participate in an assessment of exercise capacity, including those who cannot use or own a smartphone, or who cannot complete a conventional face-to-face 6MWT. The majority of PH patients in the UK have a travel time of greater than 1 h to attend clinic appointments, are concerned about contracting nosocomial infections while in hospital and 93% would be happy for some of aspects of their PH care to be remote.[16] Previous work has demonstrated that patients are willing to participate in remote exercise capacity assessments and felt this was feasible.[17] The Remote Exercise Testing in Pulmonary Hypertension (PHRET) study aimed to assess the feasibility, safety, and validity of four exercise capacity tests that could be performed by patients with PH when tested at home while further examining patients' opinions on such tests.

METHODS

Patient selection

Patients were recruited between June 2021 and November 2022, at the time of their diagnosis with PH during a diagnostic admission at the Scottish Pulmonary Vascular Unit (SPVU), the PH referral center for Scotland. Patients aged ≥16 years old, who were able to give informed consent and with PH based on the European Respiratory Society/European Society of Cardiology 2015 guidelines (mean pulmonary artery pressure ≥ 25 mmHg) from any clinical classification were included.[18] Patients who were deemed to be clinically unstable or who could not perform any of the four tests (either due to the severity of PH symptoms or mobility) were excluded.

Study exercise tests

Four exercise tests were studied; a 3-m Timed Up and Go test (TUG), a 2-min Step Test (ST), a 1-min Sit-to-Stand test (STS), and a tele-6MWT (T6MWT). The tests were chosen as they were felt to represent a spectrum of user-friendliness for PH patients, with previous work demonstrating that patients felt they were feasible to perform at home.[17] Previous studies have demonstrated the clinimetric properties, including the test retest reliability, of these four tests.[9,10,19–21] The T6MWT employed a smartphone application (*Timed Walk)* available for free on the iOS App Store and Android Play Store which has been previously validated in healthy and PAH populations.[9,10] The research team and participant chose which of the four exercise tests the patient would prefer to perform, based on pre-existing symptoms, mobility, joint pain, whether a patient required long-term oxygen, and whether they owned and felt confident operating a smartphone. They continued to perform the same selection of tests throughout the study period. Patients were given brief verbal instructions on how to complete each test and were provided with written instructions for use at home (Supporting Information: Box S1). Participants performing the ST and/or the T6MWT were provided with a pulse oximeter (PO6L, Kinetik Wellbeing) and a 15 cm step (Fitness Step, Denny Enterprises Intl Ltd). Further details on the procedures of these tests are available in Supporting Information: Table S1.

A standard 6MWT was performed at Visit 1 and Visit 4 in a 30 m corridor according to standardized protocols.[4] Complaints and complications during administration of the tests at all stages were collected. Data were collected on safety, by noting the number of adverse events, and feasibility, by noting the number of participants taking each test. Participants were permitted to use an assistant for time keeping at home. Routine clinical data were extracted from electronic records at the time of diagnosis and first follow-up (Visits 1 and 4). The Visit structure was as follows;

1. *Visit 1*: During standard diagnostic admission. Following completion of the standard 6MWT, participants rested for

at least 30 min and then were observed in completing the selected study once fully recovered. Patients were commenced on pulmonary vasodilator treatment before discharge if clinically appropriate.
2. *Visit 2*: Within 7 days of discharge home, patients performed the selected study tests at home and relayed the results to the research team by email or telephone.
3. *Visit 3*: At home, patients performed the selected study tests within the 7 days before the first follow-up.
4. *Visit 4*: Standard first follow-up face-to-face review, including a standard 6MWT. A questionnaire concerning the study tests was completed by participants (Supporting Information: Box S2).

Statistical analysis

Statistical analysis was performed on GraphPad Prism (version 9.3.0 for Windows, GraphPad Software). Significance was set at the $p < 0.05$ level. The primary outcome was the comparison between study tests and the standard 6MWT. Agreement between tests with the same outcome measure was performed using Bland–Altman analysis.[22] Pearson's and Spearman's correlation coefficient (r) with 95% confidence intervals were used for parametric and non-parametric data, respectively. The agreement of concordance of change (where the study test agreed with improvement, no change or deterioration to the standard 6MWT) was assessed at follow-up. A sensitivity analysis was performed on the results, with outliers systematically removed and the results reviewed following each removal to detect the effect on models. The number and proportion of patients reporting test acceptance and adverse events were reported at each Visit. The study was approved by the South Central—Oxford A Research Ethics Committee (Ref 21/SC/0083).

RESULTS

Patient demographics

Fifty-nine patients were included in the baseline cohort with demographics provided in Table 1. The flow of patients into the follow-up cohort is shown in Figure 1. In total, nine patients discontinued from the study (discontinuation rate 15.3%) due to lack of engagement, death, or joint pain. Five patients became unwell following diagnosis and were unable to continue the study while three patients were discharged; hence, 42 patients completed full follow-up (71.8%). Forty-nine percent of patients were initially treated with monotherapy, as patients with chronic thromboembolic

TABLE 1 Patient demographics, haemodynamics, and treatments at baseline (Visit 1).

