Supplementary appendix
Analysis of nocturnal actigraphic sleep measures in patients with COPD and their association with daytime physical activity

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ONLINE ONLY SUPPLEMENTARY MATERIAL

This supplement includes:

Details of data sources

The objectively assessed data used in the current analysis were collected as part of previous studies which were developed in ten different countries (i.e., United Kingdom, Ireland, the Netherlands, Germany, Switzerland, Italy, Spain, the United States of America, Brazil, and Australia). The research groups that contributed to the current study were conveniently selected from recent publications (articles in peer-reviewed journals and abstracts presented at major respiratory congresses) using the SenseWear Armband continuously during day and night.

The data from the United Kingdom (UK) were collected in three cities, Leicester, Liverpool and London. In Leicester, the data were collected as part of a randomized controlled trial to evaluate the effectiveness of a self-management program of activity coping and education for COPD delivered in primary care (ISRCTN35501175). Ethical approval for the study was granted by Leicestershire, Northamptonshire and Rutland Regional Ethics Committee (reference 07/H0408/114). Participants were assessed between September 2009 and September 2012 at University Hospitals of Leicester NHS Trust. In London, the data were collected as part of two studies: 1) a multicenter study aiming to investigate the compliance of patients with COPD with wearing an activity monitor, and the relationship between physical activity and clinical outcomes (participants were recruited between 2009 and 2011 at the Royal Brompton Hospital; ethical approval was given by the ethics/review board of this institution); and 2) a multicenter study aiming to evaluate the effect of aclidinium bromide on exercise endurance, hyperinflation, and dyspnoea at rest and during exercise in patients with moderate to severe COPD (NCT01471171; this study was approved by the Independent Ethics Committees at each site, which were previously detailed by Beeh et al.).[1] In the latter study, participants were assessed between November 2011 and June 2012. In Liverpool, the data were collected between August 2009 and August 2010 at the University Hospital Aintree, as part of the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study.[2] Ethical approval was granted by the ethics/review board of the University Hospital Aintree. Some of the participants and data from the UK were part of previous publications,[3, 4] however there is no overlapping analysis.

The data from Ireland were collected in Dublin as part of a two-phase longitudinal study to examine the short term effects of pulmonary rehabilitation on standard measures and free-living physical activity in patients with COPD (NCT01530412). The study was approved by the Beaumont Hospital Ethics committee, reference numbers 07/10 and 07/48. Participants were assessed between June 2007 and July 2010 at the Beaumont Hospital. Some of the participants and data from Ireland were part of a previous report,[5] however there is no overlapping analysis.

The data from the Netherlands were collected in two cities, Eindhoven and Horn. In Eindhoven, the data were collected between February 2010 and September 2011 at the Catharina Hospital, as part of a clinical trial to investigate the pathophysiologic mechanisms of osteoporosis in COPD

(NCT01067248). Approval for the study was obtained from the Medical Ethical Committee of the Catharina Hospital (M09-1971). In Horn, the data were collected between May 2009 and September 2009 at CIRO+, a Center of Expertise for Chronic Organ Failure, as part of the ECLIPSE study.[2] Ethical approval was granted by the Stichting Therapeutische Evaluatie Geneesmiddelen (STEG/METC). Some of the participants and data from the Netherlands were part of previous publications,[4, 6, 7] however there is no overlapping analysis.

The data from Germany were collected in different cities. In Grosshansdorf, the data were collected as part of an ongoing prospective observational study aiming to examine the role of extra-pulmonary effects of COPD.[8, 9, 10] The study was approved by the local ethics committee of Schleswig-Holstein (Germany). Participants included were recruited between 2008 and 2009 at the Pulmonary Research Institute at Lung Clinic Grosshansdorf. A multicenter study aiming to evaluate the effect of aclidinium bromide on exercise endurance, hyperinflation, and dyspnoea at rest and during exercise in patients with moderate to severe COPD (NCT01471171) also contributed to the German database. Ethical approval was granted by the Independent Ethics Committees at each site, which were previously detailed by Beeh et al.[1] In this study, participants were recruited in Wiesbaden, Hamburg, Berlin, Lübeck, Hannover, Grosshansdorf, and Frankfurt, and assessed between November 2011 and June 2012. Some of the participants and data from Germany were part of previous publications,[1, 3, 11, 8, 12] however there is no overlapping analysis.

The data from Switzerland were collected in two cities, Basel and Zurich. In Basel, the data were collected between July 2011 and January 2012 at the University Hospital Basel, as part of a cross-sectional study aiming to examine the independent association of objectively measured daily physical activity and functional capacity with health-related quality of life in patients with COPD. Ethical approval was granted by the Ethics Committee of Basel (EKBB, 163/11). In Zurich, the data were collected between January 2010 and August 2011 in patients with COPD referred to the Pulmonary Division, University Hospital of Zurich, as part of a study which aimed to investigate if simple tests commonly used in clinical practice could accurately predict daily physical activity in COPD.[13] The study was approved by the Research Ethics Committee of the University Hospital of Zurich, Switzerland (EK-1734). Some of the participants and data from Switzerland were part of a previous report,[13, 14, 15] however there is no overlapping analysis.

