TITLE: Lower Limb Activity and its Determinants in Chronic Obstructive Pulmonary Disease

Authors: Paul P Walker, Angela Burnett, Paul W Flavahan and Peter M A Calverley

Institution for All Authors: Division of Infection and Immunity, School of Clinical Science, University of Liverpool, Liverpool, United Kingdom

Corresponding Author: Dr Paul Walker

Address: Clinical Science Centre, University Hospital Aintree, Lower Lane, Liverpool, L9 7AL, United Kingdom.

E-mail: ppwalker@liv.ac.uk
Telephone: +44 151 529 5886
Fax: +44 151 529 5888

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ABSTRACT

**Background**: Patients with COPD walk less than healthy older people and their self-reported activity predicts exacerbation risk. The relationship between lower limb activity and total daily activity is not known nor is there data relating objectively assessed daily activity to laboratory assessments made before and after rehabilitation.

**Methods**: We measured lower limb activity by leg actigraphy over 3 days in 45 patients with moderate to severe COPD and 18 similar age controls. Thirty-three COPD patients entered an 8-week rehabilitation programme where we measured the change in leg activity and related this to other outcomes.

**Results**: In COPD patients mean activity level measured by whole body and leg activity monitors was closely related (r=0.92; p<0.001) but leg activity was consistently reduced compared with similar age controls (p=0.001). Mean leg activity, mean intensity of leg activity and the time that patients spent mobile at home were all related to FEV$_1$ (r=0.57; p=0.001, r=0.5; p=0.003 and r=0.51; p=0.002 respectively) but intensity of activity and time spent mobile were not related. Subjects completing pulmonary rehabilitation showed significant improvements in mean activity (p=0.001) and spent more time moving (p=0.014). These changes were unrelated to improvement in muscle strength or walking distance but correlated with baseline FEV$_1$ (r=0.8; p<0.001).

**Conclusions**: Total daily activity in COPD patients is closely related to leg activity which is reduced compared to similar age controls. Individuals differ in the time spent mobile during the day but both subjective and objectively assessed activity improves after rehabilitation and is predicted by FEV$_1$. The change in activity is unrelated to improvements in corridor walking and health status.
INTRODUCTION

Symptomatic chronic obstructive pulmonary disease (COPD) is associated with impaired exercise performance, which is in turn related to reduction in health status [1] and mortality [2]. Conventionally this impairment has been documented by incremental or endurance exercise testing often using field exercise tests such as the 6-minute walking distance [3] or the endurance shuttle walking test.[4] However, exercise testing measures what an individual is capable of doing rather than their activity. The level of activity reported by COPD patients relates to the risk of hospitalisation after an exacerbation [5] and mortality.[6] More recently the availability of reliable accelerometers has made it possible to objectively monitor daily activities outside of the laboratory. COPD patients are less active than healthy age-matched controls and spend longer sitting and lying down,[7] while activity improves after a rehabilitation programme irrespective of the exercise regime used.[8]

To date, home activity monitoring has reported total body movements over a 12-hour period using a waist-mounted triaxial accelerometer, which in the case of the Dynaport system also reports the type of activity.[9] How much of the total daily activity is a result of the lower limb movement has not been determined. This is important as COPD patients are subject to loss of skeletal muscle mass most evident in the legs [10] and reduced quadriceps strength predicts both healthcare use [11] and future mortality.[12]

We hypothesised that the degree of leg activity would be an important determinant of the total daily activity of COPD patients. In addition leg activity would relate both to self-paced walking distance and muscle strength and would improve significantly after pulmonary rehabilitation. Moreover, we anticipated that the initial degree of activity impairment would predict the extent to which activity improved after rehabilitation, whether this was assessed objectively by activity monitoring or subjectively by activity questionnaire. To test these hypotheses we have monitored activity simultaneously with a leg mounted accelerometer and a Dynaport activity monitor and subsequently related leg activity to well recognised outcome measures before and after pulmonary rehabilitation.
METHODS

Subjects

We recruited patients with a clinical and physiological diagnosis of COPD [13] who had not used antibiotics or oral corticosteroids for at least six weeks and who were referred for pulmonary rehabilitation. Medication was individually optimised before assessment and remained constant throughout the study. We excluded patients using domiciliary oxygen, with unstable cardiac disease, and those unable to exercise due to musculoskeletal, neurological or vascular disorders. All patients provided written informed consent and the protocol was approved by our local Research Ethics Committee.

Study Protocol

Patients participated in one or more of three study evaluations.

1. Evaluation 1: A subset of COPD patients underwent simultaneous leg accelerometry measurements and total body activity measurements. These subjects also completed health status and activity questionnaires.

2. Evaluation 2: In a second group of COPD patients leg accelerometry measurements were compared to those of a control group of healthy volunteers of similar age and sex. Quadriceps muscle strength was also recorded.

3. Evaluation 3: A further group of COPD patients completed leg accelerometry before and after pulmonary rehabilitation and this leg activity data was related to standard measures of lung function, exercise performance, muscle strength and health status.

Pre-rehabilitation assessments were performed on two visits approximately seven days apart. Post-rehabilitation all assessments were completed on a single visit scheduled no more than 14 days after completion of the exercise programme. Each subject performed the same tests in the same order. All tests were performed before and after rehabilitation with the exception of lung function measurement and the two practice 6-minute walks.

