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## **Repeatability of the Six-Minute Walk Test and Relation to Physical Function in Survivors of a Critical Illness**

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## Repeatability of the Six-Minute Walk Test and Relation to Physical Function in Survivors of a Critical Illness

Jennifer A. Alison, Patricia Kenny, Madeleine T. King, Sharon McKinley, Leanne M. Aitken, Gavin D. Leslie, Doug Elliott

**Background.** The Six-Minute Walk Test (6MWT) is widely used as an outcome measure in exercise rehabilitation. However, the repeatability of the 6MWT performed at home in survivors of a critical illness has not been evaluated.

**Objective.** The purpose of this study was to evaluate, in survivors of a critical illness: (1) the repeatability of the 6MWT performed at home, (2) the effect on estimates of change in functional exercise capacity if only one 6MWT was performed at follow-up assessments, and (3) the relationship between the physical functioning (PF) score of the 36-Item Short-Form Health Survey questionnaire (SF-36) and the 6MWT.

**Design.** Repeated measures of the 6MWT and SF-36 were obtained.

**Methods.** Eligible participants had an intensive care unit (ICU) length of stay of  $\geq 48$  hours and were mechanically ventilated for  $\geq 24$  hours. Two 6MWTs and the SF-36 were conducted in participants' homes at weeks 1, 8, and 26 after hospital discharge.

**Results.** One hundred seventy-three participants completed the study. The participants had a mean age of 57 years ( $SD=16$ ), a mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score on admission of 19 ( $SD=10$ ), a mean ICU length of stay of 9 days ( $SD=8$ ), and a mean mechanical ventilation time of 140 hours ( $SD=137$ ). Of the 173 participants, 110 performed two 6MWTs at weeks 1, 8, and 26. There were significant mean increases in 6-minute walk distance in the second test of 15 m ( $P<.0001$ ) at week 1, 13 m ( $P<.0001$ ) at week 8, and 9 m ( $P=.04$ ) at week 26. If only one 6MWT was performed at weeks 8 and 26, the estimate of change in 6-minute walk distance from week 1 was 19 m less ( $P<.001$ ) at both weeks 8 and 26. There was a moderate to strong correlation between SF-36 PF score and 6-minute walk distance at each assessment (week 1:  $r=.62$ ,  $P<.001$ ; week 8:  $r=.55$ ,  $P<.001$ ; and week 26:  $r=.47$ ,  $P<.001$ ).

**Limitations.** Some study participants were unable to perform a second 6MWT, and these participants may have differed in important aspects of function compared with those individuals who completed two 6MWTs.

**Conclusions.** In survivors of a critical illness, the 6MWT in the home environment should be performed twice at each assessment to give an accurate reflection of change in exercise capacity over time. The SF-36 PF score was a strong indicator of 6-minute walk distance in early recovery from a critical illness.

The Six-Minute Walk Test (6MWT) is widely used as an outcome measure in exercise rehabilitation. Previous research has shown a 7% to 14% increase in distance walked in a second 6MWT in participants with chronic obstructive pulmonary disease<sup>1-3</sup> and an increase of approximately 8% in older people who were healthy.<sup>4</sup> Two 6MWTs, therefore, are recommended at baseline assessment.<sup>5</sup> However, minimal information is available on the 6MWT in survivors of a critical illness. First, repeatability of the 6MWT performed at home in survivors of a critical illness has not been evaluated. Second, although it is recommended that two 6MWTs be performed at initial assessment<sup>5</sup> to account for a learning effect, it is unknown whether it is necessary to perform two 6MWTs at follow-up assessments and whether performing only one 6MWT at follow-up assessment would affect the reporting of changes in 6MWT distance in this patient population. Third, the relationship between the 6MWT, a quantitative measure of functional exercise capacity, and the patient report of physical function in daily life using the physical functioning (PF) score of the 36-Item Short-Form Health Survey questionnaire (SF-36) has not been evaluated during the period of recovery from a critical illness. A strong relationship between SF-36 PF and 6MWT scores would enhance the value of the PF score in reflecting functional exercise capacity in this population, and may provide a proxy measure in circumstances where staff is not available to conduct a 6MWT. Track configuration has been shown to affect the distance walked in the 6MWT.<sup>2</sup> However, the effect of variations in track configuration and environment on distance walked when the 6MWT is performed at home is unknown.

