Minimum important difference of shuttle walk tests in patients with interstitial lung disease following pulmonary rehabilitation

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Shareable abstract (@ERSpublications)
The minimum important difference for incremental and endurance shuttle walk tests in ILD population is 35.0–38.5 m and 170–209 s respectively https://bit.ly/40ypJ8c

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Abstract

Background Pulmonary rehabilitation (PR) is recommended for patients with interstitial lung disease (ILD). The impact of PR on exercise capacity, symptom management and mortality risk in ILD is well established; however, there are limited studies reporting on the minimal important difference (MID) for shuttle walk tests (SWTs) in the ILD population. The aim of this study was to establish the MID for both the incremental and endurance shuttle walking tests (ISWT/ESWT) in the ILD population and to evaluate the association with survival.

Participants The study includes 207 participants with ILD (mean±SD age 71.1±9.5 years, forced vital capacity 2.32±0.79 L) who completed PR.

Results The baseline ISWT was 251.4±153.3 m and ESWT was 217.7±136.3 s. There were significant improvements for both the ISWT and ESWT following the PR programme (44.5±77.0 m ($p<0.001$) and 312.3±338.6 s ($p<0.001$)). MID was calculated through a combination of distribution (0.5×SD) and anchor-based techniques (global rating of change (GROC) and receiver operating characteristic (ROC) analysis). The distribution-based technique yielded an MID of 38.5 m for ISWT and 169.3 s for ESWT. ROC analyses yielded an MID of 35 m for ISWT and 200 s for ESWT; and the GROC yielded an MID of 58.5 m for ISWT and 209.0 s for ESWT. Survival analysis showed that improvements in exercise tolerance are associated with improved survival.

Conclusion Our data suggest an MID of 35.0–38.5 m for ISWT and 170–209 s for ESWT for patients with ILD. The size of improvements in SWT is associated with a survival advantage in ILD individuals who attend and complete PR.

Introduction

Interstitial lung diseases (ILDs) comprise a heterogeneous group of respiratory conditions commonly characterised by symptoms such as breathlessness, fatigue, cough, reduced exercise tolerance and health-related quality of life. The median survival differs based on the ILD subtype but is typically around 3–5 years after diagnosis in untreated idiopathic pulmonary fibrosis (IPF), the archetypal fibrotic ILD [1].

Pulmonary rehabilitation (PR) is a recommended treatment approach for patients with ILD [2–4], and there is now a growing body of evidence supporting the enrolment of ILD patients into these programmes for the benefit of improved exercise tolerance and symptom management [5–7]. The assessment process involves exercise testing that is used to individually prescribe exercise intensity for the programme and to evaluate the effectiveness of the intervention. Commonly, either the 6-min walking test (6MWT) or shuttle walk tests (SWT) are used. Additionally, exercise capacity is associated with survival in ILD and presents important insight into disease mortality [8–11].

The minimum important difference (MID) for the 6MWT and SWT has been previously studied in other patient groups following the completion of PR programmes to demonstrate its effectiveness. However, to our knowledge, there are limited studies exploring the MID for SWTs in patients with ILD. Nolan *et al.* [12] first estimated the MID for the incremental shuttle walking test (ISWT) in patients with IPF (n=72) as a change of 31–46 m. However, no studies have evaluated the MID for the endurance shuttle walk test (ESWT) in ILD and outside of IPF. Given that there is an established MID for SWTs in COPD, our assumption was that we could detect an MID for SWTs in the ILD population undergoing PR. Therefore the aim of our study was to evaluate the response to PR in ILD, to establish MIDs for both ISWT and ESWT in ILD, and lastly, to assess the impact of PR on survival in ILD.

Materials and methods

Study subjects and design

The study represents a retrospective service evaluation (internally registered as clinical audit 13 239) of a PR programme at University Hospitals of Leicester NHS Trust for the period April 2012 to March 2022. Stable patients with a confirmed diagnosis of ILD who were referred for PR and completed a 6-week face-to-face programme with baseline and discharge assessment were eligible for inclusion in the study. All participants provided written consent for data collection during their initial assessment with a registered member of the rehabilitation team. As this study represented clinical evaluation of the service, formal ethics committee approval was not required.

Outcome measures

The SWTs were used to assess participants' exercise tolerance and to prescribe exercise intensity for their individualised programme. All tests were performed according to contemporaneous guidelines [13] by qualified healthcare professionals. The longer distance of the two ISWTs performed at initial assessment was used to determine the speed for the ESWT, typically defined at 85% of predicted peak oxygen consumption ($V'O_{2peak}$) of the ISWT [14–16]. Participants performed another ISWT and ESWT (using the same ESWT speed as at the baseline) as part of their discharge assessment. Both baseline and discharge assessments were performed under the same circumstances with regard to the use of walking aids and/or oxygen use.

Descriptive measures like age, sex, body mass index (BMI) and lung functions were collected either from the participant or their medical records during the initial assessment.

Intervention

Patients attended a 6-week, bi-weekly, face-to-face PR programme, delivered according to the British Thoracic Society (BTS) guidelines [3].

