ERJ Express. Published on February 8, 2013 as doi: 10.1183/09031936.00134312

VALIDITY OF PHYSICAL ACTIVITY MONITORS DURING DAILY LIFE IN PATIENTS WITH COPD

Roberto A. Rabinovich[1*], Zafeiris Louvaris[2*], Yogini Raste[3], Daniel Langer[4], Hans Van Remoortel[4], Santiago Giavedoni[1], Chris Burtin[4], Eloisa M. G. Regueiro[5], Ioannis Vogiatzis[2], Nicholas S. Hopkinson[3], Michael I. Polkey[3], Frederick J. Wilson[6], William MacNee[1], Klaas R. Westerterp[7], and Thierry Troosters[4]; on behalf of the PROactive consortium.

* These authors (RR and ZL) contributed equally to this work.

[1]ELEGI Colt Laboratory, Centre for Inflammation Research. The Queen`s Medical Research Institute, University of Edinburgh, Scotland, UK. [2]Department of Critical Care Medicine, Pulmonary Rehabilitation Centre, Evangelismos Hospital, National & Kapodistrian University of Athens, M' Simou and GP Livanos Laboratories, Thorax Foundation, Athens, Greece. [3]NIHR Respiratory Biomedical Research Unit of the Royal Brompton and Harefield NHS Foundation Trust and National Heart & Lung Institute, Imperial College London, London, United Kingdom. [4]Faculty of Kinesiology and Rehabilitation Sciences, Department of Rehabilitation Sciences, Katholieke Universiteit Leuven, Leuven, Belgium. [5]Laboratory of Respiratory Physiotherapy, Universidade Federal de São Carlos - UFSCar, São Carlos, Brazil. [6]Precision Medicine, Pfizer Worldwide Research and Development, Sandwich, Kent, United Kingdom. [7]Department of Human Biology, Maastricht University, Maastricht, the Netherlands.

This work has been funded by The Innovative Medicine Initiative Joint Undertaking (IMI JU # 115011).

Supported by the NIHR Respiratory biomedical research unit at Royal Brompton and Harefield NHS Foundation Trust and Imperial College London.

Correspondence: Roberto A. Rabinovich. ELEGI Colt Laboratory, Centre for Inflammation Research. The Queen`s Medical Research Institute, University of Edinburgh. 47 Little France Crescent. EDINBURGH, U.K. EH16 4TJ. Email: roberto.rabinovich@ed.ac.uk

Authors Contributions:
Conception and design: RR, IV, NH, MP, FW, KW, TT.
Realisation, analysis and interpretation: RR, ZL, YR, DL, HVR, SG, CB, ER, IV, NH, FW, KW, TT.
Drafting the manuscript for important intellectual contents: RR, ZL, HVR, FW, WM, MP, IV, TT.

Running Title: Validation of physical activity monitors in COPD
Body Text word count: 3712.
Key words: Activity Monitoring, Chronic Obstructive Pulmonary Disease, Doubly Labelled Water, Indirect Calorimetry, Physical Activity.

This article has an online data supplement.

Abstract

Background: Symptoms during physical activity (PA) and physical inactivity are hallmarks of COPD. Our aim was to evaluate the validity and usability of six activity monitors in patients with COPD against the doubly labelled water (DLW) indirect calorimetry method.

Methods: Eighty COPD patients (age 68±6 years, FEV_1 57±19% predicted) recruited in four centres each wore simultaneously three or four of six commercially available monitors validated in chronic conditions for 14 consecutive days. *A priori* validity criteria were defined. These included the ability to explain total energy expenditure (TEE) variance through multiple regression analysis, using TEE as the dependent variable with total body water (TBW) plus several PA monitors outputs as independent variables; and correlation with DLW measured activity energy expenditure (AEE).

Results: The Actigraph GT3X and DynaPort MoveMonitor best explained the majority of the TEE variance not explained by TBW (53% and 70% respectively) and showed the most significant correlations with AEE ($r=0.71$ $p<0.001$, $r=0.70$ $p<0.0001$, respectively).

Conclusions: The results of this study should guide users in choosing valid activity monitors for research or for clinical use in patients with chronic diseases such as COPD.

Abstract word count: 185

Introduction

COPD is a debilitating and progressive disease characterised by poorly reversible airflow limitation [1] and associated with several extra-pulmonary effects of which skeletal muscle dysfunction [2] contributes, together with airflow limitation, to limit the exercise capacity of these patients [3]. In association with psychological and behavioural aspects, the reduced exercise capacity contributes, in turn, to the reduced physical activity (PA) characteristic of patients with COPD [4, 5], a factor which limits social interaction and may threaten independence.

Inactivity is associated with outcomes relevant to health care providers such as lung function progression [6], hospital admission [7] and death [8]. Enabling patients to become more physically active and less symptomatic is, therefore, an important, patient-centred goal for pharmacological and non-pharmacological therapies in COPD. Therefore, accurate assessment of PA may provide a unique perspective on treatment effectiveness.

Physical activity is defined as any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level [9]. There is consensus that PA is best evaluated by direct measurement using PA monitors (PAM) [10, 11] rather than questionnaires [12]. The number of PAM is growing with improvements in technology.

However, assessing PA in patients with less and slower activity than healthy subjects is challenging [12]. The accuracy of PAM to detect subtle changes in PA needs to be validated and their acceptability to, and usability by, patients needs to be assessed.

The EU/IMI-funded PROactive project (www.proactivecopd.com) is developing a patient reported outcome (PRO) tool directed at physical activity in COPD. As part of this process a prior systematic review [13] identified six commercially available PAM

which have previously been validated - against indirect calorimetry - in healthy adult populations and in some chronic conditions. These monitors were selected for further validation.