	Total = 59
Diagnosis, n (%)	
Group I (Pulmonary arterial hypertension, PAH)	20 (33.9)
Idiopathic PAH	9 (15.3)
Pulmonary veno-occlusive disease	1 (1.7)
Connective tissue disease PAH	6 (10.2)
DI-PAH	1 (1.7)
CHD-PAH	2 (3.4)
Portopulmonary PH	1 (1.7)
Pulmonary hypertension due to left heart disease	6 (10.2)
Pulmonary hypertension due to chronic lung disease	7 (11.9)
Chronic Thromboembolic Pulmonary Hypertension	21 (35.6)
Group V Pulmonary Hypertension	3 (5.1)
Demographics	
Age (years)	63 ± 13
Male, *n* (%)	26 (44)
BMI (kg/m^2)	29.2 ± 6.5
WHO functional class	
I	1 (2)
II	32 (54)
III	25 (42)
IV	1 (2)
NT-proBNP (pg/mL), median (IQR)	810 (236–2569)
Diffusion capacity of carbon monoxide (DL_{CO})	
mmol/(min kPa)	4.2 ± 2.0
% predicted	53 ± 21
6MWT Distance (m)	340 ± 13
COMPERA 2.0 Risk Score	
Low risk	16 (27)
Intermediate-low risk	23 (39)
Intermediate-high risk	13 (22)
High risk	7 (12)
Emphasis-10 score	28 ± 13
Internet-enabled smartphone owners, *n* (%)	50 (86)
Long-term oxygen therapy, *n* (%)	8 (14)
Comorbidities, *n* (%)	

(Continues)

TABLE 1 (Continued)

	Total = 59
Obesity (BMI ≥ 30 kg/m^2)	17 (29)
Coronary artery disease	4 (7)
Diabetes mellitus	6 (10)
Systemic hypertension	13 (22)
Atrial fibrillation	10 (17)
Chronic obstructive pulmonary disease	11 (19)
Interstitial lung disease	8 (14)
Echocardiogram	
Right ventricular end diastolic diameter (cm)	3.9 ± 0.9
Tricuspid annular plane systolic excursion (cm)	1.6 ± 0.5
Right atrial area (cm^2)	21.6 ± 6.4
Right heart catheterization	
Right atrial pressure (mm Hg)	7 ± 5
Mean pulmonary artery pressure (mm Hg)	39 ± 11
Pulmonary artery wedge pressure (mm Hg)	9 ± 4
Cardiac index (L/min/m^2)	2.5 ± 1.1
Pulmonary vascular resistance (woods units, WU)	7.5 ± 4.3
Mixed venous saturation (%)	62.7 ± 8.2
Initial therapy	
Monotherapy	29 (49)
Dual therapy	23 (39)
Triple therapy	3 (5)
No therapy	4 (7)
Prostacyclin infusion therapy	4 (7)

Note: Data are presented as mean ± SD, number (%), or median (interquartile range).

Abbreviations: BMI, body mass index; CHD-PAH, congenital heart disease PAH; DIPAH, drug-induced PAH; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; 6MWT, 6-min walk test.

pulmonary hypertension were medically managed while awaiting a surgical opinion and patients with PH due to chronic lung disease were treated with a trial of phosphodiesterase-5 inhibitor.

Performance of study tests at baseline

After consultation between the patient and research team, 59 (97%) of patients elected to participate in the TUG, 43 (73%) an ST, 54 (92%) an STS, and 29 (49%) a T6MWT. Eight patients (13.5%) cited joint pain as the predominant reason for being unable to participate in the ST and T6MWT, four patients (6.7%) wished to take part in the T6MWT at baseline, but this could not be performed outdoors due to inclement weather on that day. Forty-six percent of patients were able to perform all four study tests.

There was an excellent correlation between the T6MWT walk distance and the standard 6MWD ($r = 0.93$, 95% confidence interval [CI]: 0.85–0.96, $p < 0.001$, Figure 2a). Bland–Altman analysis shows T6MWT results were systematically higher than standard 6MWD (bias +25 m, SD ± 38) with limits of agreement from −50 to +101 m (Figure 2b). The correlation between the standard 6MWT and the ST was 0.78 (95% CI: 0.62–0.87, $p < 0.001$) and STS 0.71 (95% CI: 0.54–0.82, $p < 0.001$) (Figure 2c,d). Sensitivity analysis of the TUG demonstrated the effect from three outliers (TUG > 30 s, Figure S1) and following removal the correlation was $r = -0.76$ (95% CI −0.86 to −0.64, $p < 0.001$) (Figure 2e).

Remote study tests

Nine patients did not proceed to Visit 2 for reasons detailed in Figure 1, with 50 patients proceeding to Visit 2. All patients who proceeded to Visit 2 were able to perform the tests at home without adverse incidents. Agreement analysis was not performed between the study tests at Visit 1 and Visit 2 due to the confounding effect from targeted pulmonary vasodilator therapy between these time points.