The data from Italy were collected in Pisa, in the Cardio-Thoracic and Vascular Department, University of Pisa, as part of the baseline evaluation of patients with COPD included in an outpatient pulmonary rehabilitation program. The Italian data were de-identified to protect patient information confidentiality.

The data from Spain were collected in three regions (Catalonia, Euskadi and Balearic Islands) as part of the Phenotype and Course of COPD (PAC-COPD) study, which was a prospective longitudinal study aiming to identify clinically and epidemiologically meaningful COPD

subtypes and to validate them by assessing their relationship with clinically relevant outcomes (hospitalization and death) during a 4 year follow-up.[16, 17] Participants were recruited between January 2004 and March 2006 in 9 tertiary hospitals. The study protocol was approved by the Ethics Committees of all the participating hospitals, which were previously listed by Garcia-Aymerich et al.[17] A multicenter study aiming to evaluate the effect of aclidinium bromide on exercise endurance, hyperinflation, and dyspnoea at rest and during exercise in patients with moderate to severe COPD (NCT01471171; this study was approved by the Independent Ethics Committees at each site, which were previously detailed by Beeh et al.[1]) also contributed to the Spanish database. In this study, participants were recruited in Alicante, Madrid, and Barcelona, and assessed between November 2011 and June 2012. Some of the participants and data from Spain were part of previous publications,[3, 18, 16, 19] however there is no overlapping analysis.

The data from the United States of America (USA) were collected in Rochester, MN, as part of a cross-sectional study aiming to characterize the relationship between the 4 meter gait speed (4MGS) test and various psycho-physiologic measures in a cohort of patients with chronic lung disease. The study was approved by the the Institutional Review Board of the Mayo Clinic College of Medicine (IRB# 11-008157). Participants were recruited between July 2012 and July 2013 at Mayo Clinic. Some of the participants and data from the USA were part of previous publications,[20, 21, 22] however there is no overlapping analysis.

The data from Brazil were collected in Londrina, Paraná, as part of an ongoing prospective randomized trial aiming to compare the long term effects of two exercise/training regimens on physical activity in daily life and other relevant outcome measures in patients with COPD. The study was approved by the ethics committee of the State University of Londrina (UEL), Londrina, Brazil. Participants were recruited during the baseline assessment for the outpatient pulmonary rehabilitation program which takes place at the University Hospital of Londrina. Some of the participants and data from Brazil were part of a previous report,[23] however there is no overlapping analysis.

The data from Australia were collected in two cities, Perth and Sydney. In both cities the data were collected as part of an ongoing randomized controlled trial evaluating a walking training program versus usual care on quality of life and exercise capacity in patients with COPD (ACTRN12609000472279). Ethical approval was granted by the ethics committees of Sydney South West Area Health Service (lead Human Research Ethics Committee), The University of Sydney, Curtin University, Sir Charles Gairdner Hospital and Bentley Hospital, Australia. Participants were recruited from referrals to hospital outpatient pulmonary rehabilitation programs. Some of the participants and data from Australia were part of a previous report,[24] however there is no overlapping analysis.

Algorithm

Studies on sleep in COPD have relied on subjective information gathered from self-administered questionnaires [25] or on objective measures from lab-based polysomnography.[26] While sleep diaries lack of objectivity, in-laboratory sleep-tests have remained limited mainly because of the high costs, limitations of the unnatural environment, obtrusiveness, and the single–night measurement.[27]
Actigraphy is a useful tool that is becoming popular to objectively assess the sleep–wake cycle. It provides non-invasive objective measures of the continuity and hence quality of sleep and it has the advantage of allowing recording continuously for 24-hours a day for extended periods.[28] Actigraphy correlates well with traditional polysomnography in differentiating sleep from wake and provides a complimentary way of assessing sleep, particularly when sleep architecture and extensive physiological monitoring are not necessary.[29]

As in our case, actigraphic sleep assessment could provide a massive amount of data (big data) that may be very useful to produce new insights about sleep patterns and behaviour of subjects under study. On the other hand, such big quantity of measurements will likely be unannotated and noisy. Therefore, without an automatic procedure, it would be difficult to process such a big amount of unannotated data and investigate objective sleep quality measures.

In order to calculate sleep measures, actigraphy data need to be segmented and the time in/out of bed needs to be derived. Time in bed is usually defined as the time from *lights off* to *lights on* (i.e. time interval comprised between the moment at which participants were lying down with the intention to fall asleep and the moment at which participants stand up from the bed after the night sleep).[30] Lying down time, in turn, is defined as the time spent lying down while the participants are awake.