Each exercise session (lasting 60 min) consisted of aerobic training using both walking and cycling activity, and strength training (two upper and two lower limb exercises, three sets of 10 repetitions for each). The speed used for walking training was individualised based on the speed prescribed from the ESWT. Intensity for cycling and weightlifting was prescribed based on the patient's perception of symptoms using BORG dyspnoea (0–10) [17] and rating of perceived exertion (RPE, 6–20) [18] scales. Progression was encouraged for all the exercises to maintain the prescribed effort levels throughout the programme. Progression for walking training was focused on the duration of walks at the prescribed speed (up to 20 min); for cycling it was focused on increased resistance whilst maintaining the same cycling speed (revolutions per minute) for 5–10 min; and for strength training the progression was focused on increasing weights used over the same amount of repetitions. Each exercise session was followed by an educational lesson lasting up to 60 min on various topics, *e.g.* disease education, exercise, energy conservation, managing breathlessness and managing exacerbation. To be considered completers, participants were required to attend at least eight of the 12 scheduled sessions. In addition to the two supervised sessions, participants were encouraged to exercise at home on the remaining days of the week (walking training according to their prescription) and to perform a third strength training session.

MID calculation

We have used both anchor- and distribution-based methods to derive MIDs for the ISWT and ESWT in our study. Anchor-based methods include analyses using participants' perception of change (global rating of change), outcomes with known MIDs as anchors and receiver operating characteristics (ROC) analyses. One half of 1 standard deviation (0.5×SD) was used as a distribution-based technique.

Anchor-based methods

One of the anchors we have used is participants' perception expressed on the global rating of change (GROC) scale [19]. During the discharge assessment, participants were asked to rate any change in their exercise tolerance using the following question: "Compared to your initial ISWT before you started the rehabilitation programme, how would you rate your exercise tolerance now?" Answers were categorised on a 7-point Likert scale as: (−3) "large deterioration", (−2) "moderate deterioration", (−1) "slight deterioration", (0) "no change", (+1) "slight improvement", (+2) "moderate improvement" and (+3) "large improvement". The same scale was used for collecting the GROC for ESWT, with the question being: "Compared to your initial endurance shuttle walk test before you started in rehabilitation programme, how would you rate your exercise tolerance now?" Each of the questions was asked immediately after termination of the respective test before the participants were told about what distance or time they achieved in the walking test, and neither were they reminded about what distance and time they achieved at the initial assessment.

We have also used the Medical Research Council (MRC) dyspnoea scale [20] as a patient-reported outcome measure for anchor analysis. This measure has previously been used for MID analyses for ISWT in COPD participants following a PR programme [21]. Responses were categorised as "improved MRC", "same MRC" and "worse MRC" based on the change between baseline and discharge. ISWT change was used as another anchor, but only for the MID analysis of ESWT. Participants were considered as responders if they met or exceeded the ISWT MID [12] and non-responders if they did not meet it. Another approach that we used was ROC analyses. We coupled both ISWT and ESWT change with a GROC anchor for respective SWT and additionally used ISWT MID as anchor for ROC analysis of ESWT MID. Only anchors with acceptable correlations ($r \geqslant 0.3$, $p<0.05$) [22] with either of the SWTs and ROC curves describing meaningful relationships (area under curve (AUC) >0.7) [23] were included in MID analysis. We were not able to include any questionnaires for anchor analyses as the use of questionnaires changed significantly over the observation period in our service and we were lacking a sufficient amount of data for the study cohort.

Distribution-based methods

We calculated 0.5×SD of the change for both SWTs. This is a frequently used technique for deriving a minimal important difference value [22, 23].

Survival analysis

As the dataset covers a long period of service, participants may have been referred for PR on more than one occasion. We have therefore checked for any duplicate entries and for the purpose of survival analysis focused on the latest PR episode (*i.e.* which was closest to either death or the censoring date). Factors considered in survival analysis were whether participants achieved ISWT MID (⩾40 m *versus* <40 m) [12] and/or ESWT MID (⩾170 s *versus* <170 s, MID suggested by this study). Additionally, when we stratified participants' ESWT walking time at discharge by survival time, we discovered statistically significant differences among participants; ESWT time at discharge of at least 10 min in the surviving group (at 1- to 4-year time points following PR completion, see supplementary material). In view of this, we created another anchor for survival analysis: length of continuous walk at discharge (⩾10 min *versus* <10 min). The reason for choosing these values was to report on the role of PR in survival status reflected in the magnitude of response in exercise capacity following completion of the programme. This has been previously described in the COPD population [10].

Statistical analysis

Data were analysed using SPSS (version 20, IBM UK Ltd, Hampshire, UK). Participants with any missing data were retained for analysis of the remaining data. Parametric or non-parametric statistics were used as appropriate; data are reported as mean±SD and 95% confidence intervals. One-sample and independent-sample t-tests are used to compare outcomes before and after PR. For effect size calculations we used Cohen's d, defined as the difference between discharge and baseline divided by SD of change (within-patient variability) [24]. We used Spearman's correlation coefficient to analyse the relationship between anchors, with meaningful correlation considered as $r \geqslant 0.3$, $p<0.05$ [22]. For the ROC analysis, an AUC of at least 0.7 was required [23]. ROC analysis used the GROC categories to establish an MID in either SWT performed. Additionally, ROC analysis with MID anchor for ISWT was used to establish an MID in ESWT following PR. Subsequent sub-analysis was conducted with respect to the disease subtype stratified as IPF and non-IPF.

For the survival analysis, an independent t-test was used to determine baseline differences between deceased participants and those still alive on 1 July 2023. We conducted survival analysis using the

Kaplan–Meier log rank test and Cox regression to determine factors that independently predicted survival in our cohort.

Statistical significance was set as $p<0.05$.