Procedures

Pulmonary Function Tests

Prior to testing patients omitted short-acting inhaled bronchodilators for 8 hours and long-acting beta-agonists for 12 hours. Spirometry, static lung volumes and single breath carbon monoxide transfer factor were measured with a rolling seal spirometer (PK Morgan, Kent, UK) according to American Thoracic Society guidelines,[14] Static lung volumes were measured by helium dilution. Predicted values used were those of the European Coal and Steel Community.[15]

Health Status and Disability Questionnaires

Patients completed the St George’s Respiratory Questionnaire (SGRQ) [16] and the Hospital Anxiety and Depression (HAD) questionnaire [17] while self-reported activity was assessed using the Nottingham Extended Activities of Daily Living (NEADL) questionnaire.[18]
Quadriceps Muscle Strength

Maximum quadriceps strength \((Q_{\text{MAX}})\) was measured by isometric maximum voluntary contraction of the dominant quadriceps using a custom built set-up. Further details of this are included in the online supplement. Subjects performed three maximum voluntary contractions with a rest period of 1 minute between efforts. \(Q_{\text{MAX}}\) was defined as the peak value obtained from the 3 recordings.

Six Minute Walking Test

The tests were performed in accordance with ATS recommendations [19] with two additional practice walks at initial assessment. Perceived breathlessness was scored immediately before exercise and at maximum exercise using the modified Borg scale.[20]

Activity Measurement

i.) Leg Accelerometry Measurement

Leg activity was measured using the Actiwatch uniaxial accelerometer (Cambridge Neurotechnology, Cambridge, UK). All recordings were made continuously over 3 week days with the exception of evaluation 1 (comparison of whole body and lower limb activity) where only 2 days were recorded. Using a lightweight strap the Actiwatch was positioned just above the dominant ankle and subjects only removed the device for bathing and then repositioned the Actiwatch immediately afterwards. The Actiwatch has an event marker button and subjects pressed this button on rising in the morning, going to bed at night and when the device was removed for bathing. Subjects also documented when and why the activity monitor was removed. On the rare occasion a subject forgot to press the marker button we used the written record or period of overnight inactivity to determine the actigram. Activity monitoring was performed before and after rehabilitation with the same Actiwatch.

The Actiwatch signal is measured 32 times per second and processed to provide both amount and duration of movement. This signal is expressed as an activity count, which denotes the amplitude of the signal detected by the accelerometer. Approximately 25 counts represents gravitational acceleration. Further details about the technical specifications are included in the online supplement. Data were expressed as an activity count, which is the sum of all the epochs within each thirty-second period. Inactivity was expressed as an activity count of zero. Data extracted for analysis was aggregated over the three daytime periods and expressed as:

Mean Activity Score: The average value of each thirty-second epoch throughout the waking day including all periods of zero activity.

Mean Intensity of Activity: The average value of each 30-second epoch when activity was occurring throughout the waking day (excludes any period of zero activity).

Percentage of Time Mobile: The percentage of 30-second epochs throughout the waking day where an activity score of 1 or more was recorded. Any epoch with a mean activity score of zero is labelled immobile while any epoch with a score of 1 or more is active, although a score of 1 represents a very low level of activity.

ii.) Total Body Activity Measurement
The Dynaport Activity Monitor (McRoberts BV, Den Haag, Netherlands) is a lightweight device containing a triaxial accelerometer. It has previously been validated for use in patients with COPD.[9] The device consists of a lightweight box enclosed in a neoprene belt worn anteriorly around the waist. The box is connected to a leg sensor, which is worn around the upper third of the thigh. The signal recorded by the device precisely measures the time spent walking, cycling, standing, sitting, or lying and it also provides a measure of movement intensity during the recording period. The technical specifications of the activity monitor have been detailed previously.[21]

The Dynaport Activity Monitor provides a measure of overall activity (Movement Intensity) and a measure of intensity of activity (Movement Intensity during Movement). In addition it records the proportion of the day during which the subject was moving (Time Spent Moving). Different activities can be classified and expressed as the proportion of the day spent walking, standing, sitting and lying down.

Subjects had the Dynaport activity monitor fitted and were instructed how to use it. All subjects were provided with written instructions, spare batteries and an emergency contact number. Subjects were monitored for 2 consecutive days, a time period over which reliable results have been obtained previously.[7] Monitoring lasted from rising in the morning until whatever time in the evening they had completed their usual daily activities.

Pulmonary Rehabilitation
Our 8-week outpatient pulmonary rehabilitation programme consists of 2 supervised and 1 unsupervised one-hour exercise session per week. Patients received an individualised regime of aerobic upper and lower limb exercises, which included peripheral muscle strengthening and whole body endurance exercises. Further details of the programme are included in the online supplement. Due to the ‘rolling’ nature of the programme if subjects were unable to attend particular supervised session(s) they continued the programme beyond 8-weeks until they had attended 16 supervised sessions. Subjects were defined as ‘completers’ if they attended 16 sessions.

Statistical Analysis
Group data are expressed as mean (standard deviation) and sub-group data as mean (standard error of the mean). Statistical analysis was performed using Statistical Package for Social Scientists (SPSS) version 15.0 and Stats Direct 2.6 with significance set at p<0.05 and p values are recorded to three decimal places. Normal distribution was assessed using the Shapiro-Wilks test and all data were normally distributed except for the Actiwatch Mean Activity Score and Actiwatch Mean Activity Score When Active. These data were logarithmically transformed to normalise the distribution. Paired and unpaired students t-tests were used to detect differences in group data and Pearson’s correlation coefficient to examine the association between individual parameters. Multiple linear regression analysis was performed with the primary explanatory variables being change in activity scores after pulmonary rehabilitation. A model was constructed to examine potential exploratory variables (FEV1 (L), FEV1 (% predicted), FEV1/FVC, DLCO (% predicted), quadriceps strength, six minute walking distance, SGRQ score and NEADL score). The final model was constructed using a backwards stepwise procedure, at each step a variable was removed which reduced the amount of variation accounted for by the least amount. Using published data we considered an improvement in six-minute walk distance of 54 metres after completion of pulmonary rehabilitation to be clinically significant.[3] From pilot data we established that a change in
Actiwatch mean activity score of 30 corresponded with similar improvements in walking distance and an improvement in health status. Based on change of these 2 measures we established that 24 subjects had to complete evaluation 3 of the study to detect a difference in these outcomes with 80% power at a significance level of 5%.
RESULTS

Baseline Characteristics

The baseline characteristics of the COPD patients and healthy volunteers are shown in Table 1.