In practice, the following definitions of time in bed have been used:

1. Fixed time interval (from 21:00pm to 06:00am);[31]
2. Time interval extracted from subject's daily sleep log;[32, 33]
3. Time interval comprised between the *lights off* and *lights on* markers derived from polysomnography data.[30, 34, 35]

The first two methods are in general not reliable since sleeping behaviour varies from subject to subject and sleeping logs are inaccurate. The last one is not applicable when using only actigraphy data.

Other approaches should be used to guide the analysis of actigraphy data recordings and to cluster together, in a consistent way, sleeping epochs in order to compute sleep assessment measures as total night sleeping time or sleep fragmentations (number of sleeping epochs).

Sleep measures are essentially coupled to a biphasic model of human behaviour that assumes, within 24 hours, a sleep and a wake period. It is known that such a model does not always hold. Therefore, next to finding the *light on* and *light off* markers, it is of interest to have an indicator whether such a model is applicable at all.

The nighttime and daytime sleep measures used in this analysis together with their abbreviations are recalled for convenience in Table 1.

Table 1 Nocturnal and daytime sleep measures derived from actigraphy data.

Variable name	Abbreviation	Model abbreviation	Description
Total Night Sleeping Time	TNST	S_1	Total night sleeping time is calculated as the sum of all minutes scored as sleep during time in bed.
Number of Nocturnal Sleeping Bouts	NNSB	S_2	Number of nocturnal sleeping bouts during time in bed. A higher NNSB indicates more fragmented sleep.
Duration of Nocturnal Sleeping Bouts	DNSB	S_3	Average duration of nocturnal sleeping bouts during time in bed. A higher DNSB indicates longer sleeping bouts, and, in turn less nocturnal sleeping disturbances.
Sleep efficiency	Seff	S_4	Sleep efficiency defined as the ratio of TNST and time in bed.
Wake After Sleep Onset.	WASO	S_5	Time awake during time in bed after the first nocturnal sleep onset.
Total day sleeping time	TDST	S_6	Total day sleeping time defined as the total time spent asleep during the out of bed period.
Number of daytime sleeping bouts	NDSB	S_7	Number of daytime sleeping bouts indicates how many naps a subject takes during the day.
Average duration of daytime sleeping bouts	DDSB	S_8	Average duration of daytime sleeping bouts during the day. A higher DDSB indicates longer naps.

Multi-sensor activity monitors, such as the SenseWear Armband (SWA), allow the assessment of sleep and wakefulness period. In particular, in the SWA, actigraphy data is classified in a binary form into wake = 0 and sleep = 1 for each specific minute. The same minutes are also classified into lying down = 0 or not lying down = 1 according to the activity monitor's proprietary algorithm.

The method to find *light on* and *light off* markers relies on an algorithm able to segment several days of continuous actigraphy data in time in bed and time out of bed. The algorithm is based on the minutes assessed as lying down moments by the SenseWear armband. A probability distribution and a measure of uncertainty are derived and used to initialize a biphasic model (time in bed-time out of bed). The model is further refined according to the closest lying epochs assessed by the multi-sensor activity monitor.

In a nutshell the algorithm clusters together sleeping epochs related to the time in bed of the subject and it quickly classifies the sleeping pattern of a subject during the assessed days as regular or irregular (i.e. not fitting to the concept of a biphasic model).

In essence the approach is a three-step procedure. In the first step, an average sleep-awake probability distribution or model is created together with an uncertainty distribution or model. The second step is to adapt this average model to each specific day (24 hours sequence) in order to determine the specific time in bed period for that particular sequence. As a third step, the sleep measures depending on the bed/awake segmentation are calculated per day. The first step also directly yields means to generate indicators for the properness of a biphasic model.

Supplementary Materials Fig. 1 shows the output of the SenseWear activity monitor including metabolic equivalent of task (MET), sleep and lying down periods. As can be seen both the lying

down (light green) and the sleep (magenta) periods yield fragmented episodes within each 24 hours preventing a straightforward association with desired sleep /awake indicator.

Based on the activity monitor's recording of several continuous days the probability of the subject of being in the lying down status for each minute of a 24h day is calculated. Standing epochs during night time (21:00pm-06:00am) that are shorter than 1 hour are removed and considered as sleeping.[30] When calculating quality sleeping measures this assumption will not be taken into account and the real measured epochs of standing and sleeping considered.

For a Bernoulli distribution as the light green line in the Supplementary Materials Fig.1 (i.e., 0 = the subject is not lying down, 1 = the subject is lying down) the probability distribution is equal to the sample mean (blue line in Supplementary Materials Fig. 2).
The standard deviation of the sample mean is considered as a measurement of uncertainty (red dashed line in Supplementary Materials Fig. 2).