Results

Patient cohorts

The study included data from 207 participants (126 male, 61%) with ILD (IPF (n=112), autoimmune ILD (n=14), idiopathic nonspecific interstitial pneumonia (n=20), hypersensitivity pneumonitis (n=16), sarcoidosis (n=21), exposure and drug-related ILDs (n=9), unclassifiable ILDs (n=13) and other ILDs (n=2)) who completed the 6-week PR programme (figure 1). Baseline variables were normally distributed. The mean±SD age was 71.1±9.5 years and BMI was 27.8±5.8 $kg \cdot m^{-2}$, and more than half of participants had IPF (n=112, 54%). Baseline characteristics of all participants are shown in table 1.

Participants with missing data were retained in the cohort for analysis of the remaining data. Variables in question included pre/post ISWT outcomes (206 cases available), pre/post ESWT outcomes (203 cases available), GROC anchor for ISWT (164 cases available) and GROC anchor for ESWT (196 cases available).

Response to the intervention

There was a significant improvement in exercise tolerance as measured by the SWTs following the intervention. The mean±SD ISWT distance increased from 251.4±148.3 to 296.2±162.7 m representing a change of 44.5±77.0 m ($p<0.001$, effect size 0.58), and mean ESWT time increased from 217.7±136.3 to 529.8±375.4 s representing a change of 312.3±338.6 s ($p<0.001$, effect size 0.92). Subjective evaluation of breathlessness using the MRC dyspnoea scale changed from 3.12±0.92 to 2.65±0.96 ($p<0.001$). On completion of the PR programme, 46% of participants improved their MRC category, 44% of participants rated their MRC to be the same as at baseline and 10% rated their MRC to be worse than at baseline.

In subgroup analysis of IPF participants alone, there was a mean±SD improvement in ISWT of 41.6±66.8 m (from 264.0 to 305.6 m), and the ESWT improved by 331.5±351.5 s (from 234.6 to 566 s). Similarly in the non-IPF subgroup, the ISWT distance improved by 48.0±87.9 m (from 236.4 to 285 m), and the ESWT time improved by 288.7±322.3 s (from 197.5 to 485.2 s).

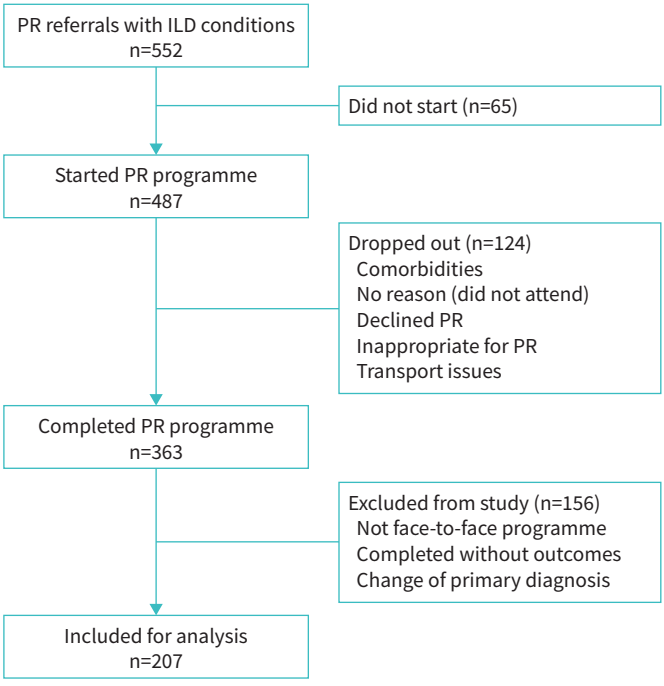

FIGURE 1 Flow diagram. PR: pulmonary rehabilitation; ILD: interstitial lung disease.

TABLE 1 Baseline characteristics of participants

Characteristic	ILD	IPF	non-IPF ILD
Sex, n (male/female)	207 (126/81)	112 (80/32)	95 (46/49)
Age years	71.1±9.5	73.4±8.4	68.5±10
BMI kg·m^{-2}	27.8±5.8	26.6±5.2	29.2±6.2
FEV_1 L	1.86±0.61	1.97±0.58	1.74±0.62
FVC L	2.32±0.79	2.44±0.78	2.19±0.77
FEV_1/FVC %	81.7±10.3	82.8±9.1	80.4±11.5
MRC (1–5)	3.12±0.92	3.12±0.89	3.12±0.95
ISWT m	251.4±153.3	264.0±147.5	236.4±148.7
ESWT s	217.7±136.3	234.6±146.6	197.5±120.7

Data are presented as mean±SD unless stated otherwise. ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis; BMI: body mass index; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; MRC: Medical Research Council dyspnoea scale; ISWT: incremental shuttle walk test; ESWT: endurance shuttle walk test.

MID calculation for the ISWT

The distribution-based technique using 0.5×SD yielded an MID value of 38.5 m, 33.4 m and 44.0 m (ILD, IPF and non-IPF patients, respectively).

In all ILD participants, the relationship between the change in ISWT with GROC and MRC anchors had moderate (r=0.359, p<0.001) and low correlations (r=0.167, p=0.017), respectively; therefore, the MRC anchor was not included in further analysis.

There was no significant difference between the ISWT changes observed in each of the GROC anchor categories, and therefore these had to be condensed. Large, moderate and slight deterioration categories were merged together with no change category; and the remaining categories (slight, moderate and large improvement) were also merged together. The newly formed categories "worse or same" and "improved" had a moderate correlation with the change in ISWT (r=0.388, p<0.001), and data were distributed as 27% (n=45) and 73% (n=119), respectively. The mean change (95% CI) was 0.7 m (−17.4–18.7) and 58.5 m (44.7–72.3), respectively.