Concordance of change following treatment

Eight patients did not proceed from Visit 2, with 42 patients proceeding to Visits 3 and 4 (Figure 1). The mean time between Visits 1 and 4 was 116 days (SD ± 33). Between Visit 1 and Visit 4, eight participants (14%) moved into a higher-risk COMPERA 2.0 stratum and 19 (32%) moved into a lower-risk stratum. The mean change in standard 6MWT distance was +29 (SD ± 70 m) and NT-proBNP was −1165 pg/mL (SD ± 2113).

Sensitivity analysis was performed with outliers removed from results at follow-up (Figure S2). Two participants were removed from the STS analysis (>100% increase in STS result) and one patient was removed from TUG and STS analysis (197% increase in standard 6MWT). Figure 3 demonstrates the proportion of change in each study test (at Visit 1 and Visit 3) when compared

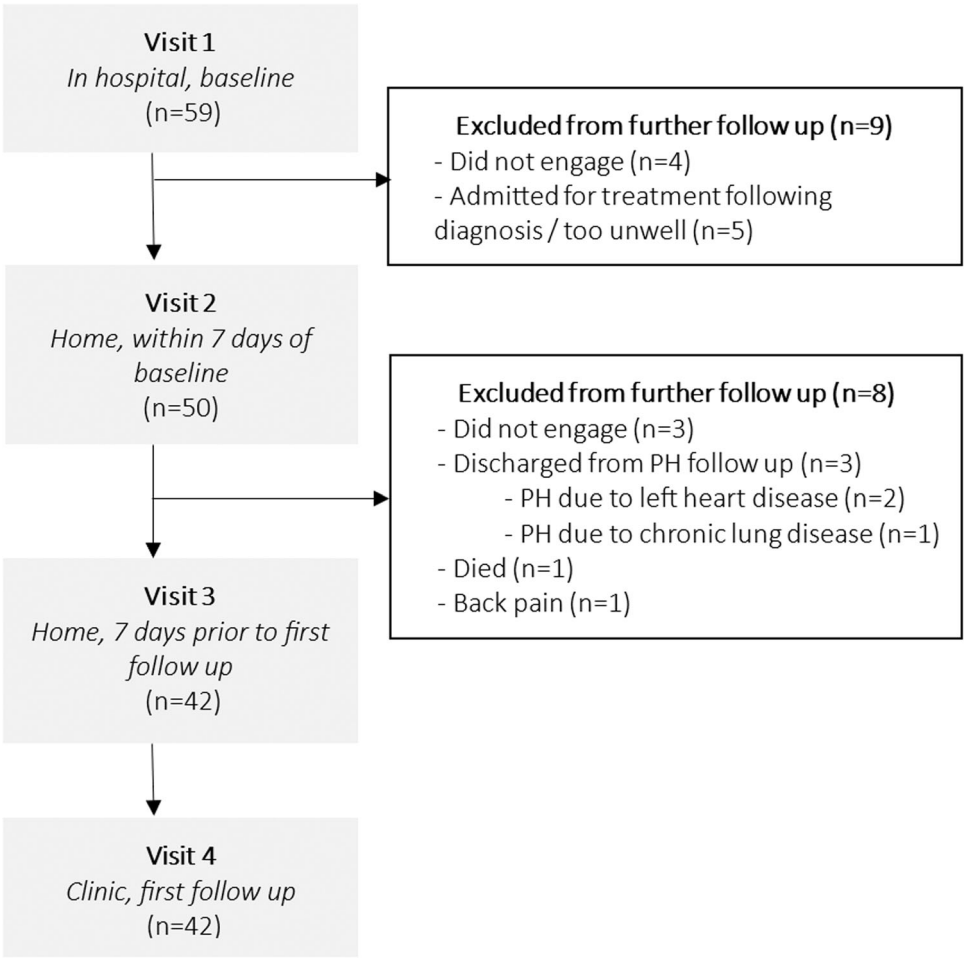

FIGURE 1 CONSORT patient inclusion flow diagram.

to the standard 6MWT (at Visits 1 and 4) and includes the numbers included in each analysis. Direction of change in the study test agreed with that in the standard 6MWT in 79% of the follow-up T6MWT, 68% of the ST, 66% of the STS, and 71% of the TUG. When the COMPERA 2.0 thresholds for 6MWD are applied[23] and when compared to the standard 6MWT, 8 of 24 (33%) participants were classed into a different risk stratum based on the T6MWT result. In 92% of cases, there was agreement of concordance with at least one of the study tests, when compared to the standard 6MWT.

Three subanalyses were performed. (i) When the concordance of change in the study tests was compared to NT-proBNP instead of the standard 6MWT, the agreement was 68% for the T6MWT, 58% of the STS, 68% of the STS, and 66% of the TUG. (ii) In patients with Group 1 PAH who were aged ≤70 years ($n = 15$), concordance of change improved to 82% for the T6MWT, 80% for the ST, 82% for the STS, and 91% for the TUG. (iii) In the 24 patients who performed a T6MWT at follow-up, the concordance of change improved to 75% for the ST, 83% for STS, and 79% for the TUG.

Between baseline and follow-up (Visit 1 and Visit 4), 66% ($n = 27$) of the participants had study tests, all of which had agreement of concordance (i.e., in these participants, the study tests all agreed there had been an improvement, deterioration, or no change). In these 27 cases, the comparison of agreement to the change in the standard 6MWT was 81%.