From Supplementary Materials Fig. 2 it can be seen that the probability for the subject to be lying in the bed is maximal around 01:00 am and its maximal uncertainty is around 19:50 pm and 03:00 am (red circles in Supplementary Materials Fig. 2).

A model can be fitted to the data to obtain a smooth curve. In our case, a Gaussian distribution (green line in Supplementary Materials Fig. 2) is fitted to the empirical probability distribution (blue line in Supplementary Materials Fig. 2).

The peaks of the uncertainty distribution closest to the 0.5 crossing point of the fitted Gaussian are used to create a biphasic model that indicates when the subject is likely to be sleeping and when he is likely to be awake (blue line in Supplementary Materials Fig. 3).
Alternatively the two extrema of the first derivative of the fitted Gaussian distribution could be used to create the biphasic model (magenta line in Supplementary Materials Fig. 2).

The biphasic model is then adapted to the lying down and standing epochs calculated by the activity monitor. In particular, firstly the rising edges of the biphasic model are matched with the closest falling edges of the standing epochs as in Supplementary Materials Fig. 4. Thus, the *light-off* moments are established.

In the same way the falling edges of the model are matched with the closest rising edges of the standing epochs as in Supplementary Materials Fig. 5.

The model is then adapted as shown in Supplementary Materials Fig. 6.

The adapted model indicates when the subject starts lying down (*light off*) and when the subject stands up (*light on*). It is possible now to calculate indices as sleeping efficiency from data provided by the multi-sensor activity monitor.

The model could be used also to quickly recognise whether a subject didn't follow a "normal/regular" sleeping pattern. There are several criteria which are inherently computed or derivable within the procedure to give indicators that a biphasic model is not proper for the data.

Two simple criteria for a binary setting are the following: (1) if the maximum value of the empirical probability distribution is smaller than a certain threshold (i.e. 0.7 works well for our purpose) it can be assumed that the subject had a very irregular sleep pattern within the observed analysis period; (2) if the distance between the two uncertainty peaks selected is less than two hours the subject had (on an average) too few hours of time in a lying position during the night. The output of the algorithm was qualitatively assessed by visual inspection in 132 cases randomly selected. From the visual inspection we concluded that were no major issues in the functioning of the algorithm.

Excluded patients

Characteristics of the patients excluded by the algorithm are provided in supplementary Table 1. Comparisons of demographic and clinical characteristics between included and excluded patients were evaluated by Mann-Whitney U-test for continuous variables and Chi-square test for categorical variables.

Patients excluded from the study because of irregular sleeping patterns and too short time spent in bed during the night (column II, supplementary Table 1) had lower FEV_1 compared to included patients. Accordingly, the excluded sample had a higher percentage of patients in GOLD 3 and GOLD 4 and a lower percentage in GOLD 1 and GOLD 2. This is line with the findings of this study showing that patients with impaired sleep had worse COPD severity.

The sample excluded due to missing data (column III, supplementary Table 1) had a higher percentage of males, lower percentage of smokers, older age, higher BMI, higher percentage of patients in GOLD 1and GOLD 3, and a lower percentage of patients in GOLD 2 and GOLD 4 compared to the sample of included patients.

Supplementary Materials Table 1 Demographic and clinical characteristics of included patients and excluded patients.

	I	II		III	
	Included COPD (n=932)	Excluded COPD due to not enough time in bed and irregular sleeping patterns (n=136)	p	Excluded COPD due to missing data (n=316)	P
Male / female (%)	66 / 34	69 / 31	0.30	71 / 29	<0.05
Smokers / non smokers (%)	33 / 67	35 / 65	0.65	23 / 77	<0.001
Age (yr)	66.4±8.3	66.0±9.3	0.75	67.5±8.4	<0.05
BMI (kg/m^2)	26.3±5.4	26.6±5.2	0.33	28.0±5.4	<0.001
FEV_1 % predicted	50.8±20.5	46.6±19.4	<0.05	54.0±23.8	0.18
GOLD 1-2-3-4 (%)	10 - 40 - 32 - 18	3 - 34 - 42 - 21	<0.05	15 - 33 - 39 - 13	<0.01
MMRC 0-1-2-3-4 (%)	14 - 27 – 22 - 18 - 6	11 - 25 - 18 - 24 - 9	0.22	10 – 29 - 27 - 21 - 8	0.14

Data in the table are expressed as absolute numbers, percentages, or means ± standard deviation. BMI: Body Mass Index, FEV_1: forced expiratory volume in 1 second, GOLD: Global Initiative for Chronic Obstructive Lung Disease stage, MMRC: modified Medical Research Councils scale. Not for all the patients we had MMRC data, in particular: I=MMRC data for 805 patients, II=MMRC data for 119 patients, III=MMRC data for 229 patients. P-values are calculated using Mann-Whitney U-test for continuous variables and Chi-square test for categorical variables, respectively.