The primary aims of the study were to evaluate, in survivors of a critical

illness: (1) the repeatability of the 6MWT performed at home, (2) the effect on estimates of change in functional exercise capacity in the longer term if only one 6MWT was performed at follow-up assessments, and (3) the relationship between the SF-36 PF score and the 6MWT at weeks 1, 8, and 26 following hospital discharge. A further aim was to evaluate the effect of 6MWT track on walk distance.

## Method

This article reports a secondary analysis of data from a multicenter randomized controlled trial designed to test the effects of an 8-week, home-based rehabilitation program compared with usual care on health-related quality of life and physical functioning for individuals who survived a critical illness. The study methods have been published previously.<sup>6</sup> Briefly, eligible patients had an ICU length of stay of  $\geq 48$  hours and were mechanically ventilated for  $\geq 24$  hours. Blinded assessments of outcome measures of exercise capacity using the 6MWT<sup>5</sup> and of physical functioning using the SF-36 (version 2)<sup>7</sup> were conducted by trained assessors in participants' homes at weeks 1, 8, and 26 after hospital discharge. Relevant institutional review board approvals were obtained prior to study commencement, and all participants provided informed consent. A safety protocol was used to support assessors during home visits.<sup>6</sup>

For the 6MWT, a flat track was marked out in each participant's home or local environment. A detailed record of the track was kept, including the track distance and type (circuit or shuttle), to ensure an identical track was used for subsequent tests. Two 6MWTs (test 1 and test 2) were performed at each time point, with a 30-minute rest period between tests. Standardized instructions and encouragement

were used based on the guidelines for the 6MWT<sup>5</sup> and detailed in the Pulmonary Rehabilitation Toolkit.<sup>8</sup> During the 6MWT, participants were directly observed by the assessor. Pulse rate and oxygen saturation were monitored continuously via a portable pulse oximeter (PalmSAT 2500 Digital Pulse Oximeter, Nonin Medical Inc, Plymouth, Minnesota) and exertion levels were assessed using the Borg Perceived Exertion Scale.<sup>9</sup>

Initial study findings have been published previously.<sup>10</sup> No significant effect of the intervention on physical functioning or 6-minute walk distance was demonstrated compared with changes over time during recovery in the usual care group. Therefore, data from both groups were pooled for further analyses.

## Data Analysis

Repeatability of the 6MWT was assessed at each time point (weeks 1, 8, and 26) using data from respondents who completed two 6MWTs at all time points. The paired *t* test was used to examine whether the mean difference between the first and second 6MWTs was significantly different from zero at each time point. The individual test variability was examined using plots of individual test difference against the individual test average distance and limits of agreement (twice the standard deviation of the difference between test 1 and test 2).<sup>11</sup>

To evaluate whether it was necessary to perform two 6MWTs at

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**Table 1.**

Characteristics of Participants (N=173)

Measure	Values
Age (y)	57 (16)
Sex, female/male	40%/60%
APACHE II score	19 (10)
Ventilation (h)	140 (137)
ICU LOS (d)	9 (8)
Hospital LOS (d)	24 (19)
6MWT (m)	313 (132)
SF-36 PF score	37 (26)

<sup>a</sup> All values are presented as mean (SD) unless otherwise indicated. APACHE II=Acute Physiology and Chronic Health Evaluation II, ICU=intensive care unit, LOS=length of stay, 6MWT=Six-Minute Walk Test, SF-36 PF=36-Item Short-Form Health Survey physical functioning scale.

follow-up assessments to ensure the accurate reporting of change in 6-minute walk distance at weeks 8 and 26, the longer walk distance of the two 6MWTs at week 1 was compared with: (1) the longer of the two 6-minute walk distances at week 8 and week 26 and (2) the first 6-minute walk distance at week 8 and week 26. This analysis used the mean change at follow-up and 95% confidence intervals (95% CIs).

The analysis to determine whether the SF-36 PF score was reflective of exercise capacity measured by the 6MWT had several aspects. First, the correlation between the longer 6-minute walk distance and the SF-36 PF score was assessed at weeks 1, 8, and 26 using the Pearson correlation coefficient. Second, the variance in 6-minute walk distance explained by the SF-36 PF score was assessed at week 1 using multiple regression. A 2-stage analysis was performed where the effect of patient characteristics potentially associated with exercise capacity and physical functioning (age and sex), as well as indicators of illness severity (Acute Physiology and Chronic Health Evaluation II [APACHE II] score and days in hospital), were included as covariates in the regression analysis, with 6MWT as the dependent variable.