Our operational definition of validity was determined *a priori* at a consortium meeting in which stakeholders were represented. We considered that the activity measure should show a good correlation with more direct measures of energy expenditure (EE). As a direct measure of energy expenditure we used the doubly labelled water (DLW) indirect calorimetry technique [14]. In addition, we considered a series of highly desirable criteria for an activity monitor to be a valid tool to assess physical activity in COPD patients, as follows. Firstly, a monitor should be able to capture small changes in PA [15]. Such differences are observed during weekends in patients with COPD [4]. Secondly, PAM should be user friendly in order to be accepted by the patient measured.

Therefore to further assess the utility of PAM for use in clinical trials and in the PRO being developed; we conducted a multicentre evaluation of the six commercially available monitors.

Methods

STUDY GROUP

Eighty patients with COPD [16] (61 male) were recruited across 4 European centres (Athens, Edinburgh, Leuven and London) (20 patients per centre). All had a diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease [1]. They were clinically stable and free of exacerbations for 4 weeks prior to the study. Patients were excluded if they had co-morbidities which would interfere with their movement, cognitive impairment or if they were on variable doses of diuretics which would potentially interfere with the doubly labelled water (DLW) method. The study was approved by the local Ethics Committee's in each country as well as the independent ethical board of the PROactive project (www.proactivecopd.com) and written informed consent was obtained from the participants.

STUDY DESIGN

This was a multi-centre crossectional validation study with 14 days of continuous assessment. The six monitors were randomly assigned to the different centres (three monitors per centre). Patients were asked to wear simultaneously during wakefulness up to 4 PAM (including the three monitors assigned to the centre) out of the six monitors selected for validation [13]: two uniaxial monitors [Lifecorder plus, Kenz Suzuken Co Ltd., Nagoya, Japan)] and [Actiwatch Spectrum (Philips Respironics, Bend, OR,USA)], three triaxial monitors [Actigraph GT3X (Actigraph LLC Pensacola, FL, USA)], [DynaPort MoveMonitor (McRoberts BV, The Hague, The Netherlands)] and [RT3 (StayHealthy Inc. Monrovia CA, USA)] and one multisensor

monitor, a triaxial accelerometer with different sensors [SenseWear Armband (Bodymedia Inc. Pittsburgh PA, USA)] (**Table 1**).

Patients wore the activity monitors during wakefulness for 14 consecutive days, and were instructed not to wear them whilst bathing or swimming. Their outputs over this period were compared to a gold standard of indirect calorimetry as obtained from doubly labelled water (see below). The monitors provide **measured** outputs derived from accelerometer data and **estimated** energy expenditure outputs derived from these and other variables (i.e. anthropometric data of the patient) using prediction equations (**Table 1**). We aimed at providing validity for the **measured** outputs of the devices rather than their prediction of energy expenditure as this is highly dependent on reference equations (which are not available to users in some cases for commercial reasons and are not provided by all six monitors) to convert accelerometer data into energy equivalents.

At the end of the monitoring period, patients also completed a usability questionnaire for each monitor, which assessed factors such as ease of use, comfort and obtrusiveness. The questionnaire is available in the online supplement.

The following *A priori* criteria for validation of the monitors were established: 1) Significant relationship with DLW-derived active energy expenditure, 2) Ability to capture day-to-day variability on PA levels throughout the period of assessment since these are a recognised feature of COPD [15], 3) Ability to capture the lower levels of activity levels during WE characteristic of COPD patients [4]; and, 5) Acceptable patient-reported usability criteria.

Patients visited the centres on three occasions, with one week in-between.

Assessments

All patients had the following baseline assessments: anthropometric measurements, pulmonary function tests (spirometry, lung diffusion capacity and lung volumes), six–minute walking distance (6MWD), incremental cardiopulmonary exercise test and COPD-specific health-related quality of life questionnaires (St. George's Respiratory Questionnaire, SGRQ), COPD Assessment Tool (CAT), modified Medical Research Council (mMRC) dyspnoea scale and usability questionnaire. Full details of the assessments are listed in the online supplement.

DLW method

The total energy expenditure (TEE) over the 14 day period of monitoring was measured using doubly labelled water (DLW), according to the Maastricht protocol [14]. On the morning of day 0, body weight was recorded, and after the collection of a background urine sample, subjects drank a weighed amount of DLW (enriched with $^{2}H_{2}$ and ^{18}O such that baseline levels of DLW (normally present in tap water and in urine) were increased by 100 ppm for ^{2}H and 200 ppm for ^{18}O). Urine samples were collected in the afternoon of day 0 approximately 6 hours post ingestion and from the second voiding. Further samples were collected on the mornings of day 1, day 7, and day 14, and in the evening of day 6, and day 13. Patients were asked to note carefully the exact time of each urine sample. The DLW method provides an average value of Total Energy Expenditure per day during the period of assessment.

Resting energy expenditure (REE) was measured using the ventilated hood method [17]. An open-circuit, computerised indirect calorimeter (Deltatrac TM; Datex Division, Helsinki) connected to a transparent hood system was used. Patients were instructed to fast overnight and measurements were taken first thing in the morning of the first

day of the study period. The calorimeter was calibrated before each patient measurement using a span gas (20% CO_2, 1% O_2), and to nitrogen for a zero calibration.

Patients were asked to lie still under the hood for 20-30 minutes until the readings of VO_2 and VCO_2 had reached equilibrium. The mean of the following 10 minutes of readings were taken to calculate resting energy expenditure. A second measurement was taken during the second week of the study and a mean of the two values was used. The Weir equation [18] was used to calculate resting energy expenditure from the VO_2 and VCO_2 values obtained.

Active energy expenditure (AEE) was measured as (0.9 × TEE) − REE, assuming diet-induced thermogenesis to be 10% of TEE [19].

Due to technical problems, some of the measurements of REE were not accurate (i.e. very low values of REE) and eleven patients have to be excluded from any analysis involving AEE. Three other patients were excluded due to technical problems with the DLW assessment.