Evaluation 1: Relationship between leg and whole body activity in COPD patients

Fourteen subjects were studied and all completed 2 days of recording with the Actiwatch. However, Dynaport measurements were unsuccessful in 2 patients due to unrecognised lack of battery power (both patients) plus incorrect operation of the device (1 patient). Therefore simultaneously recorded data were available in 12 patients with a mean recording duration of 18.7 (1.5) hours.

Mean data for the activity outcomes and body position are shown in Table 2. There was good agreement between the mean leg activity score recorded by the Actiwatch and the mean whole body activity level recorded by the Dynaport device (Table 3 and Figure 1a) and also between Actiwatch mean intensity of activity and all Dynaport activity assessments (Table 3 and Figure 1b). No relationship was seen between the time spent in specific positions and the activity levels assessed by the leg accelerometer. However, the mean number of counts recorded in each position for each patient was significantly different between the sitting and walking (online data supplement table 1).
Table 1: Baseline characteristics and number of subjects in each study evaluation. Data presented as mean (standard deviation). AW = Measurement of leg activity using the Actiwatch accelerometer. DP = Measurement of whole body activity using the Dynaport activity monitor. PR = pulmonary rehabilitation. Where “Not Known” is documented this measurement was not recorded in the particular group. FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, IC = inspiratory capacity, MVC = maximum voluntary contraction, SGRQ = St George’s Respiratory Questionnaire, NEADL = Nottingham Extended Activities of Daily Living Questionnaire.

<table>
<thead>
<tr>
<th>Study Evaluation</th>
<th>Evaluation 1</th>
<th>Evaluation 2</th>
<th>Evaluation 3</th>
<th>Evaluation 2 &amp; 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>COPD Subjects who had Concurrent DP and AW Measurement</td>
<td>Similar Age Normal Subjects who had AW Measurement</td>
<td>COPD Subjects who had AW Measurement Before and After PR</td>
<td>COPD Subjects who had AW Measurement</td>
</tr>
<tr>
<td>Number of Subjects</td>
<td>12</td>
<td>18</td>
<td>23</td>
<td>33</td>
</tr>
<tr>
<td>Gender (Male:Female)</td>
<td>9:3</td>
<td>8:10</td>
<td>12:11</td>
<td>17:16</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63 (7)</td>
<td>70 (6)</td>
<td>66 (9)</td>
<td>67 (8)</td>
</tr>
<tr>
<td>Smoker (Current:Ex:Never)</td>
<td>3:9:0</td>
<td>5:9:4</td>
<td>5:18:0</td>
<td>7:26:0</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>1.01 (0.43)</td>
<td>2.5 (0.6)</td>
<td>0.93 (0.32)</td>
<td>0.96 (0.4)</td>
</tr>
<tr>
<td>FEV1 %</td>
<td>33.4 (12.2)</td>
<td>105.1 (17.7)</td>
<td>36.4 (11.6)</td>
<td>38.2 (12)</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.83 (0.93)</td>
<td>3.3 (0.8)</td>
<td>2.27 (0.46)</td>
<td>2.36 (0.9)</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>0.36 (0.07)</td>
<td>0.77 (0.04)</td>
<td>0.41 (0.13)</td>
<td>0.42 (0.12)</td>
</tr>
<tr>
<td>IC %</td>
<td>73.3 (14.5)</td>
<td>Not Known</td>
<td>71.6 (15.8)</td>
<td>77.6 (20.8)</td>
</tr>
<tr>
<td>Quadricep MVC (N)</td>
<td>Not Known</td>
<td>415 (98)</td>
<td>315 (106)</td>
<td>308 (116)</td>
</tr>
<tr>
<td>SGRQ Total</td>
<td>63.4 (16.2)</td>
<td>Not Known</td>
<td>62.1 (13)</td>
<td>62.2 (12.5)</td>
</tr>
<tr>
<td>SGRQ Activity</td>
<td>77.2 (19.4)</td>
<td>Not Known</td>
<td>79.1 (13.1)</td>
<td>80.1 (13.7)</td>
</tr>
<tr>
<td>NEADL</td>
<td>18.9 (2.3)</td>
<td>Not Known</td>
<td>16.4 (2.7)</td>
<td>15.7 (2.8)</td>
</tr>
<tr>
<td>Actiwatch Measures:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Activity (x10³ counts/hour)</td>
<td>123 (110)</td>
<td>143 (61)</td>
<td>82 (53)</td>
<td>82 (49)</td>
</tr>
<tr>
<td>Mean Intensity of Activity (x10³ counts/hr)</td>
<td>190 (162)</td>
<td>232 (90)</td>
<td>156 (69)</td>
<td>156 (63)</td>
</tr>
<tr>
<td>% of Time Mobile</td>
<td>63.2 (14.5)</td>
<td>61.4 (11.2)</td>
<td>50 (13.9)</td>
<td>50.8 (15.4)</td>
</tr>
</tbody>
</table>
Table 2: Measurements of activity obtained from the Actiwatch (leg) and Dynaport (whole body) systems during the 2 days of recording in 12 patients with COPD (Evaluation 1). Data are presented as mean (standard deviation).