The model also was adjusted for trial randomization group to ensure the secondary analysis was not affected. The analysis then was repeated with SF-36 PF score added to the model as an explanatory variable. The difference in the  $R^2$  between the 2 models provided an estimate of the variance in 6-minute walk distance explained by the SF-36 PF score. The third aspect of the analysis investigated which items within the SF-36 PF score were more closely related to the 6MWT. For this analysis, the mean and 95% CI of the 6MWT were plotted against the individual SF-36 PF item responses at week 1.

The impact of track characteristics on the 6-minute walk distance was assessed at week 1 using multiple regression analysis, with 6-minute walk distance as the dependent variable and track characteristics of length (circular or straight, indoor or outdoor) as explanatory variables. This analysis was adjusted for participant characteristics of age, sex, APACHE II score, and days in hospital.

**Results**

One hundred seventy-nine study participants completed at least one 6MWT; of this sample, 173 participants had complete data for the

6MWT and the SF-36 PF at week 1 and were included in the analyses. Participant characteristics are presented in Table 1. On average, the sample had low physical functioning, with a mean SF-36 PF score of 37 (95% CI=33- 41), and a low exercise capacity, with a mean 6-minute walk distance of 313 m (95% CI=293-333) at week 1.

**Repeatability of the 6MWT**

At each assessment time point, several participants declined to perform a second 6MWT (14 of 176 participants at week 1, 7 of 147 participants at week 8, and 15 of 143 participants at week 26). Reasons given for declining to repeat the 6MWT included exhaustion or fatigue, despite the 30-minute rest period. For the 110 participants who completed two 6MWTs at each time point, the 6-minute walk distance, on average, was significantly longer at the second 6MWT (weeks 1 and 8,  $P<.001$ ; week 26,  $P=.04$ ) (Tab. 2). Individual mean 6MWT distance and differences between the first and second tests at weeks 1, 8, and 26 and the limits of agreement are presented in Figure 1. Although the mean differences were relatively small, the distribution of individual differences indicated considerable variability, with a majority of participants performing a longer 6-minute walk distance in the second test, as indicated by the points above zero in Figure 1. The limits of agreement were  $\pm 71$ ,  $\pm 60$ , and  $\pm 92$  m at weeks 1, 8, and 26, respectively. The mean percent difference when test 2 was compared with test 1 showed an increase of 5% (SD=13%), 3% (SD=8%), and 2% (SD=12%) at weeks 1, 8, and 26, respectively (Tab. 2).

**Effect of Performing Only One 6MWT at Follow-up (Weeks 8 and 26) on Estimate of Change Over Time**

The calculated improvement in 6-minute walk distance was approx-

**Table 2.**

 Repeatability of Six-Minute Walk Test (6MWT) Distance (Difference Between Test 1 and Test 2) and Impact of Using 1 or 2 Follow-up Tests on the Estimate of Change Over Time (n=110)<sup>a</sup>

Week	Test 1 X̄ (SD)	Test 2 X̄ (SD)	Test 2 – Test 1 Mean Difference (95% CI)	% Difference <sup>b</sup> X̄ (SD)	Proportion Improved at Test 2 <sup>c</sup>	Longer Follow-up Minus Longer Week 1 (A) Mean Difference (95% CI)	First Follow-up Minus Longer Week 1 (B) Mean Difference (95% CI)	Difference in Estimate of Change (A – B) Mean Difference (95% CI)
1	322 (109)	337 (116)	15 (9–22)	5 (13)	0.67			
8	419 (126)	432 (135)	13 (7–19)	3 (8)	0.69	95 (79–111)	76 (60–91)	19 (15–23)
26	447 (137)	456 (142)	9 (0.3–18)	2 (12)	0.55	122 (102–143)	103 (83–124)	19 (12–26)

<sup>a</sup> 6MWT results in meters. 95% CI=95% confidence interval; Longer=the longer 6MWT distance of the 2 tests performed at that time point; First=the first 6MWT performed at the assessment time point.

