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**Cardiorespiratory measurements during field tests in CF:
Use of an ambulatory monitoring system**



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Keywords:	respiratory inductive plethysmography, LifeShirt, cystic fibrosis, 6 Minute Walk Test, Modified Shuttle Test



Title: Cardiorespiratory measurements during field tests in CF: Use of an ambulatory monitoring system

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Short title: Field exercise tests in CF

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4 **Summary:** Respiratory inductive plethysmography (e.g. LifeShirt) may offer in-depth
5 study of the cardiorespiratory responses during field exercise tests. The aims of this
6 study were to assess the reliability, discriminate validity and responsiveness of
7 cardiorespiratory measurements recorded by the LifeShirt during field exercise tests in
8 adults with CF. To assess reliability and discriminate validity, participants with CF and
9 stable lung disease and healthy participants performed the 6 Minute Walk Test (6MWT)
10 and Modified Shuttle Test (MST) on 2 occasions. To assess responsiveness, participants
11 with CF experiencing an exacerbation performed the 6MWT at the start and end of an
12 admission for intravenous antibiotics. The LifeShirt was worn during all exercise tests.
13 Reliability and discriminate validity were assessed in 18 participants with CF (mean (SD)
14 age: 26 (10)years; FEV₁%predicted: 69.2 (23)%) and 18 healthy participants (age: 24
15 (5)years, FEV₁%predicted: 92 (8)%). There was no difference in 6MWT and MST
16 performance between days and reliability of cardiorespiratory measures was acceptable
17 (bias $p>0.05$; CV<10%). Participants with CF demonstrated a significantly greater
18 response to exercise (e.g. ventilation, respiratory rate) compared to healthy participants
19 indicating discriminate validity. Responsiveness was assessed in 12 participants with CF:
20 clinical measurements and 6MWT performance improved (61(81)m; $p<0.05$) however
21 cardiorespiratory measurements recorded by the LifeShirt remained the same (bias:
22 $p>0.05$; CV<10%). This study provides evidence that cardiorespiratory responses can be
23 measured non-invasively during field exercise tests in adults with CF. Reliability and
24 discriminate validity of key cardiorespiratory measurements recorded by the LifeShirt
25 were demonstrated. Some information on responsiveness is reported.
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Keywords

respiratory inductive plethysmography;
LifeShirt;
cystic fibrosis;
6 Minute Walk Test;
Modified Shuttle Test

For Peer Review

INTRODUCTION

In cystic fibrosis (CF) exercise tests enable assessment of functional capacity and limitations, determination of level of fitness, safe and effective exercise recommendations, and evaluation of interventions.^{1,2} Field exercise tests are often used in CF centres when clinical laboratories are unavailable. While field exercise tests provide information on exercise performance (i.e. how far a patient can walk or run) they do not provide in-depth information on the cardiorespiratory responses to exercise or what factors contribute to exercise limitation. Measuring cardiorespiratory responses during field exercise tests using ambulatory monitoring has been limited by the technology available. Some available ambulatory monitoring systems record a narrow range of measurements and others are too cumbersome. Respiratory inductive plethysmography (e.g. the LifeShirt) may offer the opportunity for more in-depth study of the cardiorespiratory responses during field exercise tests and potentially provide additional valuable information.³

The LifeShirt[®] (Vivometrics, Inc., Ventura, CA, U.S.A.) is a multi-function ambulatory system capable of detecting several cardiorespiratory measures of interest to clinicians and researchers working in CF, for example timing and volume components of breathing and heart rate. The LifeShirt consists of a CoolMax[®] garment, data recorder, and computer-based analysis software (VivoLogic). The core technology is respiratory inductive plethysmography which provides non-invasive assessment of respiratory pattern. Unlike direct methods which must be coupled to the individual (e.g. pneumotach via a face-mask or mouthpiece and nose-clips), respiratory inductive plethysmography is

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3 unobtrusive and so can be used for extended periods in an ambulatory setting. The
4 LifeShirt system incorporates a Lycra vest into which the respiratory inductive
5 plethysmography bands are embedded in order to limit displacement. Before systems
6 such as the LifeShirt can be used in clinical or research practice information is required
7 on clinimetric properties (i.e. reliability, validity and responsiveness).
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17 Assessment of clinimetric properties of the LifeShirt has mainly been conducted in
18 healthy participants in a laboratory environment.³⁻⁶ We have previously demonstrated
19 that the LifeShirt can provide valid and reliable cardiorespiratory data across multiple
20 assessments in healthy participants tested in a laboratory environment.³ There has been
21 one previous study that has used the LifeShirt during exercise in clinical populations and
22 demonstrated the ability of cardiorespiratory measurements recorded by the LifeShirt
23 (ventilation, respiratory rate and heart rate) to discriminate between patients with
24 congestive heart failure, chronic obstructive pulmonary disease and healthy participants.⁴
25 There is no available information on the clinimetric properties of cardiorespiratory
26 measurements recorded by respiratory inductive plethysmography (i.e. the LifeShirt)
27 during exercise tests in patients with CF.
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45 The aims of this study were:

- 46 • to assess the reliability of cardiorespiratory measurements recorded by the
47 LifeShirt during the 6 Minute Walk Test (6MWT) and Modified Shuttle Test
48 (MST) in participants with CF and healthy controls (i.e. degree to which the
49 results are consistent over two occasions)
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- to assess the discriminate validity of cardiorespiratory measurements recorded by the LifeShirt during comparable stages of the MST (i.e. ability to detect a difference in cardiorespiratory responses to exercise between participants with CF versus healthy age matched controls)
- to assess the responsiveness of cardiorespiratory measurements recorded by the LifeShirt system during the 6MWT in participants with CF admitted for intravenous antibiotic therapy (i.e. ability to detect treatment induced changes in cardiorespiratory response to exercise).

The hypotheses for this study were that cardiorespiratory measurements recorded by the LifeShirt during field tests in participants with CF 1) are reliable, 2) can discriminate between participants with CF and healthy age matched participants, and 3) are responsive to intravenous antibiotic therapy.

MATERIALS AND METHODS

Ethics

The protocol was approved by the Queen's University Belfast and Belfast Trust City Hospital ethics and research governance procedures and written informed consent obtained. Recruitment commenced in November 2003 and ended in October 2007.

LifeShirt

LifeShirt data relating to various cardiorespiratory measurements were recorded during field exercise tests. These included inspiratory tidal volume (V_{iVol} , mL); ventilation (V_E , $L \cdot \text{min}^{-1}$); respiratory rate (Br/M, $\text{breaths} \cdot \text{min}^{-1}$); ratio of inspiratory time to total respiratory time (T_i/T_t); and heart rate (HR, $\text{beats} \cdot \text{min}^{-1}$). The method of calibrating the volume components of breathing was recommended by the manufacturers and involved patients inflating and deflating a fixed volume (400mL/800mL) bag seven times whilst wearing nose clips. This was performed in standing.