Statistical analysis

To study which factors influence measures of sleep quality in people with COPD, we constructed a linear mixed-effect model (LMM) for each sleep parameter (S_i), with GOLD and MMRC as ordinal explanatory variables; smoking status, country of origin, gender and parts of the week (i.e. weekday vs. weekend day) as categorical explanatory variables; age and BMI as continuous explanatory variables.

To account for repeated measurements, we use random effects on two levels. On the highest level, we include a random intercept per patient. The second level, within patients, has a random intercept for each parts of the week (weekdays vs. weekends). The residuals then account for the differences between days within the same parts of the week. The model had the form:

$$S_i \sim GOLD + MMRC + Smoking\ status + Country + Gender + Part\ of\ the\ week + Age + BMI + (1 \mid patient\ ID) + (1 \mid Day\ group{:}\ patient\ ID) + \varepsilon. \quad (1.1)$$

where ε is a random error and the notations (1| patient ID) and (1| Parts of the week: patient ID) indicate that the model accounts for by-subject and by-parts of the week variability.[38]

Next, sleep quality parameters were further categorized into quartiles to examine potential relationships with daytime measurements. Each of the physical activity measurements (PA_i) was considered the response variable of a separate LMM. Sleep parameter quartiles (Q) and MMRC were ordinal explanatory variables; smoking status, country of origin, gender and parts of the week were categorical explanatory variables; FEV_1, age and BMI were continuous explanatory variables of the model. Repeated measurements and parts of the week were included as random effects. The model had the form:

$$PA_i \sim Q + MMRC + Smoking\ status + Country + Gender + Part\ of\ the\ week + FEV1 + Age + BMI + (1|patient\ ID) + (1|Day\ group{:}\ patient\ ID) + \varepsilon. \quad (1.2)$$

This kind of analysis was chosen to focus on differences between effects, while accounting simultaneously for different sources of variance (i.e. controlling for several confounding factors and distinguishing between weekdays and weekend days/nights) and repeated measurements.

Moreover, applying linear mixed effects models on the time-specific data, we assessed the association of sleep quality with physical activity levels during the following day taking into account repeated measurements of sleep and physical activity for each participant without disregarding between-subject variations.

To construct the models we used the *lmer* function of the package lme4 in R.=[36]=[36]

Analyses were carried out using MATLAB R2015a (The MathWorks, Inc., Natick, Massachusetts, United States) and R (R Core Team, 2012) software.

Relationship between daytime physical activity levels and objective sleep quality

Supplementary Materials Table 2 shows the quartile ranges for each sleep quality indicator together with the corresponding least-square average of the daytime actigraphy measures. Spearman's rank correlation is used to calculate the p-trends between the quartiles for each daytime actigraphy measure.

Supplementary Materials Table 2 Quartiles of night sleep variables and corresponding LS-means of the daytime actigraphy measures.

		Total night sleeping time (TNST)				
Quartiles (min)		$Q_1 < 347$	$347 \leq Q_2 < 416$	$416 \leq Q_3 < 480$	$Q_4 \geq 480$	***p-trends***
STEPS	**(#)**	4952	4882	4759	4503	0.08
TDST	**(% awake time)**	2.26	1.76	1.75	1.59	0.08
TIME VL	**(% awake time)**	73.42	73.45	73.22	74.01	0.75
TIME L	**(% awake time)**	15.3	15.61	15.64	15.13	0.91
TIME MV	**(% awake time)**	7.42	7.77	7.97	7.79	0.33
		Number of nocturnal sleeping bouts (NNSB)				
Quartiles	***(#)***	$Q_1 < 2$	$2 \leq Q_2 < 3$	$3 \leq Q_3 < 4$	$Q_4 \geq 4$	***p-trends***
STEPS	**(#)**	5136	4874	4664	4484	0.08
TDST	**(% awake time)**	1.71	1.91	1.94	1.79	0.75
TIME VL	**(% awake time)**	72.78	73.32	73.60	74.25	0.08
TIME L	**(% awake time)**	16.00	15.45	15.35	15.08	0.08
TIME MV	**(% awake time)**	8.18	7.83	7.60	7.39	0.08
		Average duration of nocturnal sleeping bouts (DNSB)				
Quartiles	***(min)***	$Q_1 < 86$	$86 \leq Q_2 < 136$	$136 \leq Q_3 < 225$	$Q_4 \geq 225$	***p-trends***
STEPS	**(#)**	4559	4759	4861	4987	0.08
TDST	**(% awake time)**	1.97	1.82	1.89	1.70	0.33
TIME VL	**(% awake time)**	74.05	73.40	73.55	72.98	0.33
TIME L	**(% awake time)**	15.06	15.56	15.32	15.81	0.33
TIME MV	**(% awake time)**	7.39	7.76	7.74	8.12	0.33
		Sleep efficiency				
Quartiles	***(%)***	$Q_1 < 71$	$71 \leq Q_2 < 82$	$82 \leq Q_3 < 91$	$Q_4 \geq 91$	***p-trends***
STEPS	**(#)**	4524	4758	4798	5111	0.08
TDST	**(% awake time)**	2.01	1.81	1.82	1.73	0.33
TIME VL	**(% awake time)**	73.32	73.50	73.43	72.62	0.08
TIME L	**(% awake time)**	14.89	15.41	15.54	15.98	0.08
TIME MV	**(% awake time)**	7.24	7.76	7.76	8.30	0.08
		Time awake during time in bed after the first sleeping onset (WASO)				
Quartiles	***(min)***	$Q_1 < 57$	$57 \leq Q_2 < 104$	$106 \leq Q_3 < 165$	$Q_4 \geq 165$	***p-trends***
STEPS	**(#)**	5076	4967	4687	4355	0.08
TDST	**(% awake time)**	1.75	1.88	1.87	1.89	0.33
TIME VL	**(% awake time)**	73.02	73.11	73.59	74.23	0.08
TIME L	**(% awake time)**	15.84	15.56	15.35	15.01	0.08
TIME MV	**(% awake time)**	8.03	7.98	7.71	7.29	0.08