The subgroup analysis presented similar findings; the MRC anchor was not suitable for further analysis due to weak correlation and the GROC anchor categories had to be condensed into "worse or same" and "improved" categories as described for ILD group. The IPF subgroup data distribution was 32% "worse or same" (n=27) and 68% "improved" (n=57), with mean change (95% CI) −4.8 m (−30.7–21.1) and 64.9 m (48.2–81.6), respectively. The non-IPF subgroup data distribution was 23% "worse or same" (n=18) and 77% "improved" (n=62), with mean change (95% CI) 8.9 m (−16.8–34.6) and 52.6 m (30.6–74.6), respectively.

The ROC curve analysis was performed using the "improved" GROC anchor (AUC >0.7), which was associated with a change of 35.0 m in all ILDs (0.622 sensitivity and 0.778 specificity); as well as IPF (0.667 sensitivity and 0.741 specificity) and non-IPF participants (0.581 sensitivity and 0.833 specificity).

Figure 2 visualises results from all techniques of MID delivery for the ISWT in all ILD participants as well as in IPF and non-IPF subgroups.

MID calculation for the ESWT

The distribution-based technique using 0.5×SD yielded an MID value of 169.3 s, 175.8 s and 161.1 s in ILD, IPF and non-IPF patients, respectively.

In all ILD patients, the relationship between the change in ESWT with the GROC, ISWT MID [12] and MRC anchors had moderate (r=0.496, p<0.001), moderate (r=0.491, p<0.001) and low (r=0.240, p=0.001) correlations, respectively. The MRC anchor, therefore, was not included in further analysis.

There was no significant difference between the ESWT changes observed in each of the GROC anchor categories, and therefore these had to be condensed. Large, moderate and slight deterioration categories were merged with no change category; and moderate improvement category was merged with the large improvement category. The newly formed categories "worse or same", "slightly improved" and "largely improved" had moderate correlation with the ESWT change (r=0.493, p<0.001), and the data distribution

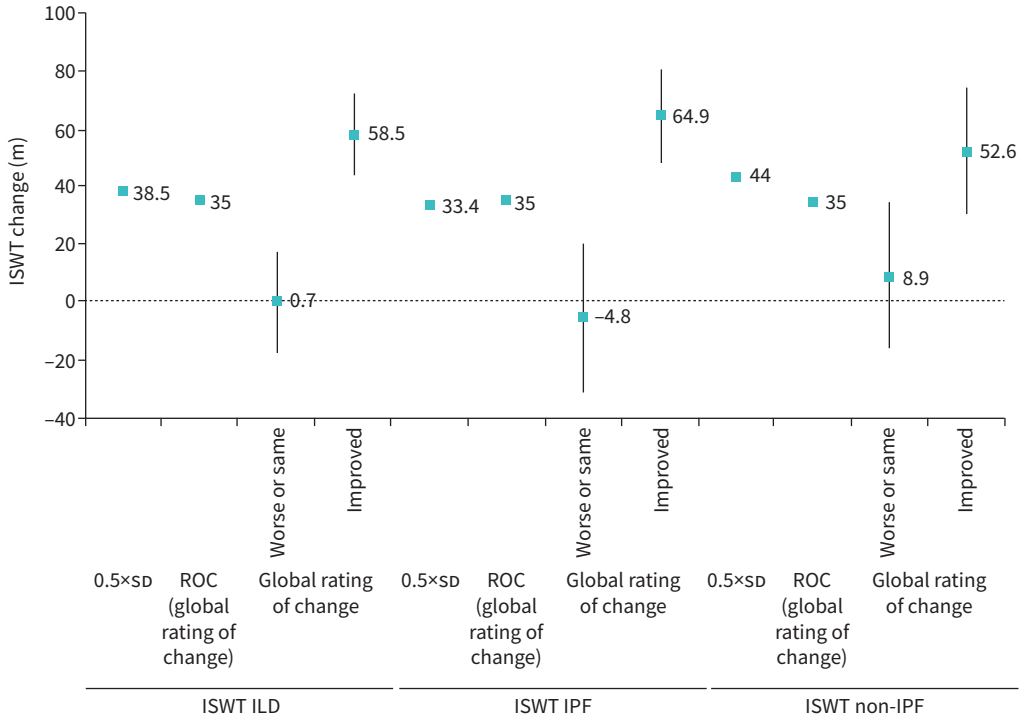

FIGURE 2 Means for the incremental shuttle walking test (ISWT) change following pulmonary rehabilitation completion in interstitial lung disease (ILD) participants. ROC: receiver operating characteristics; IPF: idiopathic pulmonary fibrosis.

was 17% "worse or same" (n=34), 31% "slightly improved" (n=61) and 52% "largely improved" (n=101) with mean change (95% CI) being 69.2 s (1.3–137.0), 209.0 s (153.0–265.0) and 467.5 s (397.4–537.7), respectively. The distribution of data using the ISWT MID anchor was "less than 40 m" in 48% (n=98) and "40 m or more" in 52% (n=105), with mean change (95% CI) of 145.7 s (97.3–194.0) and 467.8 s (401.4–534.2), respectively.