Spirometry and exercise tests

Spirometry was performed according to ATS/ ERS guidelines for standardisation of spirometry⁷ and expressed as percentage of predicted normal values according to the equations developed by Quanjer et al. (1993)⁸. Lung disease was classified by FEV_1 as normal ($>90\%$ predicted), mild (70-89% predicted), moderate (40-69% predicted) or severe ($<40\%$ predicted).⁹ For the 6MWT participants were asked to walk as fast as they could around a 30 metre course for a period of six minutes according to the ATS

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3 guidelines.¹⁰ For the MST participants were asked to walk or run around a 10 metre
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5 course at increasing speeds dictated by an external bleep from a tape recorder.¹¹⁻¹⁴
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10 **Part 1: Reliability and discriminate validity**

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12 Patients with CF and stable lung disease were recruited from the Northern Ireland Adult
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14 CF Centre in Belfast City Hospital. Age matched controls were recruited from staff and
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16 students at Belfast City Hospital and the University of Ulster. All participants wore the
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18 LifeShirt system during a 6MWT and MST performed on two occasions at least one
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20 week apart (Time 1 and Time 2). Exercise tests were carried out according to
21
22 standardised protocols and in a standardised order. Sufficient rest periods were used
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24 between exercise tests for Borg breathlessness score and heart rate to return to resting
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26 values. All participants performed spirometry on each occasion.
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34 **Part 2: Responsiveness**

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36 Participants with CF undergoing intravenous antibiotic therapy for an acute exacerbation
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38 of respiratory disease were recruited from Northern Ireland Adult CF Centre in Belfast
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40 City Hospital. A course of intravenous antibiotics was chosen as a test platform to assess
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42 responsiveness of cardiorespiratory measurements recorded by the LifeShirt. This has
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44 been used in previous studies that have investigated the ability of an outcome measure to
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46 detect clinically important changes.¹⁵ All patients also performed spirometry and had C-
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48 reactive protein (CRP) levels determined on two occasions (Time 1= beginning of
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50 admission for intravenous antibiotic therapy and Time 2= end of admission for
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3 intravenous antibiotic therapy). All participants also wore the LifeShirt system during a
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5 6MWT on each occasion.
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10 **Statistical analysis**

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12 The significance of differences in clinical measurements and exercise performance
13 between Time 1 and Time 2 were analysed using paired t-tests. Breath-by-breath data
14 recorded by the LifeShirt were summarised into minute means to facilitate analysis.
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16 Exploratory assessment of the 6MWT (using repeated measures ANOVA) revealed that a
17 steady state work rate was achieved by the fourth minute therefore minute means of the
18 final two minutes were analysed. It was not possible to perform repeated measures
19 ANOVA on the submaximal stages of the MST due to an unbalanced design (i.e. there
20 was a large range of performances resulting in differences in the number of completed
21 stages), therefore the minute means were calculated for the last two stages that
22 participants reached on both days (i.e. the two highest comparable stages). When the two
23 days were compared (Part 1 and Part 2), differences (residual errors) were found to be
24 associated with the size of the measurements (heteroscedasticity) and as such, all data
25 were log transformed.¹⁶ Reliability and responsiveness were then assessed using
26 repeated-measures ANOVA performed in Minitab (Minitab Ltd, Coventry, UK). Results
27 are reported as significance of bias (systematic differences between measurements in a
28 particular direction) and within-subject mean-square errors reported as coefficients of
29 variation (CV) (unexplained error differences between measurements).^{17,18} Bias was
30 considered to be significant at $p < 0.05$ level and a CV below 10% was considered
31 acceptable. For discriminate validity means were calculated for each stage of the MST
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3 completed for Time 1 and Time 2 combined. The significance of the difference in
4 cardiorespiratory measurements between participants with CF and healthy participants
5 was assessed by 2-sample t-tests (significant at $p < 0.05$ level) on a stage by stage basis.
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RESULTS

Part 1: Reliability and discriminate validity

Eighteen patients and eighteen age matched healthy participants were recruited [CF: 9M:9F, age 26 (10) years, FEV₁ %predicted: 69.2 (23)%, controls: 8M:10F, age: 24 (5) years, FEV₁ %predicted: 92 (8)%]. Within the group of participants with CF there was a range of severity in lung disease (normal: n=2; mild: n=11; moderate: n=4; severe: n=3). There was no significant difference in FEV₁ %predicted over the two occasions in either group indicating that health status of participants was stable.

In order to facilitate analysis of the reliability of cardiorespiratory measurements recorded by the LifeShirt system it was essential that performance on the exercise tests was reliable between Time 1 and Time 2. There was no difference in exercise performance between Time 1 and Time 2 in any of the tests in either the patients with CF (mean difference [95%CI] Time 1 vs. Time 2: 6MWT: -10 [-33 to 13]m; MST: -29 [-65 to 7]m) or the controls (mean difference [95%CI] Time 1 vs. Time 2: 6MWT: 10 [-8 to 28]m; MST: 38 [-59 to 136]m). As there were no differences between Time 1 and Time 2 for either group, this enabled us to combine the groups to determine the reliability of the cardiorespiratory measurements recorded by LifeShirt over a wide range of exercise capacities.

For both the 6MWT and the MST reliability of cardiorespiratory measures recorded by the LifeShirt was acceptable with no significant bias (i.e. $p > 0.05$) and CV below 10% (Table 1). The mean absolute differences between Time 1 and Time 2 for all

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3 cardiorespiratory measurements were small and not clinically important (Table 2).
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5 Analysis for SpO₂ was not performed due to the large amount of missing values.
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10 Patients had a significantly lower mean (SD) exercise capacity as measured by the
11 6MWT (CF: 546 (90)m vs. controls: 705 (61)m (p<0.01)). Therefore since the two
12 groups were exercising at different intensities the cardiorespiratory responses were not
13 assessed for discriminate validity. Participants with CF also had a lower exercise
14 capacity as measured by the MST (CF: 757 (266)m vs. controls: 1201 (232)m (p<0.01)).
15 However, exercise intensity at each stage of the MST was externally controlled (i.e.
16 patients with CF and healthy participants exercised at the same intensity) and therefore
17 discriminate validity in the cardiorespiratory measurements could be assessed for each
18 stage fully completed.
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34 Cardiorespiratory measurements recorded by the LifeShirt generally demonstrated an
35 exaggerated response to exercise. Significant differences (p<0.05) between participants
36 with CF and healthy controls were observed from stages 1 to 8 for ViVol, stages 1 to 10
37 for V_E, stages 1 to 12 for Br/M, stages 7 to 10 for Ti/Tt, and stages 8 to 12 for HR
38 (Figures 1 to 5). Abnormalities in cardiorespiratory responses were still apparent when
39 only participants with CF and normal lung function or mild CF-related lung disease
40 (FEV₁>70 %predicted, n=11) were compared to healthy participants: significant
41 differences were observed from stages 1 to 8 for ViVol, stages 1 to 10 for V_E, and stages
42 1 to 10 for Br/M. Ti/Tt and HR showed a trend for being higher in later stages however
43 there were fewer participants completing these stages.
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Part 2: Responsiveness

Twelve participants with CF were recruited (6M:6F). Mean (SD) FEV₁ %predicted at the start of admission for antibiotics was 45 (19)% and mean (SD) length of stay was 13 (4) days. FEV₁ %predicted (Mean(SD): Time 1: 45(19) vs. Time 2: 52(16), p=0.024) and distance walked during the 6MWT (Mean(SD): Time 1: 544(80), vs. Time 2: 605(98), p=0.025) improved significantly indicating a treatment benefit. A trend towards improvement, which approached significance was observed for CRP (Mean (SD): Time 1: 12 (15) vs. Time 2: 7 (11), p=0.061). There was no significant difference from Time 1 to Time 2 for ViVol, V_E, Br/M, Ti/Tt and HR recorded by the LifeShirt during the 6MWT (Tables 3 and 4). Analysis for SpO₂ was not performed due to the large amount of missing values.