<sup>b</sup> % Difference=test 2 – test 1 as percentage of test 1.

<sup>c</sup> Proportion of participants who walked farther in test 2 than in test 1.

imately 95 m at week 8 and 122 m at week 26, when the longer distance of the two 6MWTs at each time point was used. When the first 6MWT at weeks 8 and 26 was used, the calculated improvement in 6-minute walk distance was 19 m less ( $P<.001$ ) at both weeks 8 and 26 (Tab. 2).

### Relationship Between 6MWT Distance and SF-36 PF Score

All participants who completed at least one 6MWT and the SF-36 PF domain items at week 1 were included in the analysis of the relationship between 6-minute walk distance and SF-36 PF score. The 6-minute walk distance showed a moderate to strong, significant correlation with the SF-36 PF score (week 1:  $r=.62$ ,  $P<.001$ ; week 8:  $r=.55$ ,  $P<.001$ ; and week 26:  $r=.47$ ,  $P<.001$ ).

At week 1, the SF-36 PF score was significantly associated with 6-minute walk distance and explained a further 26% of the variance in 6-minute walk distance beyond that explained by covariates, as indicated by the differences in  $R^2$  between models 1 and 2 in Table 3. Figure 2 illustrates the relationship between individual items within the SF-36 PF score and the 6-minute walk

distance at week 1. The responses (“not limited,” “limited a little,” and “limited a lot”) to items “climbing one flight of stairs” and “walking 100 m” were most able to differentiate 6-minute walk distance. For the item “climbing one flight of stairs,” the mean distance walked for those reporting:

1. “limited a lot” (n=50) was 216 m (95% CI=187–245)
2. “limited a little” (n=75) was 318 m (95% CI=293–343)
3. “not limited” (n=49) was 403 m (95% CI=365–439).

The mean difference between subgroups 1 and 2 was 102 m (95% CI=64–140) ( $P<.0001$ ) and between subgroups 2 and 3 was 85 m (95% CI=42–128) ( $P<.0001$ ).

For the item “walking 100 m,” the mean distance walked for those reporting:

1. “limited a lot” (n=37) was 189 m (95% CI=157–222)
2. “limited a little” (n=62) was 302 m (95% CI=274–329)

3. “not limited” (n=75) was 383 m (95% CI=357–410).

The mean difference between subgroups 1 and 2 was 113 m (95% CI=70–154) ( $P<.0001$ ) and between subgroups 2 and 3 was 81 m (95% CI=44–120) ( $P<.0001$ ).