Daytime actigraphy measures: STEP = Steps performed; TDST = Total Day Sleeping Time, TIME VL = Time spent in Very Light activity, TIME L = Time spent in Light activity, TIME VM = Time spent in Moderate-to-Vigorous activity. Q_i = i-th quartile. Data in the table are expressed as least-square means or percentage of wake time. p-trends between quartiles evaluated by Spearman's correlation.

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Figure legends

Supplementary Materials Figure 1: Several days of data recordings. In yellow: on=standing, in light green: on=lying down, in magenta: on=sleeping, in dark green and red metabolic equivalent of tasks (METs) estimates for weekdays and weekend days, respectively. For clarity, the lying down and standing are scaled to the intervals [0, 1.5] and [0, 2], respectively.

Supplementary Materials Figure 2: Lying down probability distribution over hours of the day. In blue: probability distribution of minutes classified as lying down across 24 hours. The probability estimation is calculated empirically taking into consideration all the minutes of the assessed days. In dashed red: standard deviation of sample mean taken as uncertainty measurement. In light green: Gaussian distribution fitted to the empirical distribution (blue). Red circles: uncertainty peaks that are closer to the 0.5 crossing point of the fitted Gaussian. In dashed magenta: first derivative of fitted Gaussian distribution. The derivative was rescaled to assume values between 0 and 1 for graphical inspection.

Supplementary Materials Figure 3: Biphasic model of time in bed – time out of bed (in blue) derived from the analysis of the assessed days.

Supplementary Materials Figure 4: Finding the start of the time in bed epochs (light off). The rising edges of the biphasic model (green circles) are matched with the closest falling edges of the standing epochs (red circles).

Supplementary Materials Figure 5: Finding the end of the time in bed epochs (lights on). The falling edges of the model (green circles) are matched with the closest rising edges of the standing epochs (red circles).

Supplementary Materials Figure 6: Segmentation of recorded days in time in bed (on segment of the blue line) and time out of bed (off segment of the blue line).