DISCUSSION

This is the first study to use the LifeShirt to examine the cardiorespiratory responses to the 6MWT and MST in participants with CF and in healthy participants. The study showed that the LifeShirt had good reliability and discriminate validity, and could assess the cardiorespiratory responses to an exercise test at the beginning and end of an admission for intravenous antibiotics. The 6MWT (endurance test) and the MST (peak test) are frequently used, both in the CF clinical setting and as an endpoint in clinical trials, and offer the opportunity to examine the full range of physiological responses (i.e. resting ventilation to ventilation experienced during exercise).^{1,2} This study confirms previous findings showing that performance (distance completed) is reliable for both the 6MWT and the MST.^{13,19,20}

All cardiorespiratory measurements recorded by the LifeShirt during the 6MWT and MST showed no significant bias ($p>0.05$) and acceptable CVs ($<10\%$) over two occasions during a period of stability, indicating acceptable reliability. The results also indicate that cardiorespiratory measurements recorded by the LifeShirt can discriminate between groups of participants with CF and healthy participants at comparable exercise intensities during the MST. The patterns of cardiorespiratory response demonstrated in this study are in line with previously reported abnormalities in cardiorespiratory response to exercise in CF.²¹ Ventilatory response is exaggerated in CF compared to healthy participants. The data in this study suggest that initially this is due to both an increase in ViVol and Br/M. After stage 8 of the MST ViVol recorded in participants with CF appears to converge with that of healthy participants (i.e. no longer significantly

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3 different), however V_E and Br/M continue to be significantly different to that of healthy
4 participants until stage 10. This is in agreement with previous reports that as exercise
5 intensity increases limitation of ViVol occurs and greater increases in Br/M must
6 compensate in order to meet ventilatory demands.²¹ This is due to the increased residual
7 volume to total lung capacity ratio as a consequence of hyperinflation and increased
8 deadspace.²¹ Ti/Tt also demonstrated some significant differences during stages 7 to 10
9 however the difference is small and unlikely to be of clinical relevance. From stage 8 of
10 the MST the difference between participants with CF and healthy participants in HR
11 response becomes significant with participants with CF having an exaggerated response.
12 There may be several reasons that this does not appear to be significant until later stages
13 in the exercise test. Firstly there may be a compensatory increase in HR in response to
14 inefficient ventilatory response. Secondly it may be due to a lower anaerobic threshold in
15 participants with CF (i.e. there is increased demand on cardiorespiratory systems when
16 individuals exercise above their anaerobic threshold). Thirdly, hyperinflation
17 additionally contributes to the increased work of breathing by forcing the inspiratory
18 muscles to work at a mechanical disadvantage and as oxygen is diverted away from
19 exercising muscles to the inspiratory muscles there is increased demand on the
20 cardiovascular system. Data on the later stages of the MST is not available for all
21 patients and therefore the findings need to be confirmed in further studies.
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51 It should be highlighted that the standard deviation appears to decrease for Ti/Tt and HR.
52 The cardiorespiratory data were log transformed as is appropriate for data demonstrating
53 heteroscedasticity (errors associated with size of measurements). For ViVol, V_E , and
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3 Br/M the heteroscedasticity was obvious and thus log transforming the data produced
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5 uniform standard deviations across the stages of the MST. For Ti/Tt and HR the data
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7 demonstrated heteroscedasticity, albeit less pronounced, and thus the log transformed
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9 standard deviations appear to decrease across the stages of the MST.
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15 The reliability study was performed in a small group of participants with CF, in particular
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17 there were few patients with moderate (n=4) or severe (n=3) lung disease. Reliability
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19 may not be equivalent across different severities of disease as patients with more severe
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21 disease experience more frequent fluctuations in health status making it difficult to assess
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23 reliability of measurements. Future research should include larger numbers of patients
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25 with moderate and severe lung disease in order to assess reliability in subgroups of
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27 patients.
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34 In this study, the distance walked during the 6MWT improved in response to an
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36 admission for intravenous antibiotic treatment for an exacerbation of lung disease in
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38 participants with CF. Cardiorespiratory measurements recorded by the LifeShirt during
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40 the 6MWT were unable to capture the mechanism by which exercise capacity improved.
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42 The 6MWT is a self-paced functional test which is frequently used both in the CF clinical
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44 setting and as an endpoint in clinical trials.²² A possible mechanism of improved
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46 performance on the test could be improved cardiorespiratory efficiency. During an
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48 exacerbation patients often present with many characteristics which would impair
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50 cardiorespiratory efficiency, such as impaired airflow and reduced gas exchange.²³
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53 Therefore it would be expected that ventilatory response would be increased at the start
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3 of an admission for intravenous antibiotic therapy. In other words more air would have
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5 to be moved in and out of the lungs (reflected by increased V_E , ViVol, Br/M) to maintain
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7 gaseous concentrations at the alveolar-capillary membrane. It could be hypothesised that,
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9 with intravenous antibiotic treatment, airway inflammation, sputum load and gas trapping
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11 would decrease leading to improvements in airflow and gas exchange, and hence
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13 improved cardiorespiratory efficiency during exercise. Patients in this study improved
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15 their exercise capacity (i.e. walked further at Time 2). Cardiorespiratory measurements
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17 recorded by the LifeShirt did not change significantly from Time 1 to Time 2 therefore
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19 this may indicate that the increase in exercise performance masked any treatment induced
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21 improvements in cardiorespiratory efficiency. These improvements would have been
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23 more clearly demonstrated using an externally controlled constant load test (e.g. treadmill
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25 walking at constant speed Time 1 and Time 2). A number of findings would suggest that
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27 patients in this study were experiencing a “mild” exacerbation: the modest level of CRP
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29 at Time 1, and the modest changes in all the clinical outcome measures from Time 1 to
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31 Time 2. Improvement may also have been more evident in participants experiencing a
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33 severe exacerbation. Further evaluation of responsiveness is needed in participants with
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35 CF taking into consideration the exercise test chosen and the severity of exacerbation.
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46 In this study, participants also wore a pulse oximeter linked to the LifeShirt. However,
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48 due to large amounts of missing data analysis was not performed on SpO₂. The reason
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50 for this may have been that movement of the upper limb during walking or running
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52 caused large amounts of movement artifact and hence a large noise-to-signal ratio. Cycle
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3 ergometry enables the upper limb to be stabilized and therefore may provide a more
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5 suitable platform for assessing the clinimetric properties of the LifeShirt pulse oximeter.
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10 This study focused on inspiratory tidal volume, ventilation, respiratory rate, fractional
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12 inspiratory time, and heart rate. Other measurements may be relevant in CF (for
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14 example, the relative contributions of the ribcage and abdomen to breathing). Further
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16 study is needed to assess the clinimetric properties of the range of cardiorespiratory
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18 measurements available from the LifeShirt.
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22 23 24 **Conclusion**

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27 In conclusion this study adds to the growing body of evidence that cardiorespiratory
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29 response can be measured non-invasively during field tests such as the MST. This study
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31 demonstrated that key cardiorespiratory measurements recorded by the LifeShirt are
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33 reliable during field exercise tests and can discriminate between adults with CF and
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35 young healthy adults. This study provides some limited information on responsiveness of
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37 cardiorespiratory measurements recorded by the LifeShirt during the 6MWT.
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41 42 43 **Acknowledgments**

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45
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49
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52 Technology (DEL CAST) with VivoMetrics. DEL CAST award entails a studentship
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54 paid to LK (VivoMetrics contribution = £14760 from 2006 to 2009). LK, JB, SE, BO'N
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3 received equipment and consumables from VivoMetrics. AN and LB do not have any
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5 conflict of interest to declare. All data analysis was performed independently by AN
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8 (VivoMetrics were not involved in the design or conduct of the study, analysis or
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10 interpretation of results, or the decision to publish).
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Figure legends

Figure 1: Mean $\ln[V_iVol]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, * $p < 0.05$, ** $p < 0.01$.

Figure 2: Mean $\ln[V_E]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, ** $p < 0.01$, *** $p < 0.001$.

Figure 3: Mean $\ln[Br/M]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, ** $p < 0.01$, *** $p < 0.001$.

Figure 4: Mean $\ln[Ti/Tt]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, * $p < 0.05$, ** $p < 0.01$.

Figure 5: Mean $\ln[HR]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, * $p < 0.05$, ** $p < 0.01$.