Total body water (TBW) was calculated as the ^2H dilution space from the ^2H enrichment of the second voiding minus the ^2H concentration of the sample before dose administration [20]. The ^2H dilution space was divided by 1.04 to correct for isotope exchange with non-aqueous hydrogen of body solids [21].

Statistical analysis

Results are described as mean±SEM unless otherwise specified. *A priori* criteria for monitor validity were established before any analyses were undertaken. Being physical activity defined as “body movement incurring in energy consumption” we

expected a significant correlation between the outputs of the monitors (based on accelerometer data to capture movement) with the energy consumed during the same period of assessment using DLW. The relationship of each activity monitor output (average of the whole period of assessment) with active energy expenditure (AEE) as assessed by DLW was tested by Pearson's correlation (see online supplement for Bland-Altman plot for those monitors giving an estimate of mean total daily energy expenditure).

A significant portion of the total energy consumed obtained with the DLW method would be related to the body composition of a particular subject. Therefore, we further explore the ability of the activity monitors to explain the variance of TEE not correlated with TBW (the portion of TEE related with movement). In order to explain the variability in TEE measured with the DLW method, a multiple stepwise regression analysis was performed with TEE as the dependent variable and DLW-measured TBW (a surrogate for metabolically active tissue and hence REE) and PAM outcomes as independent variables [22].

The PAM ability to capture variability in PA level was assessed by comparison of the coefficient of variation of monitor outcomes (one value per day of assessment) over the 14 days of assessment using one-way analysis of variance (ANOVA).

The ability to capture lower levels of activity present at weekends, characteristic of COPD patients [4] was tested by a Student's t-test to compare weekday versus weekend activity for each monitor (average of each period weekday/weekend).

Relationship with parameters of exercise (6MWD, peak VO_2) was tested with Pearson's correlation.

Acceptable patient-reported usability was based on the questionnaire results.

In order to assess the repeatability of PA outcomes assessed by PAM, we calculated the differences between outputs obtained in the two consecutive weeks of assessment. We expected 95 % of the differences between week I and week II to be less than two standard deviations (of the difference)[23]. A student's t-test was also used to compare PAM outputs between the first and second week of assessment. A comparison between the variability (standard deviation) for a representative measured variable for each of the six PAM comparing the first week of assessment to the whole period of 14 days (two weeks) was performed to evaluate if two weeks of assessment add power (reduction of the standard deviation) to the PA evaluation. The level of significance for all comparisons was set at $p<0.05$. Data were analyzed using the statistical package SAS version 9.2 (SAS Institute Inc, Cary, NC, USA).

Results

Patients had at least 2 weekends and 6 weekdays of data for each activity monitor. The first and last day were excluded to eliminate bias (as these were incomplete days and included visits to the study centres). Although subjects wore the monitor for 14 days, in some cases technical problems, or due to insufficient hours of data collection, resulted in incomplete data collection (i.e. less than 10 hours of data during daytime hours per day). Out of all possible days of assessment, the proportion of days with more than 10 h of assessment included in the validation analysis ranged from 79% to 91% for all six monitors (see online supplement for details).

No patient had to be entirely excluded from the analyses. However, incomplete days of monitoring were excluded.

Anthropometric characteristics and pulmonary function data of patients are depicted in **Table 2**. The patients had a wide spectrum of disease severity in terms of lung function (FEV_1 from 16 %pred to 96 %pred) (GOLD STAGE I=10, GOLD STAGE II= 43, GOLD STAGE III=20, GOLD STAGE IV=7) and in terms of symptoms (MRC 1=12, MRC 2=33, MRC 3=26, MRC 4=9). No differences in Total or Activity related energy expenditure measured with the DLW method were identified between patients wearing different monitors. Moreover, no differences were observed in body composition, lung function, dyspnoea score, BODE index and health related quality of life (see online supplement).

PAM validation against DLW

Measured (instead of estimated) activity monitor outputs that showed the most significant correlations with AEE measured by the DLW method are shown in **Figure 1** (for a broader list of variables see online supplement). All the monitors showed

statistically significant correlations with AEE. The better the correlation, the best the ability of a monitor to identify a patient with high AEE as a more active patient and a patient with a low AEE as a low active patients.

As expected, most of the total energy expenditure variance was explained by TBW (a surrogate of Resting Energy Expenditure) (**Figure 2**). Although all monitors significantly explained part of the residual variance with some of the variables remaining in the model ($p<0.05$), the DynaPort MoveMonitor ($r^2=0.30$) (average movement intensity+walking time+walking movement intensity), and the Actigraph GT3X ($r^2=0.24$) (activity time [AT]) were the two monitors with the largest variance explained by the monitor in the model (grey column in **Figure 2**), explaining 70% and 53% of the TEE variance not correlated with TBW respectively. The remaining monitors explained a lower portion of the TEE variance not explained by TBW (actiwatch [AC; $r^2=0.18$]); SenseWear [AvgMETs+Steps, $r^2=0.08$]; .Lifecorder [AS, $r^2=0.10$]; and, RT3 [TEE, $r^2=0.07$]). Because three different variables corresponding to the DynaPort contribute to explain the TEE variance not explained by TBW, we have conducted the analysis with the variable with the highest contribution (average movement intensity). Considering this variable alone ($r^2=0.23$) the percentage of the possible explained variance drops from 70 to 54. The RT3X and the DynaPort remain the monitors with the largest variance explained by the monitor in the model.

Ability of PA monitors to capture variability and differences in PA between weekends and weekdays

The ability of activity monitors to capture variability, assessed as the coefficient of variation for the different monitor's outputs is shown in **Figure 3A**. All monitors were able to capture variability in PA levels across the different days throughout the period

of assessment. The ability of the monitors to detect changes in physical activity levels was also assessed as the differences between weekend and weekdays PA levels (**Figure 3B**). With exception of the RT3, all monitors were capable to capture differences between weekend and weekdays.