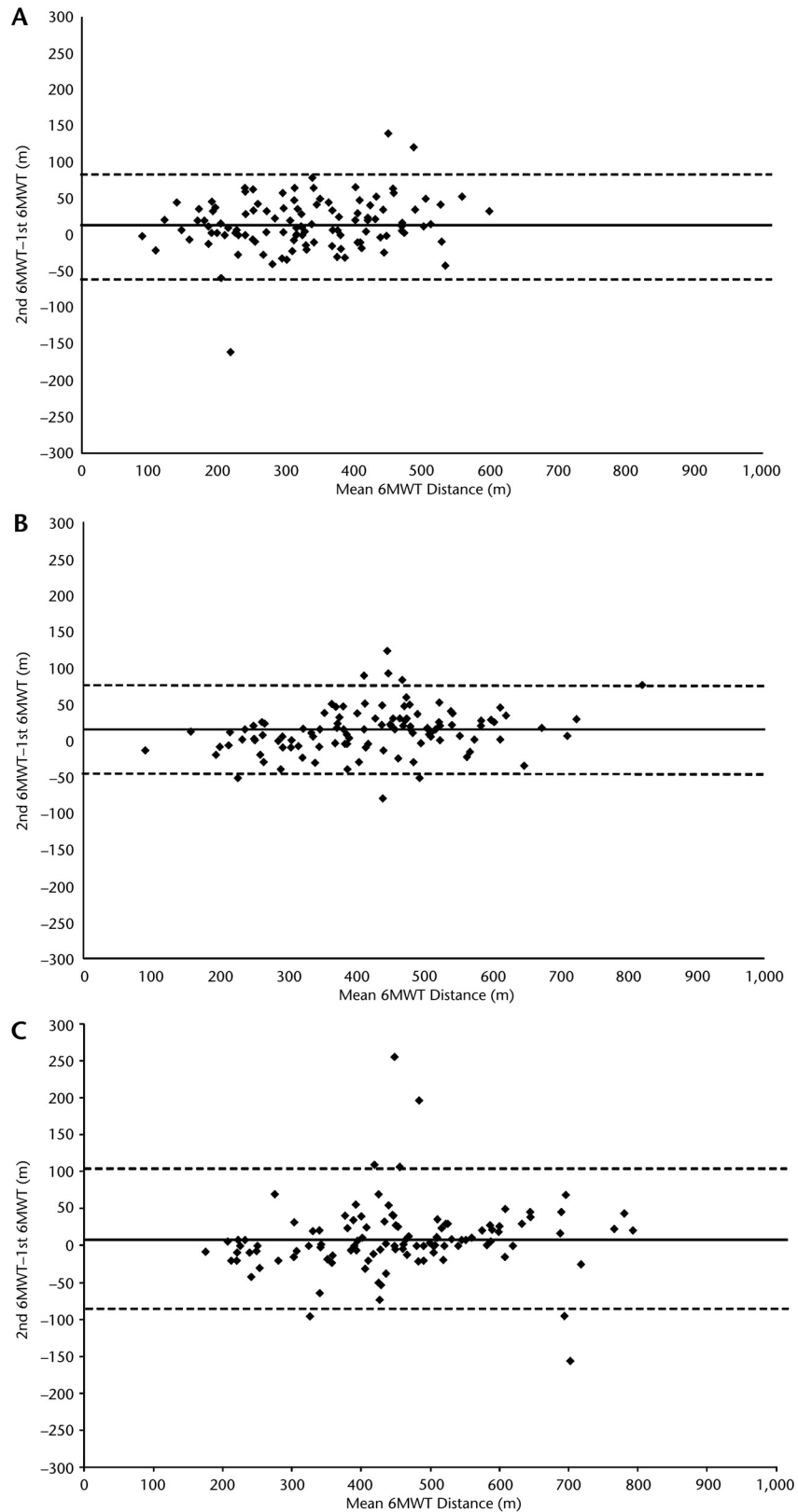
### Effect of Track Characteristics on 6MWT Distance

Track characteristics information was available for 108 participants. The mean track length was 23 m (SD=20, median=16, range=4–130 m). The majority of tracks were outside (80%) rather than inside and straight (66%) rather than circular. Using multiple regression analysis and adjusting for age, sex, APACHE II score, and days in hospital, track length was significantly associated with 6-minute walk distance at week 1 (Tab. 4). For each additional meter of track length, the 6-minute walk distance increased, on average, by 3 m.

### Discussion

The main findings were that a small but consistent and significant average increase was observed in the second 6MWT distance at each assessment time point, that the reported change in 6MWT distance at weeks 8





**Figure 1.** Scatter plots (Bland-Altman) of the mean Six-Minute Walk Test (6MWT) score (x-axis) plotted against the difference between 6MWT 1 and 6MWT 2 (y-axis) at week 1 (A), week 8 (B), and week 26 (C). The unbroken line represents mean difference, and broken lines represent limits of agreement.

**Table 3.**

Six-Minute Walk Test at Week 1: Regression Models With and Without 36-Item Short-Form Health Survey (SF-36) Physical Functioning (PF) Score (N=173)<sup>a</sup>

Parameter	Model 1			Model 2		
	Estimate	SE	P	Estimate	SE	P
Intercept	404.35	25.71	<.0001	364.33	21.81	<.0001
SF-36 PF score <sup>b</sup>				2.81	0.32	<.0001
Age <sup>b</sup>	-2.33	0.60	.0001	-1.64	0.50	.001
Female	-49.22	19.05	.010	-13.58	16.31	.41
APACHE II score	-1.08	0.97	.27	-0.54	0.80	.50
Days in hospital	-1.45	0.50	.004	-0.72	0.42	.09
Control group	-31.72	18.40	.09	-20.19	15.31	.19
R <sup>2</sup>	0.18			0.44		

<sup>a</sup> SE=standard error of the measurement, APACHE II=Acute Physiology and Chronic Health Evaluation II.