Title: Cardiorespiratory measurements during field tests in CF: Use of an ambulatory monitoring system

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Short title: Field exercise tests in CF

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4 **Summary:** Respiratory inductive plethysmography (e.g. LifeShirt) may offer in-depth
5 study of the cardiorespiratory responses during field exercise tests. The aims of this
6 study were to assess the reliability, discriminate validity and responsiveness of
7 cardiorespiratory measurements recorded by the LifeShirt during field exercise tests in
8 adults with CF. To assess reliability and discriminate validity, participants with CF and
9 stable lung disease and healthy participants performed the 6 Minute Walk Test (6MWT)
10 and Modified Shuttle Test (MST) on 2 occasions. To assess responsiveness, participants
11 with CF experiencing an exacerbation performed the 6MWT at the start and end of an
12 admission for intravenous antibiotics. The LifeShirt was worn during all exercise tests.
13 Reliability and discriminate validity were assessed in 18 participants with CF (mean (SD)
14 age: 26 (10)years; FEV₁%predicted: 69.2 (23)%) and 18 healthy participants (age: 24
15 (5)years, FEV₁%predicted: 92 (8)%). There was no difference in 6MWT and MST
16 performance between days and reliability of cardiorespiratory measures was acceptable
17 (bias $p>0.05$; CV<10%). Participants with CF demonstrated a significantly greater
18 response to exercise (e.g. ventilation, respiratory rate) compared to healthy participants
19 indicating discriminate validity. Responsiveness was assessed in 12 participants with CF:
20 clinical measurements and 6MWT performance improved (61(81)m; $p<0.05$) however
21 cardiorespiratory measurements recorded by the LifeShirt remained the same (bias:
22 $p>0.05$; CV<10%). This study provides evidence that cardiorespiratory responses can be
23 measured non-invasively during field exercise tests in adults with CF. Reliability and
24 discriminate validity of key cardiorespiratory measurements recorded by the LifeShirt
25 were demonstrated. Some information on responsiveness is reported.
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Keywords

respiratory inductive plethysmography;

LifeShirt;

cystic fibrosis;

6 Minute Walk Test;

Modified Shuttle Test

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INTRODUCTION

In cystic fibrosis (CF) exercise tests enable assessment of functional capacity and limitations, determination of level of fitness, safe and effective exercise recommendations, and evaluation of interventions.^{1,2} Field exercise tests are often used in CF centres when clinical laboratories are unavailable. While field exercise tests provide information on exercise performance (i.e. how far a patient can walk or run) they do not provide in-depth information on the cardiorespiratory responses to exercise or what factors contribute to exercise limitation. Measuring cardiorespiratory responses during field exercise tests using ambulatory monitoring has been limited by the technology available. Some available ambulatory monitoring systems record a narrow range of measurements and others are too cumbersome. Respiratory inductive plethysmography (e.g. the LifeShirt) may offer the opportunity for more in-depth study of the cardiorespiratory responses during field exercise tests and potentially provide additional valuable information.³

The LifeShirt[®] (Vivometrics, Inc., Ventura, CA, U.S.A.) is a multi-function ambulatory system capable of detecting several cardiorespiratory measures of interest to clinicians and researchers working in CF, for example timing and volume components of breathing and heart rate. The LifeShirt consists of a CoolMax[®] garment, data recorder, and computer-based analysis software (VivoLogic). The core technology is respiratory inductive plethysmography which provides non-invasive assessment of respiratory pattern. Unlike direct methods which must be coupled to the individual (e.g. pneumotach via a face-mask or mouthpiece and nose-clips), respiratory inductive plethysmography is

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3 unobtrusive and so can be used for extended periods in an ambulatory setting. The
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5 LifeShirt system incorporates a Lycra vest into which the respiratory inductive
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7 plethysmography bands are embedded in order to limit displacement. Before systems
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9 such as the LifeShirt can be used in clinical or research practice information is required
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11 on clinimetric properties (i.e. reliability, validity and responsiveness).
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18 Assessment of clinimetric properties of the LifeShirt has mainly been conducted in
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20 healthy participants in a laboratory environment.³⁻⁶ We have previously demonstrated
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22 that the LifeShirt can provide valid and reliable cardiorespiratory data across multiple
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24 assessments in healthy participants tested in a laboratory environment.³ There has been
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26 one previous study that has used the LifeShirt during exercise in clinical populations and
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28 demonstrated the ability of cardiorespiratory measurements recorded by the LifeShirt
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30 (ventilation, respiratory rate and heart rate) to discriminate between patients with
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32 congestive heart failure, chronic obstructive pulmonary disease and healthy participants.⁴
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36 There is no available information on the clinimetric properties of cardiorespiratory
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38 measurements recorded by respiratory inductive plethysmography (i.e. the LifeShirt)
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40 during exercise tests in patients with CF.
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46 The aims of this study were:

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48 • to assess the reliability of cardiorespiratory measurements recorded by the
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50 LifeShirt during the 6 Minute Walk Test (6MWT) and Modified Shuttle Test
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52 (MST) in participants with CF and healthy controls (i.e. degree to which the
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54 results are consistent over two occasions)
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- to assess the discriminate validity of cardiorespiratory measurements recorded by the LifeShirt during comparable stages of the MST (i.e. ability to detect a difference in cardiorespiratory responses to exercise between participants with CF versus healthy age matched controls)
- to assess the responsiveness of cardiorespiratory measurements recorded by the LifeShirt system during the 6MWT in participants with CF admitted for intravenous antibiotic therapy (i.e. ability to detect treatment induced changes in cardiorespiratory response to exercise).

The hypotheses for this study were that cardiorespiratory measurements recorded by the LifeShirt during field tests in participants with CF 1) are reliable, 2) can discriminate between participants with CF and healthy age matched participants, and 3) are responsive to intravenous antibiotic therapy.

MATERIALS AND METHODS

Ethics

The protocol was approved by the Queen's University Belfast and Belfast Trust City Hospital ethics and research governance procedures and written informed consent obtained. Recruitment commenced in November 2003 and ended in October 2007.

LifeShirt

LifeShirt data relating to various cardiorespiratory measurements were recorded during field exercise tests. These included inspiratory tidal volume (ViVol, mL); ventilation (V_E , $L \cdot \text{min}^{-1}$); respiratory rate (Br/M, $\text{breaths} \cdot \text{min}^{-1}$); ratio of inspiratory time to total respiratory time (Ti/Tt); and heart rate (HR, $\text{beats} \cdot \text{min}^{-1}$). The method of calibrating the volume components of breathing was recommended by the manufacturers and involved patients inflating and deflating a fixed volume (400mL/800mL) bag seven times whilst wearing nose clips. This was performed in standing.

Spirometry and exercise tests

Spirometry was performed according to ATS/ ERS guidelines for standardisation of spirometry⁷ and expressed as percentage of predicted normal values according to the equations developed by Quanjer et al. (1993)⁸. Lung disease was classified by FEV₁ as normal (>90% predicted), mild (70-89% predicted), moderate (40-69% predicted) or severe (<40% predicted).⁹ For the 6MWT participants were asked to walk as fast as they could around a 30 metre course for a period of six minutes according to the ATS

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3 guidelines.¹⁰ For the MST participants were asked to walk or run around a 10 metre
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5 course at increasing speeds dictated by an external bleep from a tape recorder.¹¹⁻¹⁴
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10 **Part 1: Reliability and discriminate validity**

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12 Patients with CF and stable lung disease were recruited from the Northern Ireland Adult
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14 CF Centre in Belfast City Hospital. Age matched controls were recruited from staff and
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16 students at Belfast City Hospital and the University of Ulster. All participants wore the
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18 LifeShirt system during a 6MWT and MST performed on two occasions at least one
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20 week apart (Time 1 and Time 2). Exercise tests were carried out according to
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22 standardised protocols and in a standardised order. Sufficient rest periods were used
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24 between exercise tests for Borg breathlessness score and heart rate to return to resting
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26 values. All participants performed spirometry on each occasion.
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34 **Part 2: Responsiveness**