Safety and feasibility

There were no adverse events reported during any of the study Visits. Four participants provided results demonstrating their end exercise oxygen saturation was <80% but did not report syncope, chest pain, or presyncope during the test. Three participants reported difficulties using the pulse oximeter at home.

Thirty-nine participants completed the end of study questionnaire. One hundred percent of participants reported they were able to complete their allocated study tests at home. Ninety-seven percent of respondents were "Very happy" or "Happy" to continue performing the

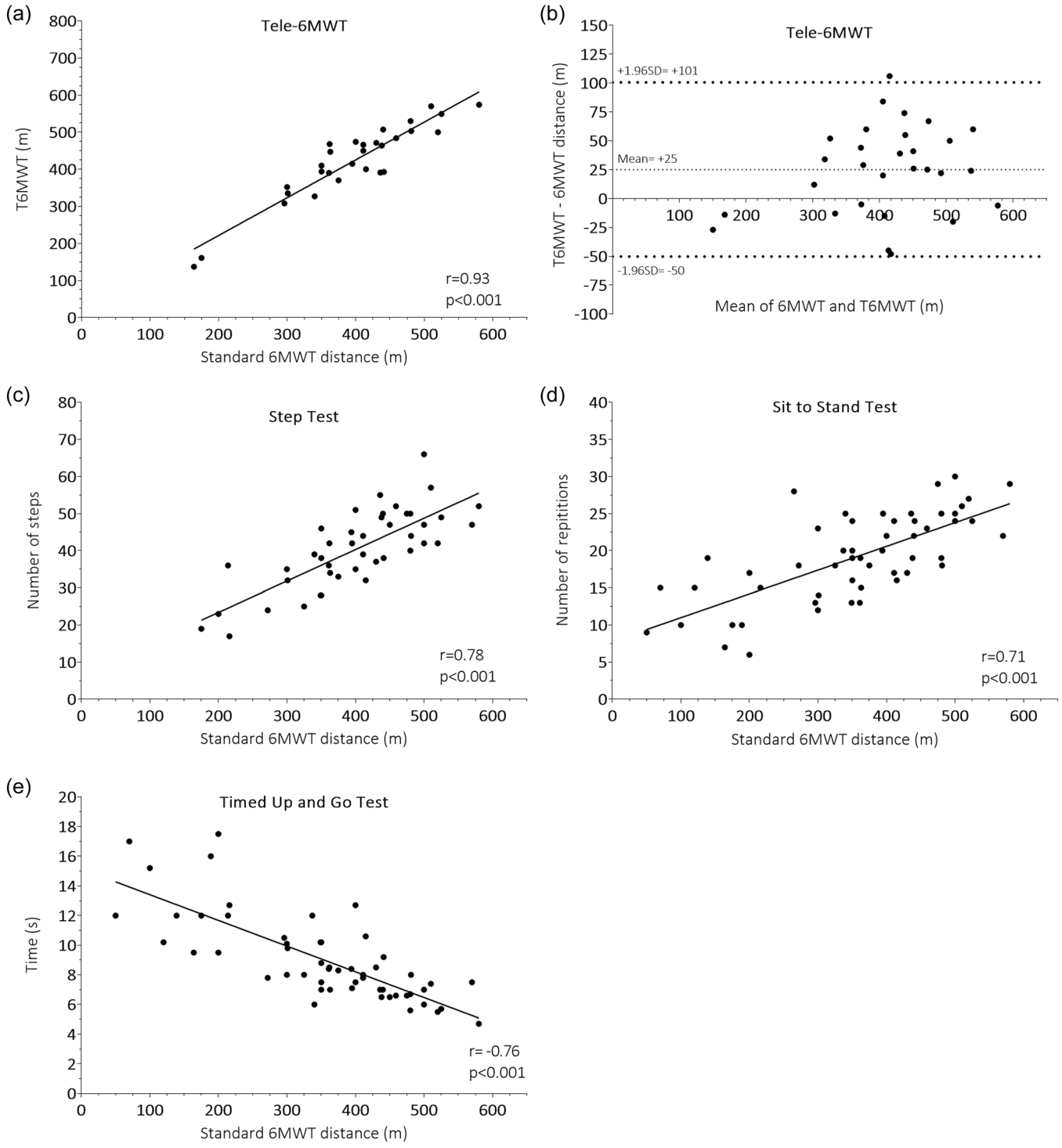

FIGURE 2 Performance of the study tests at baseline (Visit 1) as compared to the standard 6-min walk test. Correlation (a) and Bland–Altman analysis (b) are shown for the Tele-6MWT. Correlation is shown for the (c) Step Test, (d) Sit to Stand Test, and (e) Timed Up and Go Test.