<table>
<thead>
<tr>
<th>ACTIWATCH</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Spent Mobile (% of recording)</td>
<td>63.3 (14.5)</td>
<td></td>
</tr>
<tr>
<td>Mean Activity Score (x10^3 counts/hour)</td>
<td>123 (110)</td>
<td></td>
</tr>
<tr>
<td>Mean Intensity of Activity (x10^3 counts/hour)</td>
<td>190 (162)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DYNAPORT</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Spent Moving (%)</td>
<td>13.5 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Movement Intensity</td>
<td>0.2 (0.1)</td>
<td></td>
</tr>
<tr>
<td>Movement Intensity During Movement</td>
<td>1.48 (0.21)</td>
<td></td>
</tr>
<tr>
<td>Time Spent Walking (%)</td>
<td>3.6 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Time Spent Standing (%)</td>
<td>32.1 (15.2)</td>
<td></td>
</tr>
<tr>
<td>Time Spent Sitting (%)</td>
<td>58.7 (17.6)</td>
<td></td>
</tr>
<tr>
<td>Time Spent Lying Down (%)</td>
<td>5.3 (4.9)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Correlation between different activity measures obtained from the Actiwatch and Dynaport Activity Monitor in 12 patients with COPD (Evaluation 1). Data recorded are Pearson’s correlation coefficient, 95% confidence interval of the correlation and p value.

<table>
<thead>
<tr>
<th>ACTIWATCH</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Mean Activity Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Intensity of Activity Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time Spent Mobile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time Spent Moving (%)</td>
<td>r = 0.83</td>
<td>95% CI = 0.48-0.95</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>Movement Intensity</td>
<td>r = 0.92</td>
<td>95% CI = 0.72-0.98</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Movement Intensity During Movement</td>
<td>r = 0.81</td>
<td>95% CI = 0.45-0.95</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>Time Spent Walking (%)</td>
<td>r = -0.42</td>
<td>95% CI = -0.8-0.2</td>
<td>p = 0.171</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DYNAPORT</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Spent Moving (%)</td>
<td>r = 0.76</td>
<td>95% CI = 0.32-0.93</td>
<td>p = 0.004</td>
</tr>
<tr>
<td>Movement Intensity During Movement</td>
<td>r = 0.88</td>
<td>95% CI = 0.63-0.97</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Movement Intensity During Movement</td>
<td>r = 0.83</td>
<td>95% CI = 0.49-0.95</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>Time Spent Walking (%)</td>
<td>r = -0.32</td>
<td>95% CI = -0.76-0.31</td>
<td>p = 0.306</td>
</tr>
<tr>
<td>Time Spent Standing (%)</td>
<td>r = 0.35</td>
<td>95% CI = -0.28-0.77</td>
<td>p = 0.27</td>
</tr>
<tr>
<td>Time Spent Sitting (%)</td>
<td>r = 0.54</td>
<td>95% CI = -0.54-0.61</td>
<td>p = 0.883</td>
</tr>
<tr>
<td>Time Spent Lying Down (%)</td>
<td>r = -0.42</td>
<td>95% CI = -0.8-0.2</td>
<td>p = 0.169</td>
</tr>
</tbody>
</table>
Evaluation 2: Leg activity in COPD and health volunteers

The patients and volunteers were of similar age and by definition differed in lung function (Table 1). Quadriceps muscle strength was significantly less in the COPD patients (Difference = 107N, 95% CI = 48 – 139N; p=0.001). The COPD patients spent significantly less of the day mobile (Difference = 10.6%, 95% CI 3.1 – 18.2%; p=0.007) and had a lower mean activity level (Difference = 61, 95% CI 27 – 96; p=0.001) and lower intensity of activity score (Difference = 77, 95% CI = 27 – 126; p=0.004). Leg activity recordings were relatively stable between the days for both COPD patients and volunteers. The mean (range) coefficient of variation was, 21.6% (2.2% to 47.4%) for mean activity score, 15.7% (3.2% to 42%) for mean intensity of activity and 11.5% (1.5% to 31.3%) for percentage of time spent mobile. When different leg activity measures, recorded in the COPD patients, were compared mean activity scores were closely related to the mean intensity of activity (r=0.86, 95% CI 0.73 – 0.93; p<0.001) with a weaker relationship between the mean activity score and the percentage of time scored as mobile (r=0.68, 95% CI 0.44 – 0.83; p<0.001). However, the intensity of activity when exercising was not related to the amount of time spent mobile (r=0.27, 95% CI = -0.08 – 0.56; p=0.122).

Evaluation 3a: Lower limb activity and laboratory assessments of exercise capacity

In this evaluation the Actiwatch accelerometer was worn for an average of 15.7 (0.2) hours per day on each of the 3 days of recording.

All functional measurements whether lung mechanics, muscle strength, walking distance or self-completed questionnaires were related to each other to a varying degree (online data supplement Table 2). There was a significant or near significant relationship between measures of leg activity and many of these variables (on-line data supplement Table 3). Mean activity of the legs was most closely related to absolute FEV1 as was the percentage of time spent mobile (r=0.57, 95% CI = 0.28 – 0.76; p<0.001 and r=0.51, 95% CI = 0.2 - 0.73; p=0.002 respectively). There was a significant relationship between FEV1 percent predicted and mean intensity of activity when exercising (r=0.5, 95% CI = 0.19 – 0.72; p=0.003), although in this case the best univariate correlation was with gas transfer (r=0.6, 95% CI = 0.25 – 0.81; p=0.003). There was a relationship both between mean leg activity and the subjective assessment of activity using the NEADL. However, this relationship was weak: r=0.35, 95% CI = 0 – 0.62; p=0.049.

Evaluation 3b: Lower limb activity and pulmonary rehabilitation

The number of patients participating in and completing the pulmonary rehabilitation programme is shown in Figure 2. The change in outcome variables after completion of rehabilitation is presented in Table 4. Subjects completing rehabilitation showed significant improvements in self-paced walking distance, quadriceps strength, breathlessness at rest and peak exercise, health status and level of anxiety and depression. In general these changes exceeded the minimum clinically important difference and they were paralleled by significant improvements in leg activity. However, the magnitude of change in walking distance and muscle strength were unrelated to the change in any index of leg activity.