The subgroup analysis presented similar findings. The anchor-based analysis was possible with the GROC and ISWT MID anchors. The GROC anchor categories in the IPF subgroup had to be condensed due to lack of difference between categories into "worse or same", "slight improvement" and "large improvement" (as described for ILD group) with data being distributed as 20% "worse or same" (n=22), 29% "slight improvement" (n=32) and 51% "large improvement" (n=56); and with mean change (95% CI) of 77.0 s (−24.9–178.9), 243.2 s (157.6–328.9) and 502.6 s (409.0–596.3), respectively. In the non-IPF subgroup, the GROC anchor categories had to be merged due to lack of difference between some of the categories (large, moderate and slight deterioration, and no change categories). The newly formed categories were "worse or same", "slight improvement", "moderate improvement" and "large improvement" with data being distributed as 14% "worse or same" (n=12), 34% "slight improvement" (n=29), 31% "moderate improvement" (n=27) and 21% "large improvement" (n=18); and with the mean change (95% CI) of 54.8 s (−15.3–124.9), 171.2 s (97.8–244.5), 327.6 s (215.1–440.1) and 568.1 s (358.5–777.6), respectively. The ISWT MID anchor data distribution in the IPF subgroup was "less than 40 m" in 47% (n=53) and "40 m or more" in 53% (n=59) with mean change (95% CI) of 129.6 s (67.4–191.8) and 512.8 s (422.5–603.2), respectively. In the non-IPF subgroup the data distribution for the same anchor was "less than 40 m" in 49% (n=45) and "40 m or more" in 51% (n=46) with mean change (95% CI) of 164.6 s (86.6–242.6) and 410.1 s (311.0–509.2), respectively.

The ROC curve analysis was not possible using the GROC anchor in any of the participant groups (AUC <0.7), and therefore the analysis was performed only using the ISWT MID anchor ("40 or more metres", AUC >0.7) which was associated with 199.5 s change (0.695 sensitivity and 0.684 specificity) in ILD participants, 242.0 s change (0.695 sensitivity and 0.698 specificity) in the IPF subgroup and 171.5 s change (0.652 sensitivity and 0.689 specificity) in the non-IPF subgroup.

Figure 3 visualises results from all techniques of MID delivery for the ESWT in all ILD participants as well as in IPF and non-IPF subgroups.

Survival analysis

The baseline characteristics of all ILD participants (n=195, out of which 105 had IPF) with respect to their survival status ascertained for 1 July 2023 are shown in table 2. The 3-year survival was 59.1% and 5-year survival was 28.4%. Figure 4a–c presents the Kaplan–Meier survival trajectories for responders and non-responders to a PR programme in terms of achieving MIDs. The ISWT MID was achieved by 53% of participants (Chi square 0.993, p=0.319), the ESWT MID was achieved by 54% of participants (Chi square 8.591, p=0.003) and the 10-min continuous walk at discharge was achieved by 37% of participants (Chi square 12.380, p<0.001). Figure 4d shows survival trajectories when meeting/not meeting ISWT and ESWT MIDs (Chi square 9.195, p=0.027). Similar results were observed for those meeting/not meeting ISWT MID and ESWT MID when adjusted for sex, age and forced expiratory volume in 1 s/forced vital capacity using Cox regression analysis; and for achievers and non-achievers of 10-min continuous walk at discharge and overall response in SWTs with respect to meeting/not meeting MIDs when adjusted for sex and age.

Discussion

To our knowledge, this study contains the largest cohort with ILD individuals reporting on MIDs calculated using multiple accepted techniques. The reason we conducted subanalyses based on the disease subtype was to: 1) check how similar or different MIDs are for patients with ILD, IPF and non-IPF ILD; and 2) have direct comparison with the only available study describing MID for ISWT in the IPF population. Our data suggest a similar value for the ISWT MID as seen in COPD participants (35.0–38.5 and 33.4–35.0 m for ILD and IPF, respectively; 35.0–36.1 m for COPD [21]), and validates findings in the previous study of 72 IPF participants [12] for MID of ISWT (31–46 m). The ISWT MID for a COPD population suggested by Evans and Singh [21] was derived using the same techniques as the MID range in our study (ROC analysis using GROC anchor and 0.5×sd method). Nolan *et al.*'s MID suggestion [12], however, is combining distribution-based methods (standard error of measurement and 0.5×sd) with participants' perception (GROC analysis) suggesting 31, 35 and 46 m, respectively. As we did not perform a calculation of standard error of measurement, we can only compare results of the 0.5×sd and GROC