Usability of Activity Monitors

Patient adherence with the use of the monitors (despite using three or four simultaneously) was good throughout the period of assessment as reflected by the compliance range from 79% to 91% (**Table S1**) and by the usability questionnaire. **Figure 4** illustrates the scores from the questionnaire used to assess usability. Most patients declare willingness to wear most devices for more than a week, and the devices were generally not perceived as intrusive. Patients also provided an overall score on the monitors. In general the scores were good, ranging from 75 to 91 on a scale from 0 (worst score) to 100 (best score).

Discussion

The main findings of this multi-centre study were that the output from all monitors demonstrated a significant relationship with AEE derived from DLW measurements in line with those typically observed in field validation studies [13, 24-28]. The DynaPort MoveMonitor and the Actigraph GT3X best explained the activity related energy from total energy expenditure not related to total body water. Few studies have individually validated these PAM (or their older versions) in the field in chronic disease populations [13]. This is the first multi-centre trial where several activity monitors were validated head-to-head against directly measured EE in different stages of COPD.

The validity of the PAM against energy expenditure measured by the DLW method in the present study was assessed using correlation analysis rather than a measure of agreement (e.g. Bland and Altman analysis [see online supplement]). There are two main arguments in support of this approach: Firstly, we were more interested in providing validity for the **measured** outputs of the devices rather than their prediction of energy expenditure as this is highly dependent on reference equations to convert accelerometry into energy equivalents (which are not available to users in some cases for commercial reasons). In addition, only three out of the six monitors explored provide estimated values of total energy expenditure. Physical activity is defined as any bodily movement produced by skeletal muscle resulting in energy consumption. It is therefore reasonable to expect and investigate a relation between movement measured by accelerometers and energy expenditure assessed with indirect calorimetry (DLW) throughout the same period as proof of validity. Secondly, energy expenditure is driven to a large extent by subject specific characteristics including body weight, age, height and specific factors such as mechanical efficiency.

It is not feasible to take mechanical efficiency into account in predicting energy expenditure, especially in patients with COPD.

COPD patients have a poor mechanical efficiency yielding larger energy expenditure compared to healthy subjects [29-32]. Consequently, AEE remains relatively well preserved, whereas it is well recognised that patients are moving less [32]. It cannot be expected that an activity monitor would be able to take the individual's mechanical efficiency into account and provide very accurate estimates of AEE. Hence, we suggest that activity monitors should be used to assess the activities (i.e. movements) of patients in terms of amount and/or intensity of activity and that greater weight should be given to direct monitor outputs (steps, activity count, vector magnitude units, etc.). We acknowledge that the derivation of energy expenditure is difficult by default and likely inaccurate when based on acceleration signals only, but consider that this, does not render activity monitors invalid for the assessment of bodily movement and, perhaps even more importantly, intervention-associated changes. Therefore, comparing the raw data from the monitors with the AEE (derived from the DLW method) by using correlation analysis was judged as the appropriate statistical method [33].

All monitors were able to capture variability in activity levels across the different days throughout the period of assessment. Moreover, with the exception of the RT3 device, monitors were able to capture differences between weekend and weekdays.

Another interesting finding was the good correlation between activity monitors variables and physiological variables reflecting exercise capacity (see online). It is to be expected that patients with higher exercise capacity perform higher levels of activity and this should be captured by the monitors. The Lifecorder plus monitor

showed weak correlations with exercise capacity variables whereas the Actigraph GT3X showed the best correlations with all outcomes of exercise capacity. For the DynaPort MoveMonitor and the SenseWear Armband the correlations were in line with those reported previously with older models of these monitors [4, 5, 34].

Besides the concepts of validity and reliability, other factors such as size and scope of the study, usability and cost of the monitor must be taken into consideration when selecting a monitor for clinical trials. Patients participating in the present study were asked to rate their perception of wearing the devices using a twelve item questionnaire designed for this purpose. Most patients did not mind wearing most devices for more than a week, and the devices were generally not perceived as intrusive (**Figure 5**).

Our analysis comparing the first and second week of activity assessment showed repeatable data in two consecutive weeks in this population of COPD patients (see online). Moreover, adding a second week of measurements did not significantly change the variability whether it was based on one or two weeks of measurement indicating that there would be little or no advantage, in terms of a reduction in the sample size required, of extending the period of assessment from one week to two weeks.

Limitations of the study

Although patients of all GOLD stages were studied, there was not an even distribution. However, there was a wide range in activity levels (as energy consumed during activities [AEE] assessed with DLW) (55.4-1581.2) and 6MWD (149-675m), so we consider this study group to be representative of the spectrum of activity levels in COPD, and of patients typically entering clinical trials.

None of the patients wore all six monitors simultaneously, which precluded direct comparison of all six monitors in the same group of patients. This does not compromise the results of the present study since the main results are based in the individual comparison of each monitor with DLW derived variables. Moreover, wearing all monitors would have been onerous and could have introduced other errors such as poorer compliance. We felt that each patient wearing up to 4 monitors was a good compromise. Another potential limitation of the study relates to the exclusion of 11 patients for the calculation of AEE due to technical problems in the assessment of resting energy expenditure. We could have calculated resting energy expenditure from Harris-Benedict equations but we didn't feel that this approach was more appropriate than using our own data on resting energy expenditure due to known elevated resting energy expenditure in patients with COPD. However, we have run the validation analysis with AEE data calculated with Harris-Benedict equations which lead us to similar conclusions that the present analysis.