TUG at home, 97% the STS, 93.3% the ST, and 92% the T6MWT. No patients reported they would be "Unhappy" or "Very Unhappy" to continue any of the tests. Positive feedback was similar for all four tests; 12 patients felt the tests allowed them to see improvement within themselves. Two participants reported the tests built their confidence in performing exercise at home independently, two patients reported the T6MWT was a better reflection of their capacity than an inside corridor walk test, one person reported the *Timed Walk* app was

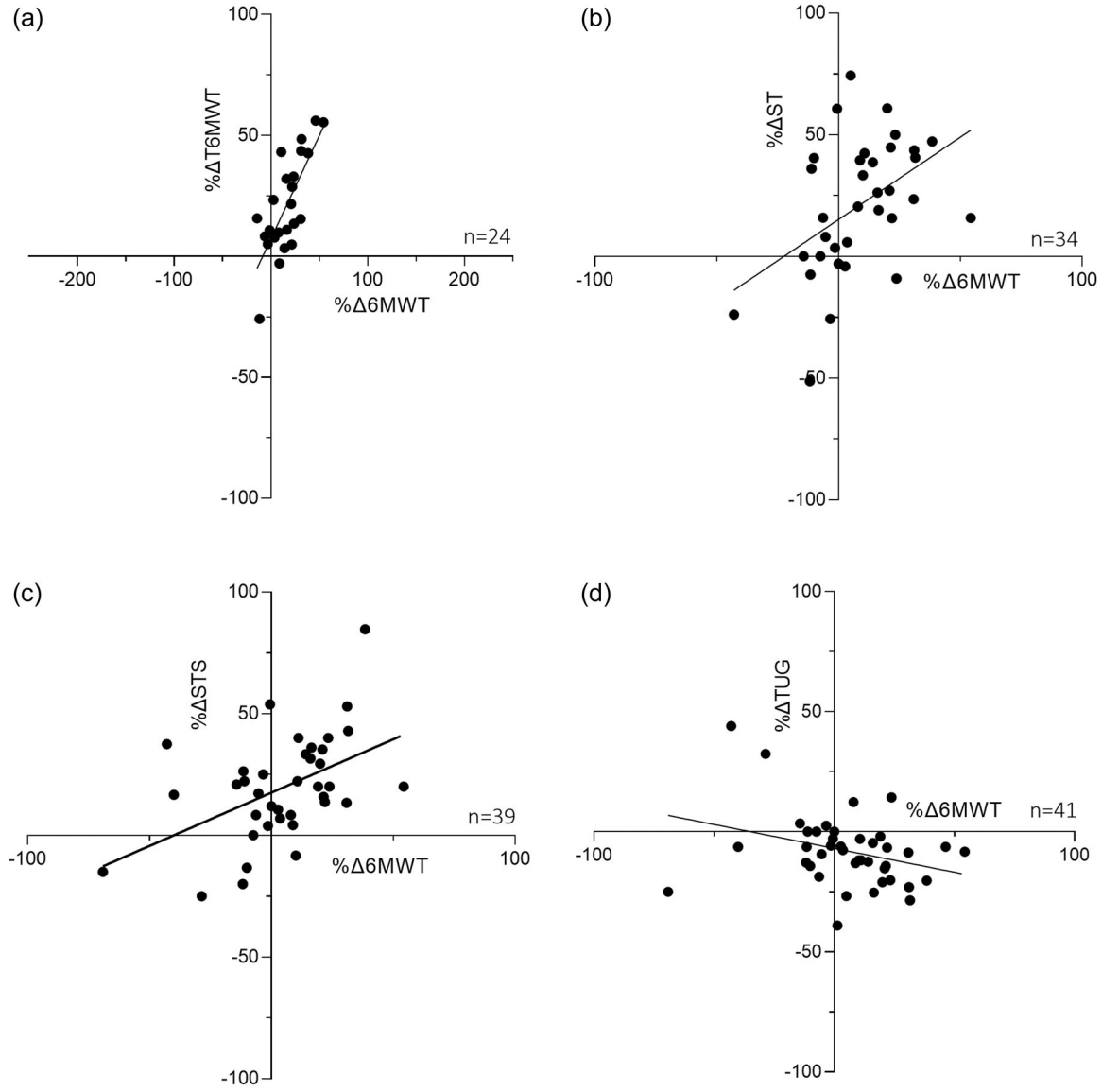

FIGURE 3 The percentage change of the (a) T6MWT, (b) Step Test, (c) Sit to Stand Test, and (d) Timed Up and Go Test between Visit 1 and Visit 3 when compared to the percentage change in the standard 6MWT between Visit 1 and Visit 4.

easy to use, and two participants reported finding the instructions easy to use. Negative feedback included four patients reporting the test was limited due to joint pain (particularly for the step test), three patients reported finding the tests made them feel very breathless, three patients reported the TUG was too short, and one patient reported that the T6MWT was difficult to perform outside in poor weather.

Discussion

Remote risk assessment in PH introduces benefits such as reducing lengthy transport to specialist centers, reducing patient exposure to commensal infections, and allowing ad hoc assessments at home.[24] However, remote assessment must be informed by objective results that can allow an accurate quantification of whether a patient is stable, improving, or deteriorating. This study demonstrates that the remote assessment of exercise capacity is feasible and safe in an incident PH population, but that results may not be as reliable as those obtained during on-site testing. There was a relatively high discontinuation rate which may impact the utility of remote tests in a remote clinic.