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36 Participants with CF undergoing intravenous antibiotic therapy for an acute exacerbation
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38 of respiratory disease were recruited from Northern Ireland Adult CF Centre in Belfast
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40 City Hospital. A course of intravenous antibiotics was chosen as a test platform to assess
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42 responsiveness of cardiorespiratory measurements recorded by the LifeShirt. This has
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44 been used in previous studies that have investigated the ability of an outcome measure to
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46 detect clinically important changes.¹⁵ All patients also performed spirometry and had C-
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48 reactive protein (CRP) levels determined on two occasions (Time 1= beginning of
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50 admission for intravenous antibiotic therapy and Time 2= end of admission for
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3 intravenous antibiotic therapy). All participants also wore the LifeShirt system during a
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5 6MWT on each occasion.
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10 **Statistical analysis**

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12 The significance of differences in clinical measurements and exercise performance
13 between Time 1 and Time 2 were analysed using paired t-tests. Breath-by-breath data
14 recorded by the LifeShirt were summarised into minute means to facilitate analysis.
15 Exploratory assessment of the 6MWT (using repeated measures ANOVA) revealed that a
16 steady state work rate was achieved by the fourth minute therefore minute means of the
17 final two minutes were analysed. It was not possible to perform repeated measures
18 ANOVA on the submaximal stages of the MST due to an unbalanced design (i.e. there
19 was a large range of performances resulting in differences in the number of completed
20 stages), therefore the minute means were calculated for the last two stages that
21 participants reached on both days (i.e. the two highest comparable stages). When the two
22 days were compared (Part 1 and Part 2), differences (residual errors) were found to be
23 associated with the size of the measurements (heteroscedasticity) and as such, all data
24 were log transformed.¹⁶ Reliability and responsiveness were then assessed using
25 repeated-measures ANOVA performed in Minitab (Minitab Ltd, Coventry, UK). Results
26 are reported as significance of bias (systematic differences between measurements in a
27 particular direction) and within-subject mean-square errors reported as coefficients of
28 variation (CV) (unexplained error differences between measurements).^{17,18} Bias was
29 considered to be significant at $p < 0.05$ level and a CV below 10% was considered
30 acceptable. For discriminate validity means were calculated for each stage of the MST
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3 completed for Time 1 and Time 2 combined. The significance of the difference in
4 cardiorespiratory measurements between participants with CF and healthy participants
5 was assessed by 2-sample t-tests (significant at $p < 0.05$ level) on a stage by stage basis.
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RESULTS

Part 1: Reliability and discriminate validity

Eighteen patients and eighteen age matched healthy participants were recruited [CF: 9M:9F, age 26 (10) years, FEV₁ %predicted: 69.2 (23)%, controls: 8M:10F, age: 24 (5) years, FEV₁ %predicted: 92 (8)%]. Within the group of participants with CF there was a range of severity in lung disease (normal: n=2; mild: n=11; moderate: n=4; severe: n=3). There was no significant difference in FEV₁ %predicted over the two occasions in either group indicating that health status of participants was stable.

In order to facilitate analysis of the reliability of cardiorespiratory measurements recorded by the LifeShirt system it was essential that performance on the exercise tests was reliable between Time 1 and Time 2. There was no difference in exercise performance between Time 1 and Time 2 in any of the tests in either the patients with CF (mean difference [95%CI] Time 1 vs. Time 2: 6MWT: -10 [-33 to 13]m; MST: -29 [-65 to 7]m) or the controls (mean difference [95%CI] Time 1 vs. Time 2: 6MWT: 10 [-8 to 28]m; MST: 38 [-59 to 136]m). As there were no differences between Time 1 and Time 2 for either group, this enabled us to combine the groups to determine the reliability of the cardiorespiratory measurements recorded by LifeShirt over a wide range of exercise capacities.

For both the 6MWT and the MST reliability of cardiorespiratory measures recorded by the LifeShirt was acceptable with no significant bias (i.e. $p > 0.05$) and CV below 10% (Table 1). The mean absolute differences between Time 1 and Time 2 for all

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3 cardiorespiratory measurements were small and not clinically important (Table 2).
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5 Analysis for SpO₂ was not performed due to the large amount of missing values.
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10 Patients had a significantly lower mean (SD) exercise capacity as measured by the
11 6MWT (CF: 546 (90)m vs. controls: 705 (61)m (p<0.01)). Therefore since the two
12 groups were exercising at different intensities the cardiorespiratory responses were not
13 assessed for discriminate validity. Participants with CF also had a lower exercise
14 capacity as measured by the MST (CF: 757 (266)m vs. controls: 1201 (232)m (p<0.01)).
15 However, exercise intensity at each stage of the MST was externally controlled (i.e.
16 patients with CF and healthy participants exercised at the same intensity) and therefore
17 discriminate validity in the cardiorespiratory measurements could be assessed for each
18 stage fully completed.
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34 Cardiorespiratory measurements recorded by the LifeShirt generally demonstrated an
35 exaggerated response to exercise. Significant differences (p<0.05) between participants
36 with CF and healthy controls were observed from stages 1 to 8 for ViVol, stages 1 to 10
37 for V_E, stages 1 to 12 for Br/M, stages 7 to 10 for Ti/Tt, and stages 8 to 12 for HR
38 (Figures 1 to 5). Abnormalities in cardiorespiratory responses were still apparent when
39 only participants with CF and normal lung function or mild CF-related lung disease
40 (FEV₁>70 %predicted, n=11) were compared to healthy participants: significant
41 differences were observed from stages 1 to 8 for ViVol, stages 1 to 10 for V_E, and stages
42 1 to 10 for Br/M. Ti/Tt and HR showed a trend for being higher in later stages **however**
43 **there were fewer participants completing these stages.**
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Part 2: Responsiveness

Twelve participants with CF were recruited (6M:6F). Mean (SD) FEV₁ %predicted at the start of admission for antibiotics was 45 (19)% and mean (SD) length of stay was 13 (4) days. FEV₁ %predicted (Mean(SD): Time 1: 45(19) vs. Time 2: 52(16), p=0.024) and distance walked during the 6MWT (Mean(SD): Time 1: 544(80), vs. Time 2: 605(98), p=0.025) improved significantly indicating a treatment benefit. A trend towards improvement, which approached significance was observed for CRP (Mean (SD): Time 1: 12 (15) vs. Time 2: 7 (11), p=0.061). There was no significant difference from Time 1 to Time 2 for ViVol, V_E, Br/M, Ti/Tt and HR recorded by the LifeShirt during the 6MWT (Tables 3 and 4). Analysis for SpO₂ was not performed due to the large amount of missing values.

DISCUSSION

This is the first study to use the LifeShirt to examine the cardiorespiratory responses to the 6MWT and MST in participants with CF and in healthy participants. The study showed that the LifeShirt had good reliability and discriminate validity, and could assess the cardiorespiratory responses to an exercise test at the beginning and end of an admission for intravenous antibiotics. The 6MWT (endurance test) and the MST (peak test) are frequently used, both in the CF clinical setting and as an endpoint in clinical trials, and offer the opportunity to examine the full range of physiological responses (i.e. resting ventilation to ventilation experienced during exercise).^{1,2} This study confirms previous findings showing that performance (distance completed) is reliable for both the 6MWT and the MST.^{13,19,20}

All cardiorespiratory measurements recorded by the LifeShirt during the 6MWT and MST showed no significant bias ($p>0.05$) and acceptable CVs ($<10\%$) over two occasions during a period of stability, indicating acceptable reliability. The results also indicate that cardiorespiratory measurements recorded by the LifeShirt can discriminate **between groups of** participants with CF and healthy participants at comparable exercise intensities during the MST. The patterns of cardiorespiratory response demonstrated in this study are in line with previously reported abnormalities in cardiorespiratory response to exercise in CF.²¹ Ventilatory response is exaggerated in CF compared to healthy participants. The data in this study suggest that initially this is due to both an increase in ViVol and Br/M. After stage 8 **of the MST** ViVol recorded in participants with CF appears to converge with that of healthy participants (i.e. no longer significantly