In summary, all tested monitors showed good correlations with DLW-measured active energy expenditure. The best correlations corresponded to two of the triaxial monitors tested (the DynaPort MoveMonitor and the Actigraph GT3X). These monitors were also the best able to explain variability in TEE-DLW associated with physical activity, and were therefore most representative of what patients were actually doing. These results complement the results for the previously published laboratory validation study of the same six monitors [33], and taken together may allow users to choose the most appropriate activity monitors and endpoints for research or for clinical use in patients with COPD. Our data also provide a consensus benchmark for future monitors which may emerge.

Acknowledgements

The authors would like to acknowledge the members of the PROactive consortium for the outstanding contribution to this work.

PROactive consortium: Chiesi Farmaceutici S.A.: Caterina Brindicci, Tim Higenbottam; Katholieke Universiteit Leuven: Thierry Troosters, Fabienne Dobbels; Glaxo Smith Kline: Margaret X. Tabberer; University of Edinburgh, Old College South Bridge: Roberto A Rabinovich, William McNee; Thorax Research Foundation, Athens: Ioannis Vogiatzis; Royal Brompton and Harefield NHS Foundation Trust: Michael Polkey, Nick Hopkinson; Municipal Institute of Medical Research, Barcelona: Judith Garcia-Aymerich; Universität Zürich, Zürich: Milo Puhan, Anja Frei; University Medical Center, Groningen: Thys van der Molen, Corina De Jong; Netherlands Asthma Foundation, Leusden: Pim de Boer; British Lung Foundation, UK: Ian Jarrod; Choice Healthcare Solution, UK: Paul McBride; European Respiratory Society, Lausanne: Nadia Kamel; Pfizer: Katja Rudell, Frederick J. Wilson; Almirall: Nathalie Ivanoff; Novartis: Karoly Kulich, Alistair Glendenning; AstraZeneca AB: Niklas X. Karlsson, Solange Corriol-Rohou; UCB: Enkeleida Nikai; Boehringer Ingelheim: Damijen Erzen.

TABLE 1. DETAILS OF TYPE, LOCATION AND AVAILABLE OUTPUTS FOR THE SIX ACTIVITY MONITORS

Name, Manufacturer (software)	Type	Number of subjects	Number of days	Location	Measured output	Estimated output
Lifecorder Plus Kenz Suzuken Co Ltd., Nagoya, Japan (Physical Activity Analysis Software)	Uniaxial accelerometer	40	471	Waist (left)	Activity Score (AS)	TEE
Actiwatch Spectrum, Philips Respironics, Bend, OR,USA (Respironics Actiware 5)	Uniaxial accelerometer	40	453	Wrist (left)	Activity Counts (AC)	
RT3, Stayhealthy Inc. Monrovia, CA, USA (Stayhealthy RT3 Assist Version 1.0.7)	Triaxial accelerometer	39	412	Waist (right)	Vector Magnitud Units (VMU)	TEE, AEE
Actigraph GT3X, Actigraph LLC Pensacola, FL, USA (Actilife 5)	Triaxial accelerometer	39	463	Waist (right)	Activity Time (AT), Vector Magnitude Units (VMU), Steps	
DynaPort® MoveMonitor, McRoberts BV, The Hague, The Netherlands (www.mcroberts.nl)	Triaxial accelerometer	40	443	Waist (lower back)	Steps, movement Intensity, different body positions	TEE
SenseWear Armband, Bodymedia, Pittsburgh, PA, USA (SenseWear Professional 6.0)	Multisensor device: triaxial accelerometer + sensors (heat flux, galvanic skin response and skin temperature)	73	748	Upper left arm at triceps	Steps, Time Active, Time on different activity, intensity level	TEE, Average METs

TEE, total energy expenditure, AEE activity energy expenditure

.

TABLE 2. CHARACTERISTICS OF THE STUDY GROUP

M/F		61/19
		mean ± SD
Age (Years)		68 ± 6.2
BMI ($kg.m^2$)		26.5 ± 4.7
mMRC		2.4 ± 0.9
FEV_1 (L)		1.5 ± 0.6
FEV_1 (% pred)		57 ± 19.1
FVC (L)		3.2 ± 0.8
FVC (% pred)		95 ± 20.1
FEV_1/FVC		0.5 ± 0.1
BODE		5.7 ± 1.7
6MWD (m)		435 ± 118.1
Wpeak (Watt)		81 ± 40.1
VO_2peak (ml/min/kg)		17.1 ± 5.9
SGRQt		42 ± 20.1
CAT		16 ± 7.5
AEE (kCal/kg)		11.4 ± 4.5
TBW (L)		35.6 ± 6.6

BMI=body mass index, mMRC=modified Medical Research Council dyspnoea score, FEV_1=forced expiratory volume in the first second, FVC=forced vital capacity, BODE=BODE index, 6MWD=distance walked in the six minute walking test, Wpeak=power achieved during the incremental exercise test; VO_2peak=peak oxygen uptake achieved during the incremental exercise test; SGRQt=St George Respiratory Questionnaire total score, CAT=COPD assessment test, AEE=activity energy expenditure, TBW=total body water.

FIGURE LEGENDS

Figure 1. Correlations of individual data of physical activity **measured** outcomes with active energy expenditure measured with doubly labelled water (DLW [AEE]) (kCal) for the six monitors studied: Lifecorder plus (panel A), ActiWatch Spectrum (panel B), RT3 (panel C), DynaPort MoveMonitor (panel D), Actigraph GT3X (panel E), SenseWear Armband (panel F). Solid lines (regression line) and dashed lines (95% confidence intervals). AS=activity score, AC=activity counts, VMU=vector magnitude units, Mint=movement intensity, DLW= doubly labelled water, AEE=activity energy expenditure.