Patients were willing and able to perform a range of unsupervised home tests and high satisfaction rates were recorded and no adverse events. The T6MWT had good cross-sectional correlation and agreement to the standard 6MWT. It had a mean bias of +25 m, which is less than

most estimates of the minimally important clinical difference in pulmonary arterial hypertension, which range from 33 to 41.8 m.[25–28] Longitudinally, the T6MWT had acceptable concordance of change when compared to the standard 6MWT (79%). However, the lowest proportion of patients (49%) felt they would be able to perform this test at home. The other tests were able to be performed by a greater number of patients with acceptable performance at baseline (correlation coefficients all above 0.7). Concordance at follow-up was less satisfactory, with wide limits of agreement. This improved in the subgroup of patients who were able to perform a T6MWT, suggesting the reduced performance in these tests may be attributable to the cohort of patients rather than the tests per se.

The subanalysis of younger Group 1 PAH patients suggests that the study tests may be more applicable in such a cohort, although given the low numbers for these subanalyses, strong conclusions cannot be drawn. The main objective of using remote tests in patients with PH would be the additional information it could provide on whether patients had deteriorated, remained stable, or improved from the last assessment and in 92% of cases at least one study test was able to identify this. However, to achieve this for a real cohort of patients, all four tests would have to be initially trialed for each patient, with a subsequent decision at follow-up to determine which test was best for an individual.

Other work has studied alternative and remote exercise tests in PH with similar results to this study. Keen et al. found that a 1-min STS was safe in PH and results were moderately correlated with those of the incremental shuttle walk test ($r = 0.7$).[13,29] Outdoor, remotely supervised 6MWTs have been shown to be safe with comparable results to the standard test in a study by Lapatra et al.[30] Studies by Brooks, Glinskii, and Salvi have investigated other mobile application alternatives to the standard 6MWT (*SA-6MWT)*, which derives the 6MWD from step count and the *Walk.Talk.Track* app, which uses accelerometery data from an Apple Watch).[12,14,15] Together, these demonstrated good correlation ($r = 0.83$–0.88) and agreement with standard 6MWT results and were felt to be feasible by users, with one self-limiting adverse event in the study by Glinskii.[12,14,15] Salvi developed the *Timed Walk* app used in this study, finding the results were repeatable and had good correlation ($r = 0.89$) to a standard walk test, but that agreement analysis demonstrated occasional inaccuracies.[9,10] The number of steps during a symptom-limited step test with oximetry testing was demonstrated by Fox to have a strong correlation ($r = 0.77$) with standard 6MWD.[11,31] Serum NT-proBNP has shown to be associated with parameters of exercise capacity derived from CPET[32] and the 6MWD,[33,34] yet there was imperfect correlation (correlation coefficients ranging from −0.31 to −0.6), potentially contextualizing the lack of concordance between the study tests and the change in NT-proBNP in this study.

This study had limitations. The study was not powered for between-group comparisons and could not definitely discern between remote tests. Only one study test was performed at each visit, and hence the intra-test and intra-observer variability were not recorded. There was a high discontinuation rate at follow-up (9 of 59 participants). Seven participants failed to engage with study follow- up. The reasons for this are unknown and while it could be related to the study tests themselves, this seems less likely given the positivity for the tests that was demonstrated in the questionnaire. A further five patients were unable to proceed due to the severity of their illness, reflecting that remote assessment can be difficult in a newly diagnosed PH population who can be unstable. The lack of adherence seen in this study may pose a significant barrier to real virtual clinic testing, where adherence may be poorer than in a study setting.

In conclusion, this study demonstrates that remote testing is feasible in PH and provides objective results, but there are significant challenges to be addressed before implementation could be considered. A mobile application-based 6MWT is a feasible remote exercise capacity test in patients with PH. However, there was insufficient validity demonstrated in this study to currently recommend its use and the high discontinuation rate may impact the utility of remote tests in a real virtual clinic. The other study tests may be used in patients who feel they are unable to complete an unsupervised, outdoor, home walk test although results would need to be interpreted with the above caveats.

AUTHOR CONTRIBUTIONS

Harrison Stubbs: Methodology; patient recruitment; formal analysis; investigation; data curation; writing—original draft; visualization. **Stephanie Lua** and **Jamie Ingram**: Patient recruitment; writing—review and editing. **Bhautesh D. Jani**, **Melanie Brewis**, and **Colin Church**: Supervision; writing—review and editing. **Martin Johnson**: Conceptualization; supervision; writing—review and editing; project administration; approval of the final draft for submission.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy restrictions.

ETHICS STATEMENT

The study was approved by the South Central—Oxford A Research Ethics Committee (Ref. 21/SC/0083).