Improvement in objectively measured leg activity was positively correlated with baseline FEV1 (r=0.8, 95% CI = 0.58 – 0.91; p<0.001) - shown in figure 3. The only other baseline variables that contributed to the improvement in any measure of activity were six minute walk
Baseline subjective activity level assessed using the NEADL questionnaire was related to change in the percentage of time spent mobile (r=0.56, 95%CI =0.15-0.79; p=0.006) and mean activity score (r=0.47; 95%CI =0.08-0.71; p=0.021) after completion of rehabilitation. Full details of the relationships between change in leg activity and baseline variables is shown in table 4 of the online supplement.

Table 4: The effect of pulmonary rehabilitation in the 23 COPD subjects who completed all assessments (Evaluation 3). Data shown are mean (standard error of the mean). 6MWD = Six minute walking distance (metres), HAD = Hospital anxiety and depression questionnaire score.

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>POST</th>
<th>Mean Difference After Rehabilitation</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quadriceps Strength:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quads MVC (Newtons)</td>
<td>312 (20)</td>
<td>334 (23)</td>
<td>22 (31)</td>
<td>9 - 35</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>6MWD:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6MWD (metres)</td>
<td>274 (13)</td>
<td>333 (13)</td>
<td>59 (33)</td>
<td>45 - 73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resting Borg Score</td>
<td>1.6 (0.2)</td>
<td>0.9 (0.2)</td>
<td>0.7 (1.2)</td>
<td>0.2 – 1.6</td>
<td>0.008</td>
</tr>
<tr>
<td>Peak Borg Score</td>
<td>4.6 (0.2)</td>
<td>3.2 (0.3)</td>
<td>1.4 (1.7)</td>
<td>0.7 – 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Leg Activity:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of time spent mobile</td>
<td>50.0 (2.7)</td>
<td>55.2 (2.6)</td>
<td>5.2 (9.4)</td>
<td>1.2 – 9.3</td>
<td>0.014</td>
</tr>
<tr>
<td>Mean activity score (x10^3 counts/hour)</td>
<td>81.5 (53.2)</td>
<td>117.2 (84.2)</td>
<td>35.7 (49)</td>
<td>14.5 – 56.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Mean intensity of activity score (x10^3 counts/hour)</td>
<td>156 (69.2)</td>
<td>208.5 (123.4)</td>
<td>52.5 (74.2)</td>
<td>20.4 - 84.6</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Health Status:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAD anxiety</td>
<td>7.2 (1)</td>
<td>5.6 (0.6)</td>
<td>1.6 (3.2)</td>
<td>0.2 - 3</td>
<td>0.016</td>
</tr>
<tr>
<td>HAD depression</td>
<td>6.4 (0.6)</td>
<td>4.4 (0.6)</td>
<td>2 (2.2)</td>
<td>1 – 2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SGRQ</td>
<td>62.9 (2.5)</td>
<td>47.8 (2.4)</td>
<td>15.1 (12.5)</td>
<td>8.9 – 19.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nottingham Extended ADL</td>
<td>16.4 (0.5)</td>
<td>18.2 (0.5)</td>
<td>1.8 (1.7)</td>
<td>1.1 – 2.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
DISCUSSION

Exercise limitation in COPD integrates the effect of many different aspects of this condition including abnormal lung mechanics, peripheral muscle dysfunction and altered mood states. Subjective assessments of exercise limitation range from simple reporting of activity limited by dyspnoea such as the MRC dyspnoea scale [22] through to more global reporting of disability such as the SGRQ activity score or NEADL. Cardio-pulmonary exercise testing can define the physiological limits to exercise but this and other objective exercise tests define what the patient can do rather than what they actually do at home. In comparison recording accelerometry provides insight into how much activity is undertaken. In this report we have focussed on leg activity and confirm that this variable relates well to whole body activity, distinguishes COPD patients from unaffected individuals and responds to rehabilitation. However, interpreting these data is not necessarily simple nor do they simply track changes in the variables we usually report when assessing a response to treatment.

Leg activity monitoring showed modest day-to-day variability in both COPD and healthy patients comparable to that reported with other systems. There was good agreement between the activity scores of the Dynaport, a validated whole body accelerometer, and both the mean activity scores and mean intensity of activity scores of the leg device. The differences in daily leg activity of the healthy volunteers and COPD patients are comparable to those reported for whole-body activity [7] and improvements after rehabilitation suggests that leg actigraphy both tracks other outcome measures and is responsive to intervention. The lack of agreement between leg activity and position monitoring data from the Dynaport likely reflects the strict scoring standards we used to define mobility. However, we cannot exclude an effect due to leg movements when seated or lying. The lack of complete agreement between the two methods means that lower limb activity monitors cannot be substituted for those measuring total activity when determining whole body energy expenditure.[23] Despite this lower limb activity is clearly the major determinant of whole body activity and in most circumstances lower limb measurement is likely to be an acceptable surrogate for a whole-body system.