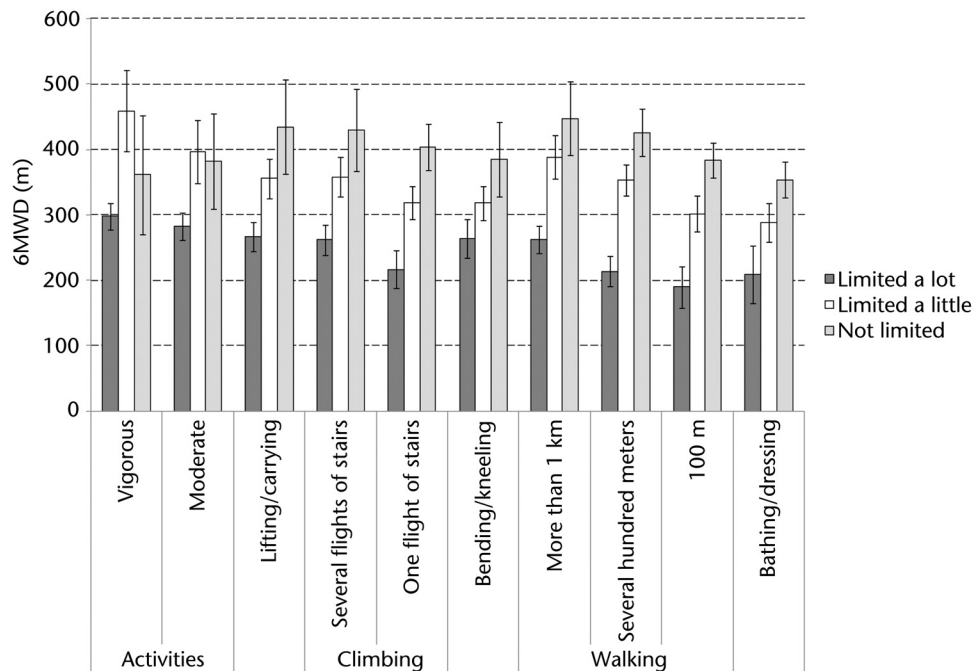
<sup>b</sup> Centered at 40 for SF-36 PF score and at 57 years for age.

and 26 was greater when the longer of the two 6MWT distances at these time points was used for analysis rather than the first 6MWT distance, and that the 6MWT distance was reflective of self-reported limitations to the SF-36 PF domain items of

“climbing a flight of stairs” and “walking 100 m.”

Performing a second 6MWT in participants who survived a critical illness resulted in a significant average increase in walk distance at all assess-

ment time points. The increase in walk distance when a second 6MWT was performed was similar to the findings for other patient cohorts, particularly those with chronic lung disease<sup>1,2,12</sup> and heart disease<sup>13</sup>; however, this is the first study that



**Figure 2.**

Week 1 36-Item Short-Form Health Survey (SF-36) physical functioning domain items (x-axis) and 6-minute walk distance (6MWD) (y-axis). Error bars are 95% confidence intervals for 6MWD.

## Repeatability of the 6MWT and Relation to Physical Function in Critical Illness

**Table 4.**

Regression Model to Investigate the Effect of Track Type (Circular or Straight, Indoor or Outdoor) and Track Length on the Six-Minute Walk Test at Week 1 (n=108)<sup>a</sup>

Parameter	Estimate	SE	P
Intercept	315.36	31.88	<.0001
Circular track	19.23	27.47	.49
Inside track	-3.38	24.88	.89
Track length	2.96	0.55	<.0001
Age <sup>b</sup>	-2.93	0.64	<.0001
Female	-42.01	21.78	.06
APACHE II score	0.05	0.92	.96
Days in hospital	-1.63	0.62	.01
R <sup>2</sup>	0.48		

<sup>a</sup> SE=standard error of the measurement, APACHE II=Acute Physiology and Chronic Health Evaluation II.

<sup>b</sup> Age centered at 57 years.

assessed repeatability of the 6MWT in people who survived a critical illness. This cohort may differ from cohorts with chronic respiratory or cardiac diseases due to younger mean age and potential for full recovery after a critical illness. The limits of agreement between test 1 and test 2 were similar to those reported in people with chronic obstructive pulmonary disease,<sup>14</sup> demonstrating the inherent within-participant variability in the 6MWT results. Although the majority of the cohort walked farther on the second 6MWT at each time point, most likely due to a familiarization or learning effect, a substantial minority walked a shorter distance at the second test (Fig. 1). The reason for this variability is unclear, but it has been reported in other cohorts.<sup>14</sup> Some contributing factors may have been lack of motivation, fatigue, and psychological issues.