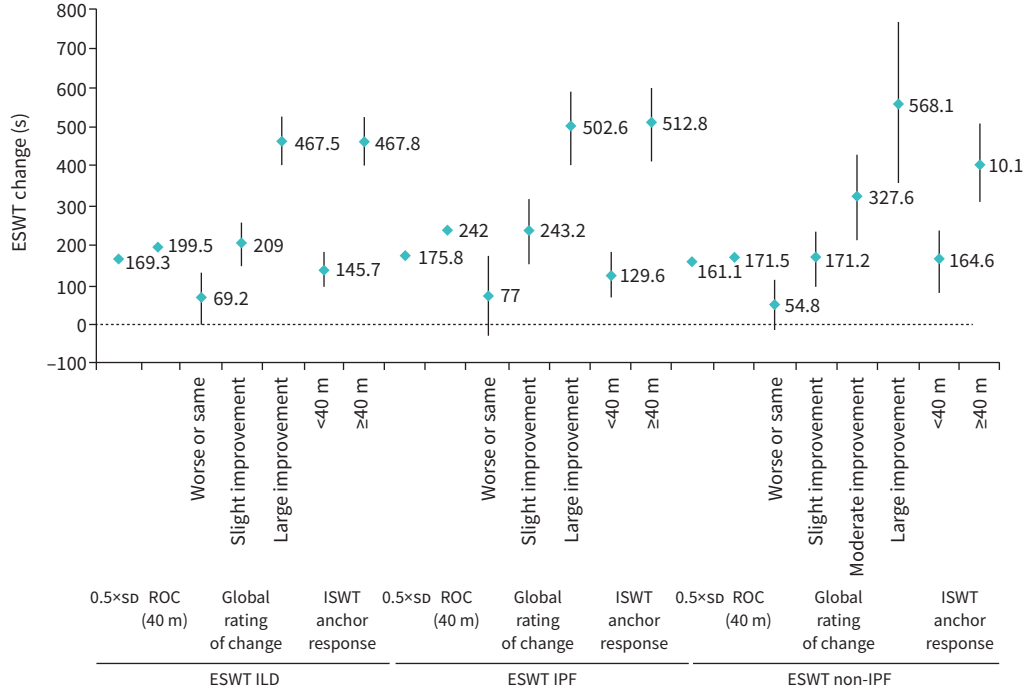

FIGURE 3 Means for the endurance shuttle walk test (ESWT) change following pulmonary rehabilitation completion in interstitial lung disease (ILD) participants. ROC: receiver operating characteristics; IPF: idiopathic pulmonary fibrosis; ISWT: incremental shuttle walking test.

TABLE 2 Baseline characteristics of interstitial lung disease (ILD) participants with respect to their survival status at the censored date

Characteristic	ILD	
	Deceased	Alive
Sex, n (male/female)	126 (86/40)	69 (33/36)
Age years	73.4±7.9	66.6±10.9
BMI kg·m^{-2}	26.9±5.7	29.0±5.7
FEV_1 L	1.86±0.60	1.85±0.63
FEV_1% pred	78.2±20	77.8±23.6
FVC L	2.27±0.76	2.40±0.83
FVC % pred	75.9±21.6	80.5±24.7
FEV_1/FVC %	0.83±0.1	0.79±0.1
MRC (1–5)	3.13±0.92	3.01±0.87
ISWT m	251.4±140.3	248.4±154.5
ESWT s	211.0±120.1	221.3±142.9

Data presented as mean±SD unless stated otherwise. BMI: body mass index; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; MRC: Medical Research Council dyspnoea scale; ISWT: incremental shuttle walk test; ESWT: endurance shuttle walk test.

anchor methods. The 0.5×SD yields similar values, unlike the GROC data. This difference is likely due to how the categories were collapsed. In the study by NOLAN *et al.*, the negative categories were merged together with "no change" category resulting in three newly formed categories: "much better", "little better" and "same/worse". Similarly in our study, we had to merge GROC into two new categories: "worse or same" and "improved". Because of this, however, we are unable to report on any discrepancy between little and bigger improvements that our participants found significant. If we were to combine the "much better" and "little better" categories in NOLAN *et al.*'s study together into a single "improved" category, we could speculate that NOLAN *et al.*'s MID suggestion would fall somewhere between 46 and 69 m (values for "little better" and "much better" categories, respectively), which would be closer to our result of 64.9 m. Singh' study [25] in a COPD population reported on the ISWT MID using the 5-point Likert scale, similar to NOLAN *et al.*'s study [12]. Singh excluded ratings of "little worse" and "worse" from the MID analysis due to insufficient number of participants and a lack of difference with other categories, resulting in three newly formed GROC categories: "better", "slightly better" and "about the same". If "slightly better" and "better" categories in Singh's study were to be combined, the MID suggestion would have been 66.7 m [21], which is close to our finding. We can see that irrespective of the MID analysis method used, the outcomes in COPD and IPF/ILD populations are comparable. As the latest MID suggestion for ISWT in a COPD population [21] is derived from statistical methods and not techniques using participants' perception, we have chosen to do the same for our MID suggestion for the ISWT in an ILD population as well; and also because the GROC produced a much higher MID estimate due to anchor categorisation of our data compared to other available studies.

In terms of the ESWT MID, there is no previously accepted suggestion for individuals with ILD to compare our data with. However, there are several studies available estimating the ESWT MID following PR in a COPD population. Our previous work in COPD [26] indicated an MID of 174–279 s where multiple methods for MID analysis were used (0.5×SD, ROC analysis and GROC). PEPIN *et al.* [27] suggested an MID of 186 s (n=132 COPD participants), which was derived by distribution-based method of analysis (0.5×SD). And lastly, Altenburg *et al.* [28] suggested an MID of 186–199 s (n=55 participants) using an anchor-based approach with 6-min walking distance (25 m), total score from the Chronic Respiratory Questionnaire (10 points) and peak power output (4 W) as anchors. However, this last study was conducted on a very specific population (COPD with respiratory failure), and the rehabilitation programme lasted 12 weeks. Data from our study indicate that the MID for ESWT is 170–209 s for individuals with ILD. The lower end of the suggested range comes from a distribution-based technique (0.5×SD), whereas the upper end is derived from an anchor-based technique using participants' perception (GROC anchor). Interestingly, the 0.5×SD technique yields a similar MID in both COPD and ILD participants, which as a reflection on the size of improvements in exercise tolerance is proving how beneficial PR programmes are irrespective of the disease specification. Even when considering results of the ROC analysis using an ISWT MID anchor, it yields a very similar MID suggestion for both COPD and ILD (207 s *versus* 200 s, respectively). It must be noted that ISWT MID used as an anchor for COPD at the time of the study was ⩾50 m, whereas for ILD in our study it was ⩾40 m. On the other hand, when