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REFERENCES

1. Galiè N, Channick RN, Frantz RP, Grünig E, Jing ZC, Moiseeva O, Preston IR, Pulido T, Safdar Z, Tamura Y, McLaughlin VV. Risk stratification and medical therapy of pulmonary arterial hypertension. Eur Respir J. 2019; 53(1):1801889.
2. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, Carlsen J, Coats AJS, Escribano-Subias P, Ferrari P, Ferreira DS, Ghofrani HA, Giannakoulas G, Kiely DG, Mayer E, Meszaros G, Nagavci B, Olsson KM, Pepke-Zaba J, Quint JK, Rådegran G, Simonneau G, Sitbon O, Tonia T, Toshner M, Vachiery JL, Vonk Noordegraaf A, Delcroix M, Rosenkranz S, Schwerzmann M, Dinh-Xuan AT, Bush A, Abdelhamid M, Aboyans V, Arbustini E, Asteggiano R, Barberà JA, Beghetti M, Čelutkienė J, Cikes M, Condliffe R, de Man F, Falk V, Fauchier L, Gaine S, Galié N, Gin-Sing W, Granton J, Grünig E, Hassoun PM, Hellemons M, Jaarsma T, Kjellström B, Klok FA, Konradi A, Koskinas KC, Kotecha D, Lang I, Lewis BS, Linhart A, Lip GYH, Løchen ML, Mathioudakis AG, Mindham R, Moledina S, Naeije R, Nielsen JC, Olschewski H, Opitz I, Petersen SE, Prescott E, Rakisheva A, Reis A, Ristić AD, Roche N, Rodrigues R, Selton-Suty C, Souza R, Swift AJ, Touyz RM, Ulrich S, Wilkins MR, Wort SJ. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022;43(38): 3618–731.
3. Demir R, Kucukoglu MS. Six-minute walk test in pulmonary arterial hypertension. Anadolu Kardiyol Derg/Anatol J Cardiol. 2015;15(3):249–54.
4. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1): 111–7.
5. Ryan JJ, Melendres-Groves L, Zamanian RT, Oudiz RJ, Chakinala M, Rosenzweig EB, Gomberg-Maitland M. Care of patients with pulmonary arterial hypertension during the coronavirus (COVID-19) pandemic. Pulm Circ. 2020;10(2): 1–7.
6. Mamzer A, Waligora M, Kopec G, Ptaszynska-Kopczynska K, Kurzyna M, Darocha S, Florczyk M, Mroczek E, Mularek-Kubzdela T, Smukowska-Gorynia A, Wrotynski M, Chrzanowski L, Dzikowska-Diduch O, Perzanowska-Brzeszkiewicz K, Pruszczyk P, Skoczylas I, Lewicka E, Blaszczak P, Karasek D, Kusmierczyk-Droszcz B, Mizia-Stec K, Kaminski K, Jachec W, Peregud-Pogorzelska M, Doboszynska A, Gasior Z, Tomaszewski M, Pawlak A, Zablocka W, Ryczek R, Widejko-Pietkiewicz L, Kasprzak JD. Impact of COVID-19 pandemics upon pulmonary hypertension patients: insights from BNP-PL national database. Eur Heart J. 2022;42(1):8423.
7. Lee JD, Burger CD, Delossantos GB, Grinnan D, Ralph DD, Rayner SG, Ryan JJ, Safdar Z, Ventetuolo CE, Zamanian RT, Leary PJ. A survey-based estimate of COVID-19 incidence and outcomes among patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension and impact on the process of care. Ann Am Thorac Soc. 2020;17(12):1576–82.
8. Milks M, Sahay S, Benza R, Farber HW. Risk assessment in patients with pulmonary arterial hypertension in the era of COVID 19 pandemic and the telehealth revolution: state of the art review. J Heart Lung Transplant. 2021;40(3):172–82.
9. Salvi D, Poffley E, Tarassenko L, Orchard E. App-based versus standard six-minute walk test in pulmonary hypertension: mixed methods study. JMIR Mhealth Uhealth. 2021;9(6): e22748.
10. Salvi D, Poffley E, Orchard E, Tarassenko L. The mobile-based 6-minute walk test: usability study and algorithm development and validation. JMIR Mhealth Uhealth. 2020;8(1): e13756.
11. Fox BD, Langleben D, Hirsch A, Boutet K, Shimony A. Step climbing capacity in patients with pulmonary hypertension. Clin Res Cardiol. 2013;102(1):51–61.
12. Glinskii V, Anderson R, Lopez A, Lin A, Del Rosario P, Hershman S, Hess J, De Jesus Perez V, Zamanian R. Feasibility and validation testing of the Walk.Talk.Track. (WTT) app for remote monitoring of the six minute walk test (6MWT) in pulmonary arterial hypertension (PAH). Eur Respir J. 2021;58:OA143.
13. Keen C, Smith I, Hashmi-Greenwood M, Sage K, Kiely DG. Pulmonary hypertension and measurement of exercise capacity remotely: evaluation of the 1-min Sit-to-Stand test (PERSPIRE)—a cohort study. ERJ Open Res. 2023;9(1):00295-2022.
14. Brooks G, Vittinghoff E, Iyer S, Marcus GM, Pletcher MJ, Olgin JE. Diagnostic accuracy of a smartphone based six-minute walk test. Circulation. 2014;130(Suppl 2):17496.
15. Brooks GC, Vittinghoff E, Iyer S, Tandon D, Kuhar P, Madsen KA, Marcus GM, Pletcher MJ, Olgin JE. Accuracy and usability of a self-administered 6-minute walk test smartphone application. Circ Heart Fail. 2015;8(5):905–13.
16. Uk Pulmonary Hypertension Association. Clinical trials: What matters to you? Emphasis-10. 2022. 2022.