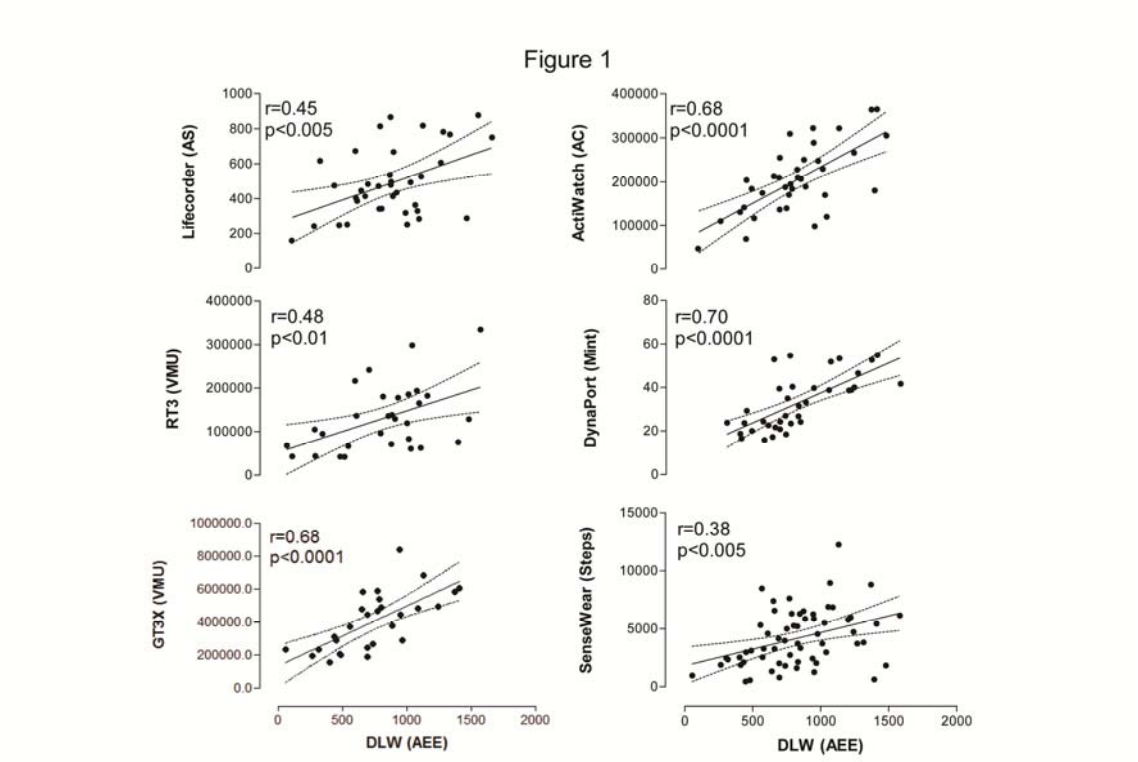


Figure 2. Percentage of boubly labelled water (DLW) measured total energy expenditure (TEE) explained by total body water (TBW) (black portion of the columns) and the six different monitors evaluated (grey portion of the columns): Lifecorder plus (activity score [AS]), ActiWatch Spectrum (activity counts [AC]), RT3 (TEE), DynaPort MoveMonitor (average movement intensity+walking time+walking movement intensity), Actigraph GT3X (activity time [AT]), SenseWear Armband (METs+Steps).

Figure 2

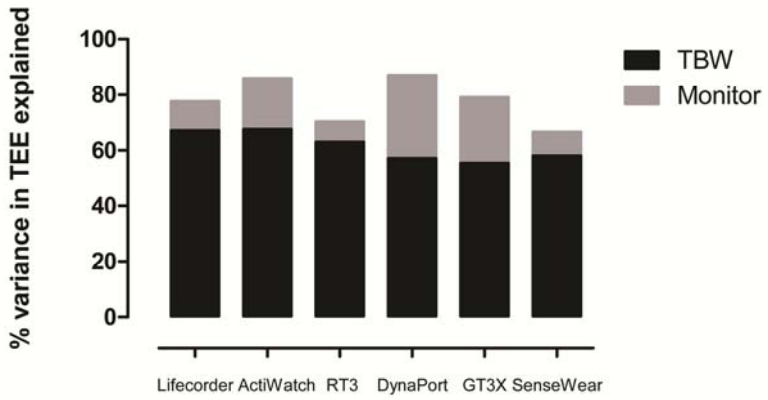


Figure 3. Variability of physical activity outcomes for the six activity monitors. Panel A shows all monitors ability to capture variability of the data throughout the 14 day period of assessment. Panel B shows ability to capture changes in physical activity between weekends (WE) and weekdays (Week) (% differences WE-Week). Error bars (SEM). VMU=vector magnitude units, AS= activity score, AC=activity counts. (* $p<0.05$).