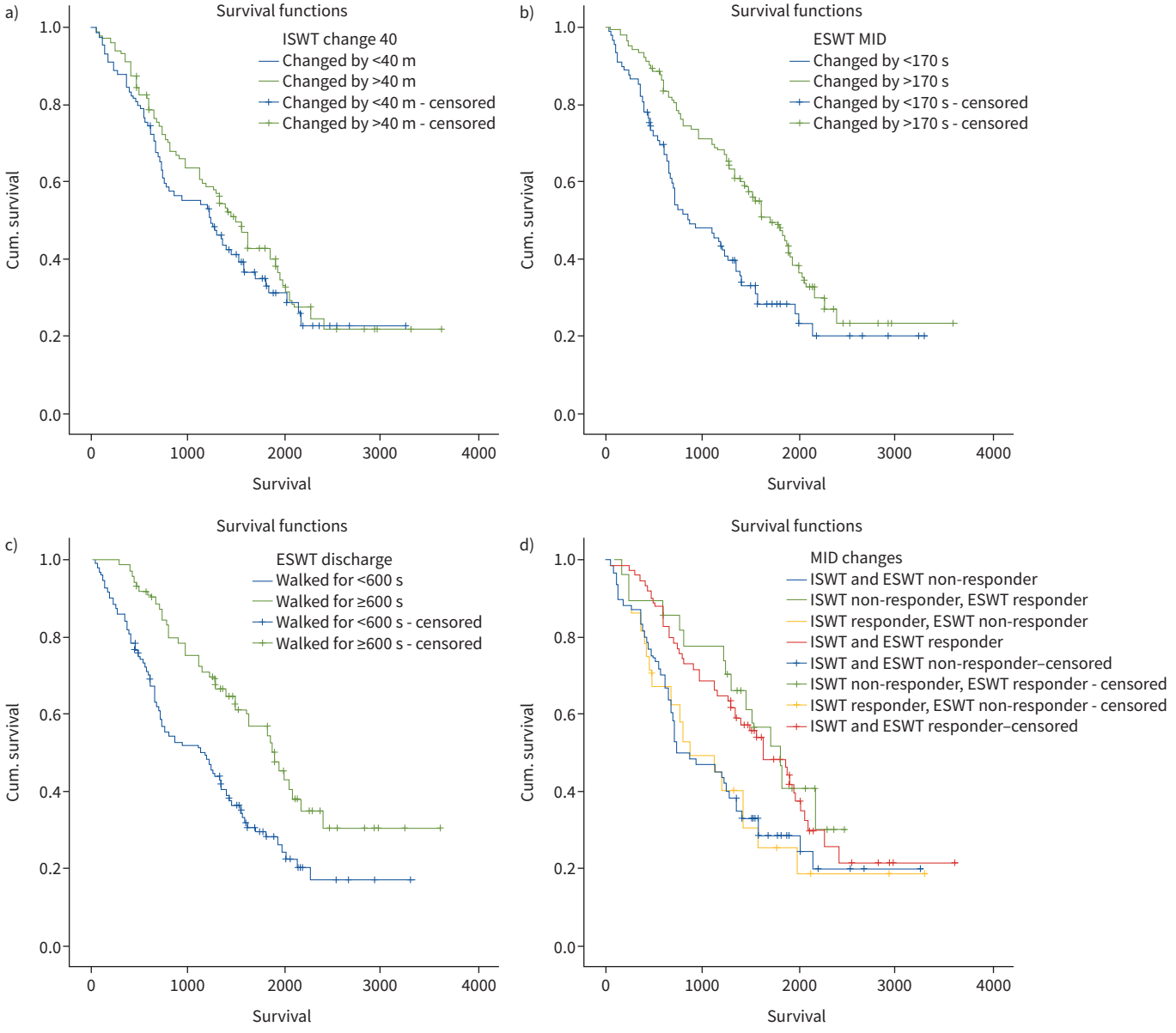

FIGURE 4 Kaplan–Meier curves expressing length of follow-up in days to end of study or death for: a) responders and non-responders to ISWT MID (40 m) following PR completion; b) responders and non-responders to ESWT MID (170 s) following PR completion; c) achievers and non-achievers of 10-min walk at discharge following PR completion; d) achievers and non-achievers of MIDs in SWTs following PR completion. cum.: cumulative; ISWT: incremental shuttle walking test; ESWT: endurance shuttle walk test; MID: minimum important difference; PR: pulmonary rehabilitation.

considering participants' perception (GROC), there is a 70 s difference between what ILD and COPD participants perceive as a meaningful change (209 s *versus* 279 s, respectively). This is likely a reflection on the difference in disease pathophysiology resulting in altered self-evaluation of a meaningful improvement in exercise capacity. It still means though that irrespective of the specific condition, the ESWT change should be around at least "3 minutes" following PR completion.