17. Stubbs H, Brewis M, Church C, Johnson M. Towards telemedicine in pulmonary hypertension: assessing the feasibility of remote quality of life and exercise capacity assessment. Pulm Circ. 2022;12(4):e12144.
18. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, Williams PG, Souza R. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53(1):1801913.
19. Tanriverdi A, Kahraman BO, Ozpelit E, Savci S. Test-retest reliability and validity of 1-minute sit-to-stand test in patients with chronic heart failure. Heart Lung Circ. 2023;32(4):518–24.
20. Ozcan Kahraman B, Ozsoy I, Akdeniz B, Ozpelit E, Sevinc C, Acar S, Savci S. Test-retest reliability and validity of the timed up and go test and 30-second sit to stand test in patients with pulmonary hypertension. Int J Cardiol. 2020;304:159–63.
21. Holland A, Malaguti C, Hoffman M, Lahham A, Burge AT, Dowman L, May AK, Bondarenko J, Graco M, Tikellis G, Lee JY, Cox NS. Home-based and remote exercise testing in chronic respiratory disease, during the COVID-19 pandemic and beyond: a rapid review. Chron Respir Dis. 2020:1479973120952418.
22. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986;1(8476):307–10.
23. Hoeper MM, Pausch C, Olsson KM, Huscher D, Pittrow D, Grünig E, Staehler G, Vizza CD, Gall H, Distler O, Opitz C, Gibbs JSR, Delcroix M, Ghofrani HA, Park DH, Ewert R, Kaemmerer H, Kabitz HJ, Skowasch D, Behr J, Milger K, Halank M, Wilkens H, Seyfarth HJ, Held M, Dumitrescu D, Tsangaris I, Vonk-Noordegraaf A, Ulrich S, Klose H, Claussen M, Lange TJ, Rosenkranz S. COMPERA 2.0: a refined four-stratum risk assessment model for pulmonary arterial hypertension. Eur Respir J. 2022;60(1):2102311.
24. Gonzalez-Garcia MC, Fatehi F, Varnfield M, Ding H, Karunanithi M, Yang I, Cordina R, Feenstra J. Use of eHealth in the management of pulmonary arterial hypertension: review of the literature. BMJ Health Care Informatics. 2020;27(3):e100176.
25. Gabler NB, French B, Strom BL, Palevsky HI, Taichman DB, Kawut SM, Halpern SD. Validation of 6-minute walk distance as a surrogate end point in pulmonary arterial hypertension trials. Circulation. 2012;126(3):349–56.
26. Gilbert C, Brown MCJ, Cappelleri JC, Carlsson M, McKenna SP. Estimating a minimally important difference in pulmonary arterial hypertension following treatment with sildenafil. Chest. 2009;135(1):137–42.
27. Moutchia J, Mcclelland RL, Al-Naamani N, Appleby DH, Blank K, Grinnan D, Holmes JH, Mathai SC, Minhas J, Ventetuolo CE, Zamanian RT, Kawut SM. Minimal clinically important difference in the 6-minute-walk distance for patients with pulmonary arterial hypertension. Am J Respir Crit Care Med. 2023;207(8):1070–9.
28. Mathai SC, Puhan MA, Lam D, Wise RA. The minimal important difference in the 6-minute walk test for patients with pulmonary arterial hypertension. Am J Respir Crit Care Med. 2012;186(5):428–33.
29. Keen C, Hashmi-Greenwood M, Sage K, Kiely DG. Pulmonary hypertension and measurement of exercise capacity remotely: the PERSPIRE study. Eur Respir J. 2022;60(66):150.
30. Lapatra T, Baird GL, Goodman R, Pinder D, Gaffney M, Klinger JR, Palevsky HI, Fritz J, Mullin CJ, Mazurek JA, Kawut SM, Ventetuolo CE. Remote 6-minute-walk testing in patients with pulmonary hypertension: a pilot study. Am J Respir Crit Care Med. 2022;205(7):851–4.
31. Fox BD, Sheffy N, Vainshelboim B, Fuks L, Kramer MR. Step oximetry test: a validation study. BMJ Open Respir Res. 2018;5(1):e000320.
32. Aueyingsak S, Khrisanapant W, Kukongviriyapun U, Pasurivong O, Ratanawatkul P, Wanitpongpan C, Pussadhamma B. Correlation between N-terminal pro-brain natriuretic peptide levels and cardiopulmonary exercise testing in patients with pre-capillary pulmonary hypertension: a pilot study. Clin Med Insights Circ Respir Pulm Med. 2020;14:1179548420954049.
33. Souza R, Jardim C, Julio Cesar Fernandes C, Silveira Lapa M, Rabelo R, Humbert M. NT-proBNP as a tool to stratify disease severity in pulmonary arterial hypertension. Respir Med. 2007;101(1):69–75.
34. Fijalkowska A, Kurzyna M, Torbicki A, Szewczyk G, Florczyk M, Pruszczyk P, Szturmowicz M. Serum N-terminal brain natriuretic peptide as a prognostic parameter in patients with pulmonary hypertension. Chest. 2006;129(5):1313–21.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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