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3 different), however V_E and Br/M continue to be significantly different to that of healthy
4 participants until stage 10. This is in agreement with previous reports that as exercise
5 intensity increases limitation of ViVol occurs and greater increases in Br/M must
6 compensate in order to meet ventilatory demands.²¹ This is due to the increased residual
7 volume to total lung capacity ratio as a consequence of hyperinflation and increased
8 deadspace.²¹ Ti/Tt also demonstrated some significant differences during stages 7 to 10
9 however the difference is small and unlikely to be of clinical relevance. From stage 8 of
10 the MST the difference between participants with CF and healthy participants in HR
11 response becomes significant with participants with CF having an exaggerated response.
12 There may be several reasons that this does not appear to be significant until later stages
13 in the exercise test. Firstly there may be a compensatory increase in HR in response to
14 inefficient ventilatory response. Secondly it may be due to a lower anaerobic threshold in
15 participants with CF (i.e. there is increased demand on cardiorespiratory systems when
16 individuals exercise above their anaerobic threshold). Thirdly, hyperinflation
17 additionally contributes to the increased work of breathing by forcing the inspiratory
18 muscles to work at a mechanical disadvantage and as oxygen is diverted away from
19 exercising muscles to the inspiratory muscles there is increased demand on the
20 cardiovascular system. Data on the later stages of the MST is not available for all
21 patients and therefore the findings need to be confirmed in further studies.
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It should be highlighted that the standard deviation appears to decrease for Ti/Tt and HR.
The cardiorespiratory data were log transformed as is appropriate for data demonstrating
heteroscedasticity (errors associated with size of measurements). For ViVol, V_E , and

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3 Br/M the heteroscedasticity was obvious and thus log transforming the data produced
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5 uniform standard deviations across the stages of the MST. For Ti/Tt and HR the data
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7 demonstrated heteroscedasticity, albeit less pronounced, and thus the log transformed
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9 standard deviations appear to decrease across the stages of the MST.
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15 The reliability study was performed in a small group of participants with CF, in particular
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17 there were few patients with moderate (n=4) or severe (n=3) lung disease. Reliability
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19 may not be equivalent across different severities of disease as patients with more severe
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21 disease experience more frequent fluctuations in health status making it difficult to assess
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23 reliability of measurements. Future research should include larger numbers of patients
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25 with moderate and severe lung disease in order to assess reliability in subgroups of
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27 patients.
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34 In this study, the distance walked during the 6MWT improved in response to an
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36 admission for intravenous antibiotic treatment for an exacerbation of lung disease in
37
38 participants with CF. Cardiorespiratory measurements recorded by the LifeShirt during
39
40 the 6MWT were unable to capture the mechanism by which exercise capacity improved.
41
42 The 6MWT is a self-paced functional test which is frequently used both in the CF clinical
43
44 setting and as an endpoint in clinical trials.²² A possible mechanism of improved
45
46 performance on the test could be improved cardiorespiratory efficiency. During an
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48 exacerbation patients often present with many characteristics which would impair
49
50 cardiorespiratory efficiency, such as impaired airflow and reduced gas exchange.²³
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53 Therefore it would be expected that ventilatory response would be increased at the start
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3 of an admission for intravenous antibiotic therapy. In other words more air would have
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5 to be moved in and out of the lungs (reflected by increased V_E , ViVol, Br/M) to maintain
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7 gaseous concentrations at the alveolar-capillary membrane. It could be hypothesised that,
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9 with intravenous antibiotic treatment, airway inflammation, sputum load and gas trapping
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11 would decrease leading to improvements in airflow and gas exchange, and hence
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13 improved cardiorespiratory efficiency during exercise. Patients in this study improved
14
15 their exercise capacity (i.e. walked further at Time 2). Cardiorespiratory measurements
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17 recorded by the LifeShirt did not change significantly from Time 1 to Time 2 therefore
18
19 this may indicate that the increase in exercise performance masked any treatment induced
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21 improvements in cardiorespiratory efficiency. **These improvements would have been**
22
23 **more clearly demonstrated using an externally controlled constant load test (e.g. treadmill**
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25 **walking at constant speed Time 1 and Time 2). A number of findings would suggest that**
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27 **patients in this study were experiencing a “mild” exacerbation: the modest level of CRP**
28
29 **at Time 1, and the modest changes in all the clinical outcome measures from Time 1 to**
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31 **Time 2.** Improvement may also have been more evident in participants experiencing a
32
33 severe exacerbation. Further evaluation of responsiveness is needed in participants with
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35 CF taking into consideration the exercise test chosen and the severity of exacerbation.
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46 In this study, participants also wore a pulse oximeter linked to the LifeShirt. However,
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48 due to large amounts of missing data analysis was not performed on SpO₂. The reason
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50 for this may have been that movement of the upper limb during walking or running
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52 caused large amounts of movement artifact and hence a large noise-to-signal ratio. Cycle
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3 ergometry enables the upper limb to be stabilized and therefore may provide a more
4
5 suitable platform for assessing the clinimetric properties of the LifeShirt pulse oximeter.
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10 This study focused on inspiratory tidal volume, ventilation, respiratory rate, fractional
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12 inspiratory time, and heart rate. Other measurements may be relevant in CF (for
13
14 example, the relative contributions of the ribcage and abdomen to breathing). Further
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16 study is needed to assess the clinimetric properties of the range of cardiorespiratory
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18 measurements available from the LifeShirt.
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22 23 24 **Conclusion**

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27 In conclusion this study adds to the growing body of evidence that cardiorespiratory
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29 response can be measured non-invasively during field tests such as the MST. This study
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31 demonstrated that key cardiorespiratory measurements recorded by the LifeShirt are
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33 reliable during field exercise tests and can discriminate between adults with CF and
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35 young healthy adults. This study provides some limited information on responsiveness of
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37 cardiorespiratory measurements recorded by the LifeShirt during the 6MWT.
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41 42 43 **Acknowledgments**

44
45
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48 (£15,000). This study formed part of a PhD programme of research which was co-funded
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50 through a Department for Employment and Learning Co-operative Award in Science and
51
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53
54 paid to LK (VivoMetrics contribution = £14760 from 2006 to 2009). LK, JB, SE, BO'N
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3 received equipment and consumables from VivoMetrics. AN and LB do not have any
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5 conflict of interest to declare. All data analysis was performed independently by AN
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8 (VivoMetrics were not involved in the design or conduct of the study, analysis or
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10 interpretation of results, or the decision to publish).
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Figure legends

Figure 1: Mean $\ln[V_iVol]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, * $p < 0.05$, ** $p < 0.01$.

Figure 2: Mean $\ln[V_E]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, ** $p < 0.01$, *** $p < 0.001$.

Figure 3: Mean $\ln[Br/M]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, ** $p < 0.01$, *** $p < 0.001$.

Figure 4: Mean $\ln[Ti/Tt]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, * $p < 0.05$, ** $p < 0.01$.

Figure 5: Mean $\ln[HR]$ at each stage of MST, data for Time 1 and Time 2 combined.

Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, * $p < 0.05$, ** $p < 0.01$.

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Title: CARDIORESPIRATORY MEASUREMENTS DURING FIELD TESTS IN CF: USE OF AN AMBULATORY MONITORING SYSTEM

Short title: FIELD EXERCISE TESTS IN CF

Authors: Judy M Bradley, Lisa Kent, Brenda O'Neill, Alan Nevill, Lesley Boyle, J Stuart Elborn

Table 1

For Peer Review

Table 1: Difference between Time 1 and Time 2 of measurements recorded by the LifeShirt during the final two minutes of 6MWT and final two comparable stages of the MST in participants with CF (n=18) during a stable period, and healthy participants (n=18) (repeated measures ANOVA)

	6MWT		MST	
	Bias (<i>p</i>)	CV (%)	Bias (<i>p</i>)	CV (%)
lnViVol	0.603	4.8	0.403	3.7
lnV _E	0.649	3.9	0.688	6.5
lnBr/M	0.799	5.0	0.056	6.2
lnTi/Tt	0.514	2.7	0.155	2.3
lnHR	0.879	6.2	0.080	8.0

Key: lnViVol: log of inspired tidal volume; lnV_E: log of ventilation; lnBr/M: log of respiratory rate; lnTi/Tt: log of ratio of inspiratory time to total respiratory time; lnHR: log of heart rate.