Of the three leg accelerometric variables we reported mean activity provided an acceptable compromise between both percent time spent immobile and the mean intensity of activity during exercise. These latter variables were unrelated in the COPD patients suggesting that the amount of time spent sitting or lying completely still was determined by different factors to those determining intensity of lower limb activity when exercise had to be undertaken. To a degree this was reflected in the relative lack of relationship between lower limb activity and conventionally used performance indicators, such as walking distance, quadriceps strength and activity questionnaires. Although these variables were related, the major factor determining leg activity was the FEV\textsubscript{1} so that the better the lung function the greater the degree of activity a patient undertook. The relationship between lung function and walking distance was much weaker, albeit not dissimilar to published data,[24] as was the relationship between activity and walking distance. Hence, level of activity does not appear to simply reflect capacity but may be affected by lifestyle and choice. The subjectively reported limitation in activity of daily living score was weakly related to mean level of activity and similar associations were seen with other subjective scores. However, unlike objective activity measures, subjective scores did not relate to measures of pulmonary function. These data suggest that level and extent of activity at home are independent measures of function which can only be approximately assessed using either currently available laboratory physiological outcomes or activity questionnaires.
Pulmonary rehabilitation produced significant improvements in health status, lower limb muscle strength and exercise performance that are comparable to the best results reported with other programmes. Significant improvement was seen in all measures of lower limb activity although even after pulmonary rehabilitation leg activity was still significantly less than that in age-matched controls. The magnitude of improvement in measures of functional capacity, such as walking distance and quadriceps strength, did not predict the change in leg activity at home, even though both were significantly greater after rehabilitation.

We initially hypothesised that the most inactive subjects would have a greater capacity to improve level of activity after rehabilitation. In fact baseline level of activity was only weakly related to the improvement after rehabilitation suggesting that even active individuals can further increase their level of activity with an effective rehabilitation programme. Instead change in leg activity after rehabilitation, however expressed, was primarily influenced by lung function, although the pre-rehabilitation 6 minute walking distance also made an independent contribution. Thus individuals with better exercise capacity and lung function did more at home and with greater intensity after completing rehabilitation. This is compatible with the subjective improvement in activity of daily living. As in previously published data patients with a better preserved FEV1 but worse perception of activity reported the greatest subjective benefit. The importance of spirometry as a predictor of outcome post-rehabilitation is not entirely surprising as previous reports have highlighted the role of ventilatory capacity in determining improvement in walking distance after rehabilitation.

The Actiwatch proved to be easy to use, acceptable to patients and carried a low failure rate. As a simple strap mounted device it could be worn under clothing and with long battery life it could be worn overnight and only needed to be removed for bathing. In contrast the Dynaport was technically more difficult to use and while light it was larger and noticeable. It includes both a waist and a leg strap and hence has to be removed overnight and during ablutions. The start-up procedure needs to be completed each morning and ideally both batteries and memory card should be changed daily. In choosing an activity monitor the ease of use of the Actiwatch has to be balanced against the more precise body position activity data obtained with the Dynaport.

Our data provide further support for the usefulness of monitoring daily activity at home in COPD patients and that simple monitoring of leg movement gives useful insights into daily activity. The intensity and amount of leg activity a patient undertakes at home gives rather different results to those predicted by more conventional measurements like walking distance, muscle strength and health status questionnaires. Understanding why people improve some forms of activity but not others after treatment and what determines how much of their improved exercise capacity post-rehabilitation they use is an important area of future research which will be greatly aided by the availability of valid monitoring methods like actigraphy.

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**Competing Interests:** No author has a competing interest to declare in respect to this manuscript

**Funding:** None
FIGURE LEGENDS

Figure 1: A – The relationship between measures of mean activity from Dynaport and Actiwatch
Figure 1: B – The relationship between measures of intensity of activity from Dynaport and Actiwatch

Figure 2: Flow chart showing the outcome for the 33 subjects referred to the pulmonary rehabilitation programme

Figure 3: A - Relationship between FEV₁ and change in Actiwatch leg mean activity after rehabilitation ($r = 0.8, p < 0.001$)
Figure 3: B - Relationship between FEV₁ and change in Actiwatch leg mean intensity of activity after rehabilitation ($r = 0.67, p < 0.001$)
REFERENCES


24 Pinto-Plata VM, Cote C, Cabral H, Taylor J, Celli BR. The 6-min walk distance: change over time and value as a predictor of survival in severe COPD. Eur Respir J. 2004;23:28-33


27 Zu Wallack RL, Patel K, Reardon JZ, Clark BA 3rd, Normandin EA. Predictors of improvement in the 12-minute walking distance following a six-week outpatient pulmonary


Figure 1: A – The relationship between measures of mean activity from Dynaport and Actiwatches.

\[ r = 0.92 \]

\[ p < 0.001 \]
Figure 1: B – The relationship between measures of intensity of activity from Dynaport and Actiwatch.

- Actiwatch Mean Intensity of Activity (log)
- Dynaport Movement Intensity During Movement

$r = 0.83
p = 0.001$
Figure 2: Flow chart showing the outcome for the 33 subjects referred to the pulmonary rehabilitation programme.

33 subjects recruited and assessed pre PR

- 24 subjects completed PR
  - 23 subjects assessed post PR
  - 1 subject declined assessment post PR
- 9 subjects did not complete PR
  - 6 subjects dropped out of PR
    - 1 chose to drop out
    - 2 exacerbated
    - 3 had other medical problems
  - 3 subjects failed to start PR
Figure 3: A - Relationship between FEV$_1$ and change in Actiwatch leg mean activity after rehabilitation ($r = 0.8$, $p < 0.001$)
Figure 3: B - Relationship between FEV\textsubscript{1} and change in Actiwatch leg mean intensity of activity after rehabilitation (\(r = 0.67, p < 0.001\))
ONLINE DATA SUPPLEMENT

METHODS

Addition details of the methods used are included in this section.

**Quadriiceps Muscle Strength**
Subjects sat in a rigid, high-backed chair with 90° flexion at hip and knee and hip position fixed using a lap strap. A further strap was positioned above the ankle and attached securely around the leg. This strap was attached to a strain gauge transducer, the signal from which was converted by connection to a MacLab Bridge Amplifier (ADInstruments, Sydney, Australia) and using the MacLab Chart and Scope software (Version 3.4). The transducer was calibrated beforehand using weights.