FIG 1

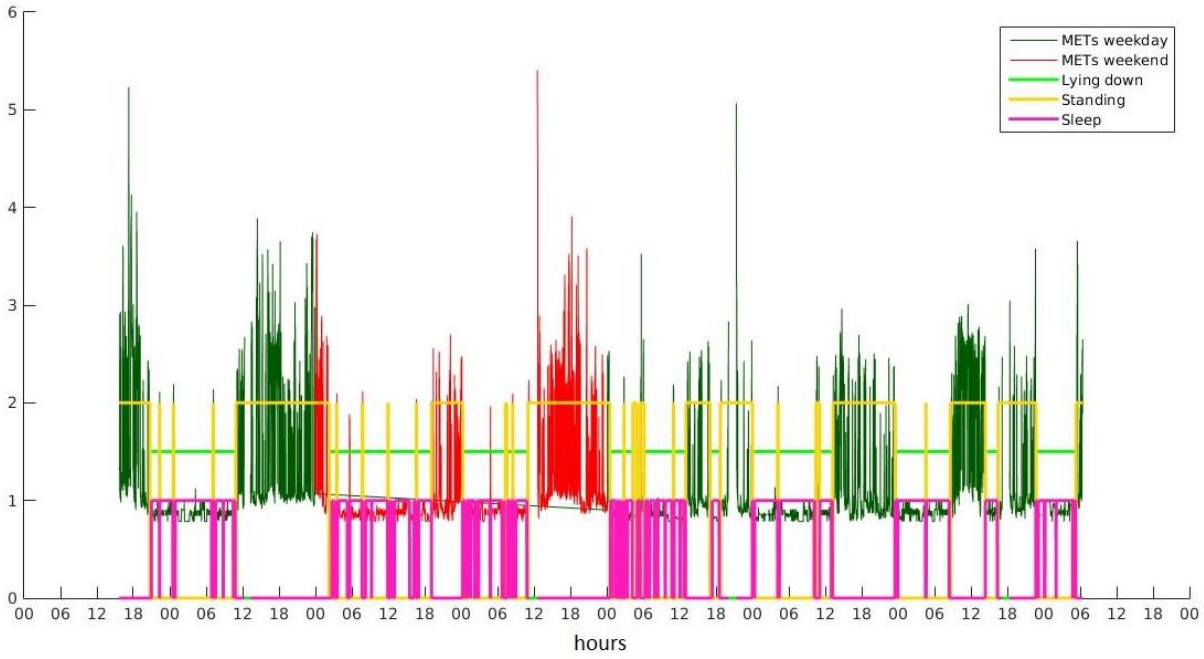

METs weekday
METs weekend
Lying down
Standing
Sleep
hours

FIG 2

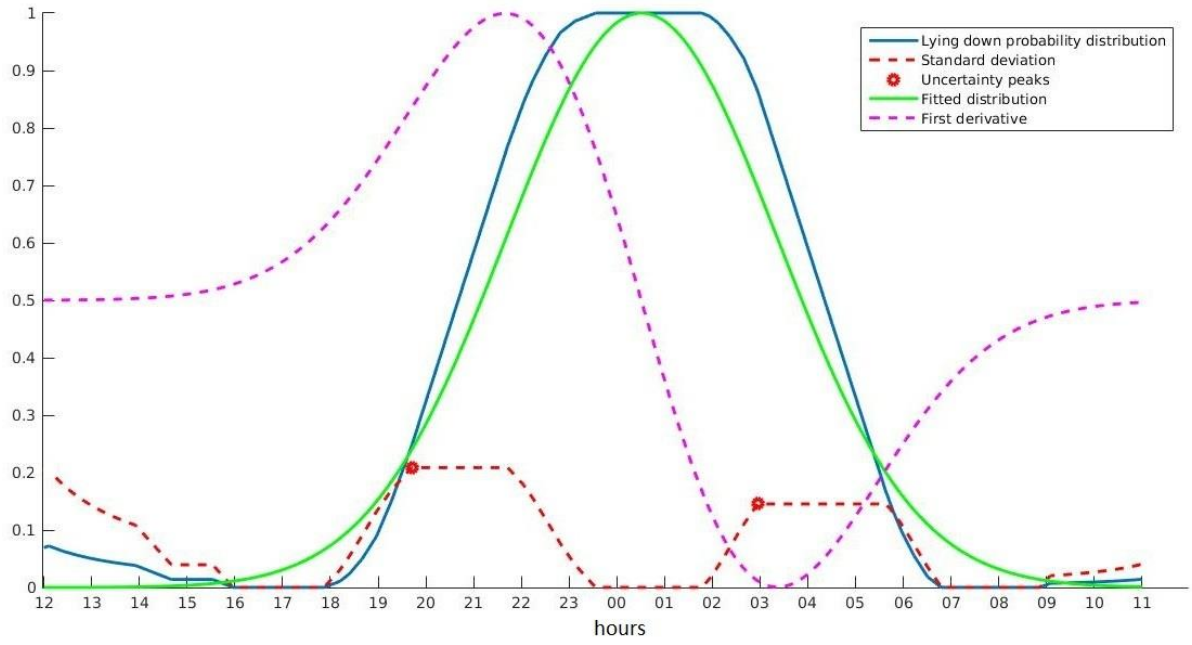

Lying down probability distribution
Standard deviation
Uncertainty peaks
Fitted distribution
First derivative
hours