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Table 2

For Peer Review

Table 2: Cardiorespiratory measurements recorded by the LifeShirt during the final two minutes of 6MWT and final two comparable stages of the MST at Time 1 and Time 2 in participants with CF (n=18) during a stable period, and healthy participants (n=18).

	6MWT			MST		
	Time 1 Mean (SD)	Time 2 Mean (SD)	Difference (SD) [95% CI]	Time 1 Mean (SD)	Time 2 Mean (SD)	Mean difference (SD) [95% CI]
ViVol (mL)	1190 (470)	1171 (536)	18.7 (529) [-106 to 143]	1808 (803)	1717 (752)	91 (675) [-67 to 250]
V _E (L·min ⁻¹)	41.1 (18.2)	41.1 (22.5)	-0.06 (19.9) [-4.7 to 4.6]	79.3 (34.9)	77.4 (36.5)	1.9 (31.0) [-5.4 to 9.2]
Br/M (br·min ⁻¹)	35.4 (6.2)	35.6 (6.5)	-0.2 (3.8) [-1.1 to 0.7]	45.0 (6.3)	45.7 (7.0)	-0.8 (4.4) [-1.8 to 0.2]
Ti/Tt	0.457 (0.029)	0.459 (0.027)	-0.002 (0.022) [-0.007 to 0.003]	0.488 (0.019)	0.490 (0.019)	-0.002 (0.015) [-0.006 to 0.001]
HR (b·min ⁻¹)	126.6 (19.7)	126.9 (19.2)	-0.4 (20.3) [-5.14 to 4.38]	167.0 (26.0)	161.2 (27.5)	5.8 (19.7) [1.16 to 10.43]

Key: ViVol: inspired tidal volume; V_E: ventilation; Br/M: respiratory rate; Ti/Tt: ratio of inspiratory time to total respiratory time; HR: heart rate.

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Table 3

For Peer Review

Table 3: Difference between Time 1 (start of admission for intravenous antibiotics) and Time 2 (end of admission for intravenous antibiotics) in measurements recorded by the LifeShirt during the final two minutes of 6MWT in patients with CF (n=12) (repeated measures ANOVA)

	% difference between Time 1 and Time 2	Bias between Time 1 and Time 2 (<i>p</i>)	CV between Time 1 and Time 2 (%)
lnViVol	4.2	0.789	4.2
lnV _E	1.8	0.907	3.3
lnBr/M	-2.4	0.414	5.6
lnTi/Tt	-1.1	0.207	2.3
lnHR	-0.4	0.126	3.1

Key: lnViVol: log of inspired tidal volume; lnV_E: log of ventilation; lnBr/M: log of respiratory rate; lnTi/Tt: log of ratio of inspiratory time to total respiratory time; lnHR: log of heart rate.

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Title: CARDIORESPIRATORY MEASUREMENTS DURING FIELD TESTS IN CF: USE OF AN AMBULATORY MONITORING SYSTEM

Short title: FIELD EXERCISE TESTS IN CF

Authors: Judy M Bradley, Lisa Kent, Brenda O'Neill, Alan Nevill, Lesley Boyle, J Stuart Elborn

Table 4

For Peer Review

Table 4: Cardiorespiratory measurements recorded by the LifeShirt during the final two minutes of 6MWT at Time 1 (start of admission for intravenous antibiotics) and Time 2 (end of admission for intravenous antibiotics).

	Time 1	Time 2	Mean difference
	Mean (SD)	Mean (SD)	(SD)
			[95% CI]
ViVol	914.5 (392.2)	830.7 (246.2)	83.8 (434.7)
(mL)			[-99.8 to 267.4]
V_E	33.0 (12.2)	31.2 (7.8)	1.8 (15.4)
(L·min ⁻¹)			[-4.7 to 8.3]
RR	39.3 (8.2)	40.2 (8.4)	-0.9 (4.3)
(br·min ⁻¹)			[-2.7 to 0.9]
Ti/Tt	0.456 (0.032)	0.461 (0.029)	-0.005 (0.016)
			[-0.012 to 0.002]
HR	128.3 (19.5)	134.5 (15.9)	-6.2 (14.5)
(b·min ⁻¹)			[-12.3 to -0.02]

Key: ViVol: inspired tidal volume; V_E : ventilation; Br/M: respiratory rate; Ti/Tt: ratio of inspiratory time to total respiratory time; HR: heart rate.

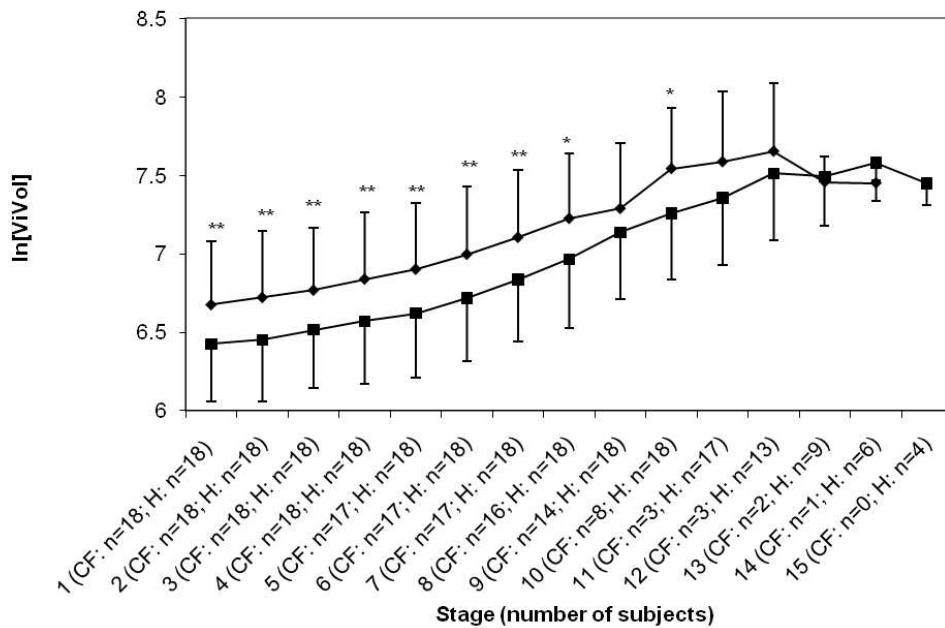


Figure 1: Mean ln[Vivol] at each stage of MST, data for Time 1 and Time 2 combined. Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, *p<0.05, **p<0.01
256x174mm (96 x 96 DPI)