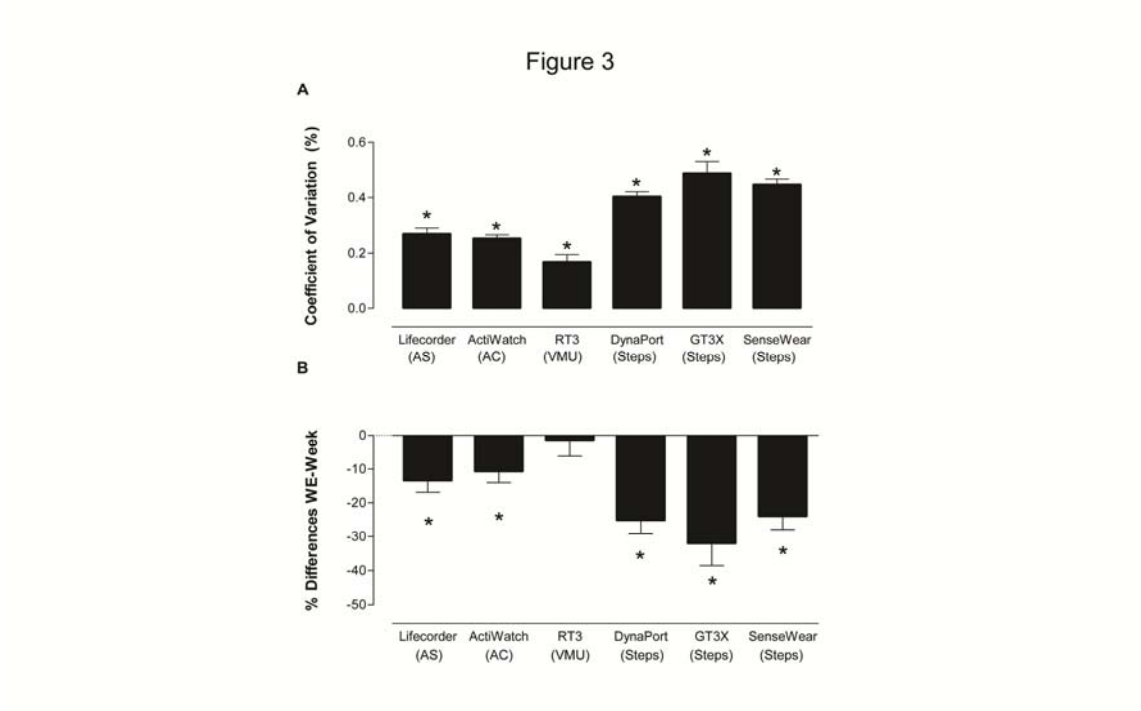
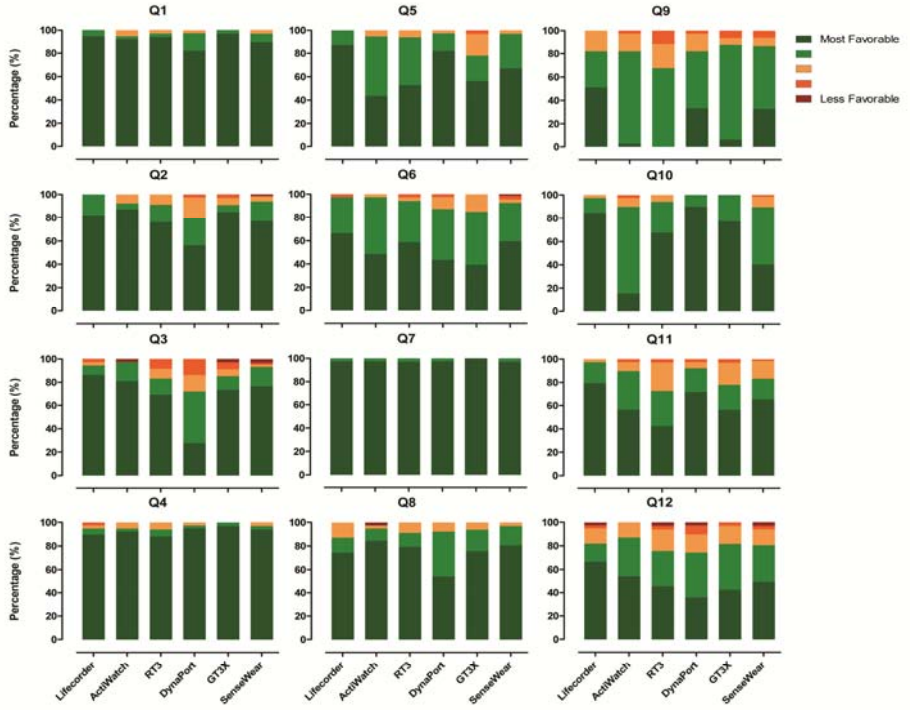


Figure 4. Usability of physical activity monitors as assessed directly from patients. This figure illustrates the responses of 71 patients who responded to the usability questionnaire. The questions were: Q1) “I experience technical problems”, Q2) “The Monitor interfered with my normal activities”, Q3) “I felt comfortable wearing the monitor”, Q4) “I felt embarrassed wearing the monitor”, Q5) “The instructions on how to use the monitor were clear”, Q6) “Using the monitor on a daily basis was easy”, Q7) “How much trouble did you have getting started with the monitor?”, Q8) “The monitors were easy to put on/take off”, Q9) “The monitors were bulky/heavy”, Q10) “The monitor bothered me in bed”, Q11) “I felt my privacy was invaded by the Monitor” ; and, Q12) ‘how long would you be willing to wear this particular monitor’. Responses to questions 1 to 11: From most favorable answer (■ dark green) to the less favorable answer (■ light green, ■ light orange, ■ dark orange and ■ brown, in that order). Responses to question 12 were: no limit (■ dark green), more than a week (■ light green), one week (■ light orange), two to four days (■ dark orange) and one day or less (■ brown).


Q1
Q5
Q9
Q2
Q6
Q10
Q3
Q7
Q11
Q4
Q8
Q12
Percentage (%)
0
20
40
60
80
100
Most Favorable
Less Favorable
Lifecorder
ActiWatch
RT3
DynaPort
GT3X
SenseWear