**Activity Measurement**

i.) *Leg Accelerometry Measurement*
The Actiwatch records all acceleration greater than 0.05 times gravitational acceleration but filters readings above 11Hz to enable capture of human movement but eliminate vibration associated with vehicular transport. The manufacturer calibrated each Actiwatch to ensure that the output from each device was produced by the same amount of motion. The signal is measured 32 times per second and processed to provide both amount and duration of movement. A reader/interface device is used to download data from the Actiwatch to a computer and Sleep Analysis software (Cambridge Neurotechnology, Cambridge, UK) is used for analysis. An activity count is obtained, which denotes the amplitude of the signal detected by the accelerometer. The number of counts is proportional to the intensity of movement with approximately 25 counts representing gravitational acceleration. The memory size of the Actiwatch is 64kB, which allows continuous recording for 22 days when data is recorded in epochs of 30 seconds. On no occasion was data lost due to battery failure.

**Pulmonary Rehabilitation**
Patients exercised to a symptom-limited intensity equivalent to a level of 3 to 4 on the modified Borg scale (moderate to somewhat severe breathlessness) [21] and were allowed 1-2 minutes rest between each exercise. Patients were encouraged to increase the time spent on each exercise at each session and the work rate of each individual was monitored and increased as necessary. An individually tailored home exercise programme was provided for the unsupervised session. After each supervised exercise session there was also a short (20-30 minutes) education session focusing on behavioural and lifestyle elements.
RESULTS

Additional data tables are included in this section

**Online Data Supplement Table 1:** Mean number of Actiwatch recorded counts in each 30-second period divided according to Dynaport recorded position in 12 patients with COPD (Evaluation 1).

<table>
<thead>
<tr>
<th>DYNAPORT CLASSIFIED ACTIVITY</th>
<th>ACTIWATCH MEAN ACTIVITY COUNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Spent Walking</td>
<td>584</td>
</tr>
<tr>
<td>Time Spent Standing</td>
<td>205</td>
</tr>
<tr>
<td>Time Spent Sitting</td>
<td>66</td>
</tr>
<tr>
<td>Time Spent Lying Down</td>
<td>5</td>
</tr>
</tbody>
</table>

**Online Data Supplement Table 2:** Relationship between measures of performance (whether based on lung mechanics, muscle strength, walking distance or self-completed questionnaires).

- Quads MVC relates to...
  - FEV1 (L) \( r=0.35 \) Effect estimate 95%CI = 0–0.62 \( p=0.048 \)
  - 6MWD \( r=0.54 \) Effect estimate 95%CI = 0.23–0.74 \( p=0.001 \)
  - HAD anxiety \( r=-0.53 \) Effect estimate 95%CI = 0.22–0.73 \( p=0.002 \)
  - SGRQ \( r=-0.48 \) Effect estimate 95%CI = -0.16–0.71 \( p=0.004 \)

- 6MWD relates to...
  - HAD anxiety \( r=-0.37 \) Effect estimate 95%CI = -0.03–0.63 \( p=0.035 \)
  - HAD depr. \( r=-0.37 \) Effect estimate 95%CI = -0.03–0.63 \( p=0.035 \)
  - SGRQ \( r=-0.47 \) Effect estimate 95%CI = -0.15–0.71 \( p=0.005 \)

- Resting Borg relates to...
  - Peak Borg \( r=0.4 \) Effect estimate 95%CI = 0.07–0.65 \( p=0.021 \)
  - SGRQ \( r=0.39 \) Effect estimate 95%CI = 0.05–0.64 \( p=0.026 \)

- SGRQ relates to...
  - HAD anxiety \( r=0.7 \) Effect estimate 95%CI = 0.48–0.84 \( p<0.001 \)
  - HAD depr. \( r=0.71 \) Effect estimate 95%CI = 0.48 – 0.84 \( p<0.001 \)

**Online Data Supplement Table 3:** Relationship between baseline activity (objective and subjective) and baseline characteristics in the COPD subjects.

**OBJECTIVE** – Leg activity measured by the Actiwatch

% Time Mobile correlates with:

- FEV1 (L) \( r=0.51 \) Effect estimate 95%CI = 0.2 - 0.73 \( p=0.002 \)
- FEV1 (%) \( r=0.38 \) Effect estimate 95%CI = 0.05 - 0.64 \( p=0.028 \)
- FVC (L) \( r=0.5 \) Effect estimate 95%CI = 0.2 – 0.72 \( p=0.003 \)
- SVC (%) \( r=0.48 \) Effect estimate 95%CI = 0.1 – 0.74 \( p=0.018 \)
- IC (%) \( r=0.45 \) Effect estimate 95%CI = 0.06 – 0.72 \( p=0.025 \)
- Quads MVC \( r=0.4 \) Effect estimate 95%CI = 0.06 – 0.55 \( p=0.023 \)
Mean Activity correlates with:

- **6MWD**  \( r=0.34 \)  Effect estimate 95%CI = 0 – 0.61  \( p=0.051 \)
- **SGRQ total**  \( r=-0.33 \)  Effect estimate 95%CI = 0.02 - -0.6  \( p=0.061 \)
- **HAD anxiety**  \( r=0.32 \)  Effect estimate 95%CI = -0.02 – 0.6  \( p=0.062 \)
- **NEADL**  \( r=0.28 \)  Effect estimate 95%CI = -0.07 – 0.57  \( p=0.113 \)

Mean Intensity of Activity correlates with:

- **FEV1 (L)**  \( r=0.57 \)  Effect estimate 95%CI = 0.28 – 0.76  \( p<0.001 \)
- **FEV1 (%)**  \( r=0.52 \)  Effect estimate 95%CI = 0.22 – 0.73  \( p=0.002 \)
- **FVC (L)**  \( r=0.36 \)  Effect estimate 95%CI = 0.02 – 0.63  \( p=0.039 \)
- **DLCO**  \( r=0.49 \)  Effect estimate 95%CI = 0.1 – 0.75  \( p=0.017 \)
- **6MWD**  \( r=0.37 \)  Effect estimate 95%CI = 0.03 – 0.63  \( p=0.034 \)
- **SGRQ total**  \( r=-0.35 \)  Effect estimate 95%CI = -0.01 - -0.62  \( p=0.047 \)
- **FEV1/FVC**  \( r=0.33 \)  Effect estimate 95%CI = -0.01 – 0.61  \( p=0.06 \)
- **IC (%)**  \( r=0.38 \)  Effect estimate 95%CI = -0.02 – 0.67  \( p=0.063 \)
- **Peak Borg**  \( r=-0.32 \)  Effect estimate 95%CI = 0.04 – -0.59  \( p=0.077 \)
- **HAD depression**  \( r=-0.32 \)  Effect estimate 95%CI = -0.02 – 0.6  \( p=0.067 \)
- **NEADL**  \( r=0.35 \)  Effect estimate 95%CI = 0 – 0.62  \( p=0.049 \)

SUBJECTIVE – Assessed by the Nottingham Extended Activities of Daily Living Questionnaire and St Georges Respiratory Questionnaire Activity score

NEADL correlates with:

- **6MWD**  \( r=0.63 \)  Effect estimate 95%CI = 0.36 – 0.8  \( p<0.001 \)
- **Quads MVC**  \( r=0.42 \)  Effect estimate 95%CI = 0.08 – 0.66  \( p=0.016 \)
- **SGRQ total**  \( r=-0.45 \)  Effect estimate 95%CI = -0.12 - -0.68  \( p=0.009 \)
- **HAD anxiety**  \( r=-0.36 \)  Effect estimate 95%CI = -0.02 - -0.63  \( p=0.037 \)
- **HAD depression**  \( r=-0.37 \)  Effect estimate 95%CI = -0.15 - -0.7  \( p=0.005 \)
- **% Time Mobile**  \( r=0.28 \)  Effect estimate 95%CI = -0.07 – 0.57  \( p=0.113 \)
- **Mean Activity**  \( r=0.35 \)  Effect estimate 95%CI = 0 – 0.62  \( p=0.049 \)
- **Mean in Active**  \( r=0.28 \)  Effect estimate 95%CI = -0.07 – 0.57  \( p=0.119 \)

**Online Data Supplement Table 4: Subject baseline characteristics that determine change in a) objective leg activity and b) subjective activity**

a.) Change in mean leg activity correlates with:
FEV1 (L) (shown in figure 2a) \( r = 0.8 \) Effect estimate 95%CI = 0.58–0.91 \( p<0.001 \)
FEV1 (% predicted) \( r = 0.59 \) Effect estimate 95%CI = 0.59-0.8 \( p=0.003 \)
FEV1/FVC \( r = 0.48 \) Effect estimate 95%CI = 0.08-0.75 \( p=0.02 \)

Regression coefficients, standard error, confidence intervals and p values from multivariate regression model in which change in leg mean intensity of activity was the outcome variable:

<table>
<thead>
<tr>
<th>Regression Coefficient</th>
<th>Standard Error</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (L)</td>
<td>119.9</td>
<td>19.6</td>
<td>79-161</td>
</tr>
</tbody>
</table>

Change in leg mean intensity of activity correlates with:

FEV1 (L) (shown in figure 2b) \( r = 0.67 \) Effect estimate 95%CI = 0.35-0.85 \( p<0.001 \)
FEV1 (% predicted) \( r = 0.55 \) Effect estimate 95%CI = 0.17-0.78 \( p=0.007 \)
6MWD \( r = 0.27 \) Effect estimate 95%CI = -0.16-0.61 \( p=0.22 \)

Regression coefficients, standard error, confidence intervals and p values from multivariate regression model in which change in leg mean intensity of activity was the outcome variable:

<table>
<thead>
<tr>
<th>Regression Coefficient</th>
<th>Standard Error</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (L)</td>
<td>164.6</td>
<td>34.3</td>
<td>93 – 256</td>
</tr>
<tr>
<td>6MWD</td>
<td>0.36</td>
<td>0.15</td>
<td>0.04 – 0.7</td>
</tr>
</tbody>
</table>

Change in time spent mobile correlates with:

FEV1 (L) \( r = 0.38 \) Effect estimate 95%CI = -0.04-0.68 \( p=0.076 \)
NEADL \( r = 0.56 \) Effect estimate 95%CI = 0.18-0.79 \( p=0.006 \)
6MWD \( r = 0.31 \) Effect estimate 95%CI = -0.11–0.65 \( p=0.136 \)

Regression coefficients, standard error, confidence intervals and p values from multivariate regression model in which change in leg mean intensity of activity was the outcome variable:

<table>
<thead>
<tr>
<th>Regression Coefficient</th>
<th>Standard Error</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (L)</td>
<td>-10.5</td>
<td>5.0</td>
<td>-21 - -0.06</td>
</tr>
<tr>
<td>NEADL</td>
<td>1.9</td>
<td>0.6</td>
<td>0.7 – 3.2</td>
</tr>
</tbody>
</table>

b.) Change in Nottingham Extended ADL score was found to correlates with:

FEV1 (L) \( r = 0.59 \) Effect estimate 95%CI = 0.24-0.81 \( p=0.003 \)
FEV1 (% predicted) \( r = 0.49 \) Effect estimate 95%CI = 0.09-0.75 \( p=0.019 \)
FEV1/FVC \( r = 0.65 \) Effect estimate 95%CI = 0.33-0.84 \( p<0.001 \)