The guidelines for the 6MWT<sup>5</sup> recommend that a practice walk test (equivalent to test 1 in our study) should be performed in people naive to the test. Therefore, two 6MWTs should be performed at initial assessment. However, there are no recommendations for whether 2 tests should be performed at follow-up

assessments for the estimate of group change in intervention research. Despite the smaller mean difference in distance walked in a second 6MWT at week 8 and week 26 compared with the difference at week 1, the difference that persisted had a significant impact on the estimate of change in 6-minute walk distance over time. If only one 6MWT had been performed at week 8 and week 26, the reported change in 6-minute walk distance (compared with week 1) would have been approximately 19 m less at week 8 and week 26 than if the longer of two 6MWT distances was used. Thus, the change in 6-minute walk distance during recovery from a critical illness would have been underestimated. This underestimation could potentially represent a substantial proportion of the effect of an intervention and result in concluding that an effective intervention was ineffective, especially if effectiveness was based on reaching a minimum clinically important difference in 6MWT distance, such as 35 m, as has been reported for people with chronic obstructive pulmonary disease.<sup>15</sup> Our findings suggest that for research evaluating the effects of an intervention over time, it is important to perform two 6MWTs at each

subsequent assessment and to use the longer test distance for analysis in reporting change in 6-minute walk distance.

A novel aspect of this study was that the 6MWTs were performed at participants' homes or in their local environment. This home environment meant that walking tracks for the 6MWT differed among participants. For example, some indoor tracks were straight "shuttle" tracks along corridors and others were circular tracks through rooms, and some outdoor tracks were straight shuttle tracks along flat pavements and others were circular tracks in flat parks. Within-participant variability was controlled by duplicating the track used for each assessment.

When examining the effect of different track types, the main finding was that only track length affected the 6-minute walk distance, with longer tracks resulting in greater distance walked. The impact of slowing down to turn more frequently on shorter tracks may explain this finding.<sup>5</sup> Our findings differed from those of a study of people with severe chronic obstructive pulmonary disease,<sup>2</sup> where straight track length had no effect on walk distance and a circular track resulted in greater 6-minute walk distance than a straight shuttle track. However, those findings could conversely support our finding that track length affected walk distance, as, by its nature, a circular track is longer than any straight track.

The SF-36 PF score correlated significantly with 6-minute walk distance at each time point (strongest at week 1). Similar positive correlations between self-reported physical function and 6-minute walk distance have previously been reported in other cohorts.<sup>16,17</sup> The week 1 SF-36 PF score was a significant predictor of 6-minute walk distance, adding 26% to the variance in 6-minute walk dis-



tance explained by other variables (age, sex, APACHE II score, and days in hospital). The closer relationship between the SF-36 PF score and 6-minute walk distance at week 1 compared with weeks 8 and 26 was likely due to the greater limitation in walk distance and physical functioning at this time point. At subsequent time points, recovery from a critical illness may have resulted in a ceiling effect in scoring of the SF-36 and the 6MWT. Both factors would reduce the strength of the relationship between SF-36 PF score and 6-minute walk distance. An interesting finding was that the SF-36 PF domain items of "walking one flight of stairs" and "walking 100 m" were able to distinguish clear differences in 6-minute walk distance at week 1. This may be a useful finding, as it suggests that these items may act as a surrogate for the 6MWT at this early stage of recovery from a critical illness.

### Limitations

A limitation of the study was that some study participants were unable to perform a second 6MWT, and these participants may have differed in important aspects of function from those individuals who completed two 6MWTs.

### Clinical Importance

Evidence from this study reinforces the need to perform two 6MWTs for home assessment of functional exercise capacity for intervention studies in people recovering from a critical illness. The use of a consistent track for all assessments of an individual should help to minimize the risk of measurement error. A longer track

length positively influenced distance walked.

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## **Repeatability of the Six-Minute Walk Test and Relation to Physical Function in Survivors of a Critical Illness**

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