References

1. Rodriguez-Roisin R, Anzueto A, Bourbeau J, Calverley P. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. www.goldcopd.com2010 [updated 2010].
2. Agusti AG, Noguera A, Sauleda J, Sala E, Pons J, Busquets X. Systemic effects of chronic obstructive pulmonary disease. *European Respiratory Journal*. 2003;21(2):347-60.
3. Saey D, Debigare R, Leblanc P, Mador MJ, Cote CH, Jobin J, et al. Contractile leg fatigue after cycle exercise: a factor limiting exercise in patients with chronic obstructive pulmonary disease. *AmJRespirCrit Care Med*. 2003;168(4):425-30.
4. Watz H, Waschki B, Meyer T, Magnussen H. Physical activity in patients with COPD. *Eur Respir J*. 2009;33(2):262-72. Epub 2008/11/18.
5. Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2005;171(9):972-7. Epub 2005/01/25.
6. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Anto JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. *Am J Respir Crit Care Med*. 2007;175(5):458-63.
7. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Anto JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax*. 2006;61(9):772-8.
8. Waschki B, Kirsten A, Holz O, Muller KC, Meyer T, Watz H, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. *Chest*. 2011;140(2):331-42. Epub 2011/01/29.
9. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep*. 1985;100(2):126-31. Epub 1985/03/01.
10. Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Physical activity and hospitalization for exacerbation of COPD. *Chest*. 2006;129(3):536-44.
11. Pitta F, Troosters T, Spruit MA, Decramer M, Gosselink R. Activity monitoring for assessment of physical activities in daily life in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil*. 2005;86(10):1979-85. Epub 2005/10/11.
12. Cyarto EV, Myers AM, Tudor-Locke C. Pedometer accuracy in nursing home and community-dwelling older adults. *Med Sci Sports Exerc*. 2004;36(2):205-9. Epub 2004/02/10.
13. Van Remoortel H, Giavedoni S, Raste Y, Burtin C, Louvaris Z, Gimeno-Santos E, et al. Validity of activity monitors in health and chronic disease: a systematic review. *The international journal of behavioral nutrition and physical activity*. 2012;9(1):84. Epub 2012/07/11.
14. Westerterp KR, Wouters L, van Marken Lichtenbelt WD. The Maastricht protocol for the measurement of body composition and energy expenditure with labeled water. *Obesity research*. 1995;3 Suppl 1:49-57.

15. Hecht A, Ma S, Porszasz J, Casaburi R. Methodology for using long-term accelerometry monitoring to describe daily activity patterns in COPD. *Copd*. 2009;6(2):121-9. Epub 2009/04/21.
16. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*. 2007;176(6):532-55. Epub 2007/05/18.
17. Maffeis C, Schutz Y, Micciolo R, Zoccante L, Pinelli L. Resting metabolic rate in six- to ten-year-old obese and nonobese children. *The Journal of pediatrics*. 1993;122(4):556-62. Epub 1993/04/01.
18. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol*. 1949;109(1-2):1-9. Epub 1949/08/01.
19. Westerterp KR. Diet induced thermogenesis. *Nutrition & metabolism*. 2004;1(1):5.
20. van Marken Lichtenbelt WD, Westerterp KR, Wouters L. Deuterium dilution as a method for determining total body water: effect of test protocol and sampling time. *The British journal of nutrition*. 1994;72(4):491-7.
21. Schoeller DA, van Santen E, Peterson DW, Dietz W, Jaspan J, Klein PD. Total body water measurement in humans with 18O and 2H labeled water. *Am J Clin Nutr*. 1980;33(12):2686-93.
22. Bonomi AG, Plasqui G, Goris AH, Westerterp KR. Estimation of free-living energy expenditure using a novel activity monitor designed to minimize obtrusiveness. *Obesity (Silver Spring)*. 2010;18(9):1845-51. Epub 2010/02/27.
23. British Standard Institution. Precision of test methods 1: Guide for the determination and reproducibility for a standard test method (BS 597, Part 1). *London: (BSI)*. 1975.
24. Adams SA, Matthews CE, Ebbeling CB, Moore CG, Cunningham JE, Fulton J, et al. The effect of social desirability and social approval on self-reports of physical activity. *Am J Epidemiol*. 2005;161(4):389-98.
25. Assah FK, Ekelund U, Brage S, Corder K, Wright A, Mbanya JC, et al. Predicting physical activity energy expenditure using accelerometry in adults from sub-Sahara Africa. *Obesity (Silver Spring)*. 2009;17(8):1588-95.
26. Leenders NY, Sherman WM, Nagaraja HN, Kien CL. Evaluation of methods to assess physical activity in free-living conditions. *Med Sci Sports Exerc*. 2001;33(7):1233-40.
27. Jacobi D, Perrin AE, Grosman N, Dore MF, Normand S, Oppert JM, et al. Physical activity-related energy expenditure with the RT3 and TriTrac accelerometers in overweight adults. *Obesity (Silver Spring)*. 2007;15(4):950-6.
28. Mackey DC, Manini TM, Schoeller DA, Koster A, Glynn NW, Goodpaster BH, et al. Validation of an armband to measure daily energy expenditure in older adults. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2011;66(10):1108-13. Epub 2011/07/08.
29. Sala E, Roca J, Marrades RM, Alonso J, Gonzalez de Suso JM, Moreno A, et al. Effects of endurance training on skeletal muscle bioenergetics in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 1999;159:1726-34.
30. Richardson RS, Sheldon J, Poole DC, Hopkins SR, Ries A, Wagner PD. Evidence of skeletal muscle metabolic reserve during whole body exercise in

patients with hronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 1999;159:881-5.
31. Franssen FM, Wouters EF, Baarends EM, Akkermans MA, Schols AM. Arm mechanical efficiency and arm exercise capacity are relatively preserved in chronic obstructive pulmonary disease. *Med Sci Sports Exerc*. 2002;34(10):1570-6. Epub 2002/10/09.
32. Baarends EM, Schols AMWJ, Pannemans DLE, Westerterp KR, Wouters EFM. Total free living energy expenditure in patients with severe COPD. *Eur Respir J*. 1997;155:549-54.
33. Van Remoortel H, Raste Y, Louvaris Z, Giavedoni S, Burtin C, Langer D, et al. Validity of Six Activity Monitors in Chronic Obstructive Pulmonary Disease: A Comparison with Indirect Calorimetry. *PloS one*. 2012;7(6):e39198. Epub 2012/06/30.
34. Troosters T, Sciurba F, Battaglia S, Langer D, Valluri SR, Martino L, et al. Physical inactivity in patients with COPD, a controlled multi-center pilot-study. *Respir Med*. 2010;104(7):1005-11. Epub 2010/02/20.