Review

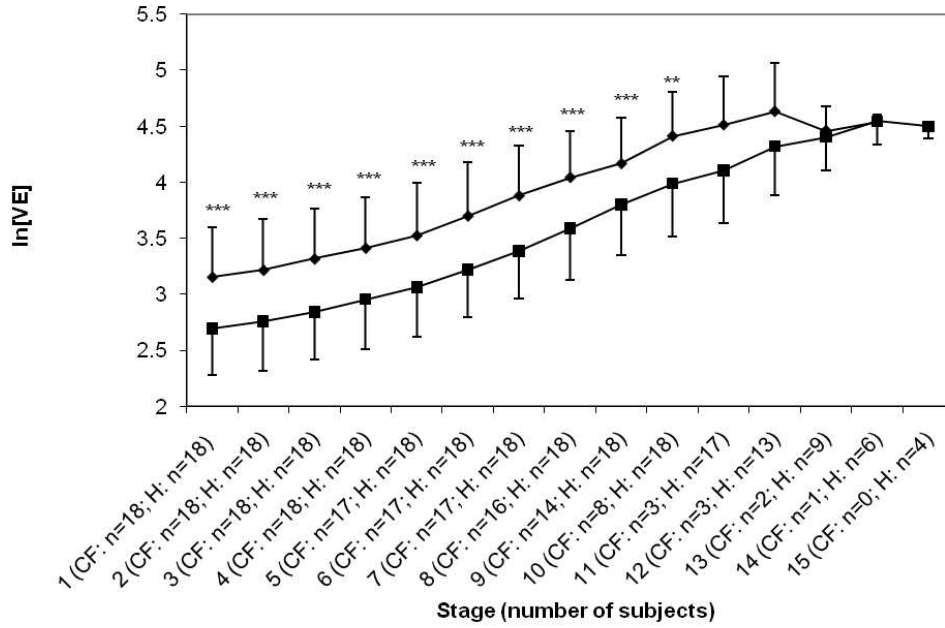


Figure 2: Mean ln[VE] at each stage of MST, data for Time 1 and Time 2 combined. Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, **p<0.01, ***p<0.001
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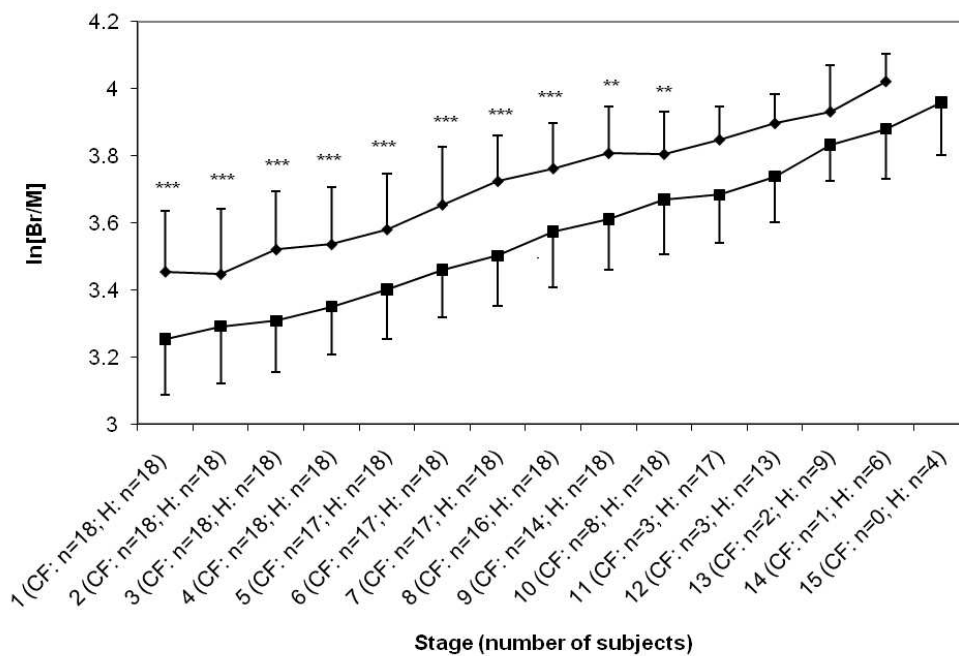


Figure 3: Mean ln[Br/M] at each stage of MST, data for Time 1 and Time 2 combined. Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, **p<0.01, ***p<0.001
256x174mm (96 x 96 DPI)

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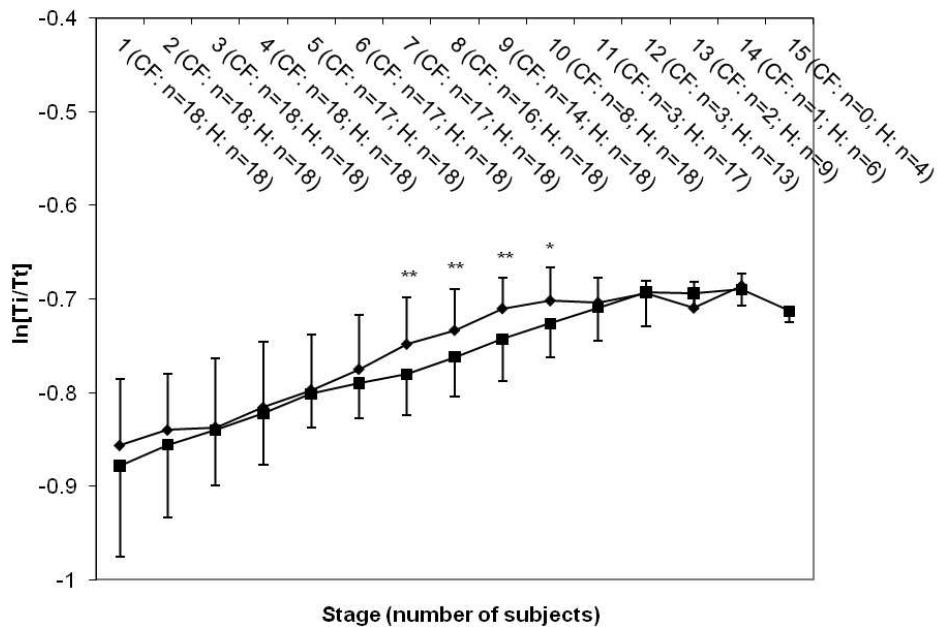


Figure 4: Mean $\ln[Ti/Tt]$ at each stage of MST, data for Time 1 and Time 2 combined. Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, * $p < 0.05$, ** $p < 0.01$
 256x174mm (96 x 96 DPI)

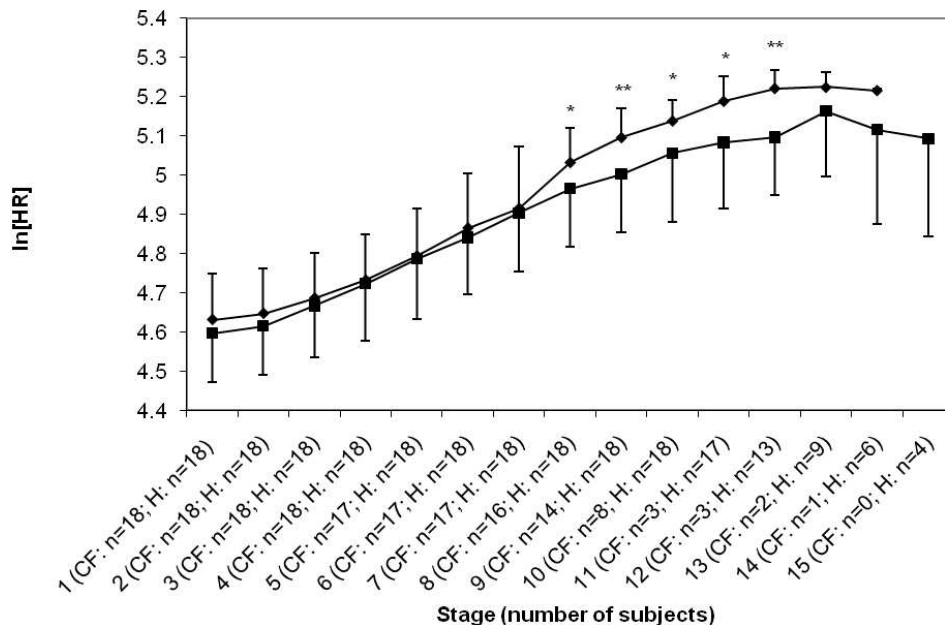


Figure 5: Mean ln[HR] at each stage of MST, data for Time 1 and Time 2 combined. Adults with CF (diamond), healthy adults (square). Error bars represent standard deviation, *p<0.05, **p<0.01