It is not unusual when reporting on MID that there are differences between MID values due to the technique adopted. Distribution-based techniques use statistical characteristics of the sample and hence report on statistically important changes. Anchor-based techniques link the change in outcome measure with a meaningful anchor reflecting participant's perspective, such as the GROC scale. However, recall bias has been reported within long-term interventions as a cause for shift in perceived response. Additionally, participants may express different meaning behind the perceived benefit or even the size of a

change with regards to being positive or negative [29, 30]. Since a PR programme is designed to improve participants' exercise tolerance, it can be difficult to accumulate a sufficient number of participants for statistical analysis who do not respond to the programme. Therefore, the suggested MIDs should not be used in terms of identifying or measuring deterioration as this is likely to have different magnitude. In our study, we merged all deteriorated categories of the GROC anchor with the category of participants reporting "no change" after completion of PR, as there were no significant differences between these Likert scale categories. This was most likely due to insufficient number of participants in the deteriorated categories. Nevertheless, the improvement in ISWT was 0.7 m in all ILD participants categorised as "worse or same" on the GROC scale. However, the ISWT is generally not as sensitive a measure for change following PR as the ESWT, which is very sensitive (as seen by the large effect size in this study). This is related to participants being trained for endurance at prescribed intensity/speed throughout their PR programme rather than progressing intensity/speed itself beyond the exercise prescription. In the case of the ESWT, we have observed that those who felt "worse or same" after PR still improved their time by 69 s on average. Interestingly, that is similar to findings in our previous work with a COPD population [26], where those who felt "worse or same" after completing the PR programme improved their ESWT time by 74 s.

Further examination of our data suggests that the ISWT might not only be less sensitive than the ESWT when establishing the gained benefits of a PR programme, but also when looking into the prospect of survival. Although there was no difference in the ISWT distance or ESWT time for ILD participants (or those with IPF/non-IPF) with respect to the survival status ("alive/deceased") at baseline (table 2), the size of induced changes in ISWT and ESWT was significantly different at discharge. The Kaplan–Meier mortality curves show that achieving the MID in the ISWT does not confer survival advantage as much as achieving the MID in ESWT (figure 4a,b,d). Nonetheless, the greatest survival advantage was conferred by the ability to walk continuously for 10 min at discharge using the prescribed speed of 85% $V'O_{2peak}$ from baseline (figure 4c). This shows that the ability to respond to the exercise programme may play a very important role in the prospect of survival for participants with ILD who complete a PR programme. Similar outcomes were previously reported in a COPD population, where completion of the PR programme and achieving the MID in ISWT were linked with significant survival advantage [10, 31]. Again, it is important to note that the ISWT MID at that time in a COPD was 47.5 m, and the newly accepted MID of 35 m [21] might have different implications on survival advantage in COPD participants following PR programme completion.

The prospect of improved exercise tolerance and survival advantage highlights some of the beneficial aspects of the outpatient supervised hospital-based PR programme, which has been proven superior to any other alternative model of delivering PR [32], and consequently, we would therefore want to limit our MID suggestions for this model of PR programme only.

There are several limitations to our study. The data we have presented are derived from a heterogeneous group of ILDs where there is likely to be differences in pathophysiology and disease trajectory. We do not report on ethnicity, comorbidities, medication and smoking history in our cohort. Neither do we report on frequency of walking aid use or oxygen use in our cohort (data not collected) which otherwise could have impact on the results (baseline *versus* discharge assessment). However, this impact is minimised by the fact that the discharge assessment was routinely performed under the same circumstances as the initial assessment (*e.g.* no walking aid at baseline, no walking aid at discharge). The observation period was of an extended duration (10 years) to enable accumulation of a sufficient sample size. During this period changes in service occurred in respect to data collection and staffing. The PR intervention itself takes 6 weeks, and therefore there is potential bias in patients' recall of exercise tolerance at baseline when trying to express perceived change. Additionally, participants may have felt obliged to report on the outcome change positively as staff performing assessments/discharges were also involved in delivering the PR programme. Another limitation could be seen as that we did not perform any sample size calculation. Nonetheless, it is difficult to accumulate equal group sizes of participants for all categories of the GROC with an intervention designed to improve the primary outcome.

Owing to the type of measures and data we collect within our service, we were restricted in selection of measures with known MID in the ILD population that we could use for anchor analysis. Therefore, there could also be an objection towards the use of MID cut-off (ESWT) for survival analysis calculated from the same cohort of participants. As there are no previous studies reporting on ESWT MID in ILD, the closest suitable for comparison would be ESWT MID in the COPD population (174 s). And as the ESWT MID in COPD is very similar to the one in ILD, we have decided to proceed in the analysis using the one for ILD. Therefore, our findings about the association between ESWT improvements and obtained survival advantage still need to be validated in another study.

With respect to the extended period of observation, some participants completed PR on more than one occasion. These 12 duplicate cases were included for MID analyses of SWTs; however, only the last PR episode for these participants was included for the survival analyses. We believe that the impact of duplicates on MID analyses should be minimal as the episodes were separated by at least 12 months and each episode constituted a new assessment of exercise capacity and subsequent relevant exercise prescription for the PR programme. Additionally, the MID analyses were focused on assessment of observed changes in the outcomes for that relevant PR episode, so any influence from previous participation in PR on baseline outcomes for either MID or survival analyses should be negligible.

Conclusion

Based on the results of our study, we propose an MID value of 35.0–38.5 m for the ISWT and 170–209 s for the ESWT in individuals with ILD following completion of a 6-week centre-based PR programme. Both MIDs have been derived from either distribution- or anchor-based methods. The magnitude of improved exercise capacity (more than suggested MIDs for SWTs) is associated with survival advantage in patients with ILD, but especially in those who are able to walk for 10 min without stopping (at the speed reflecting 85% $V'O_{2peak}$ from baseline) after PR completion.

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