FIG 3

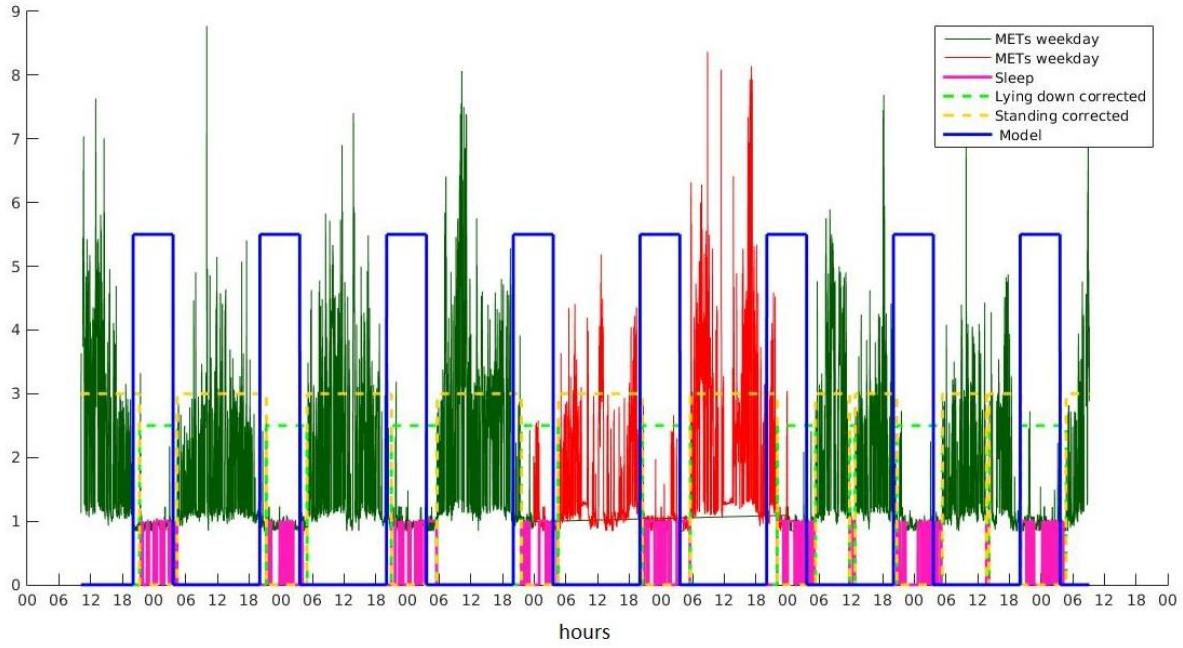

METs weekday
METs weekday
Sleep
Lying down corrected
Standing corrected
Model
hours

FIG 4

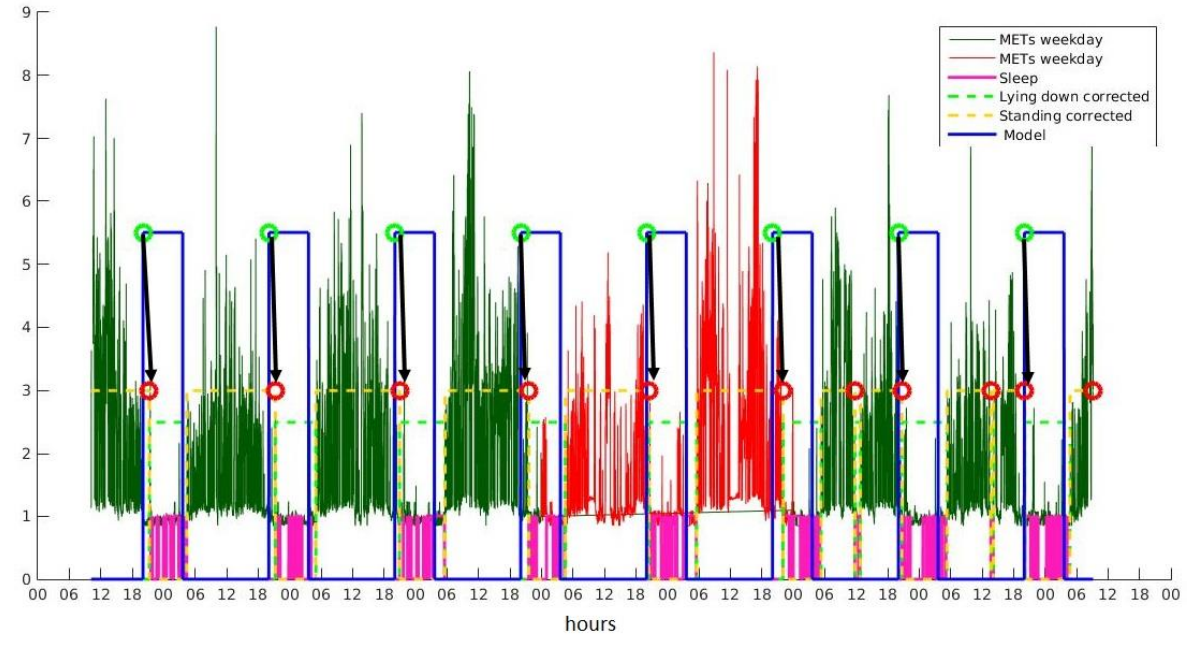

METs weekday
METs weekday
Sleep
Lying down corrected
Standing corrected
Model
hours

FIG 5

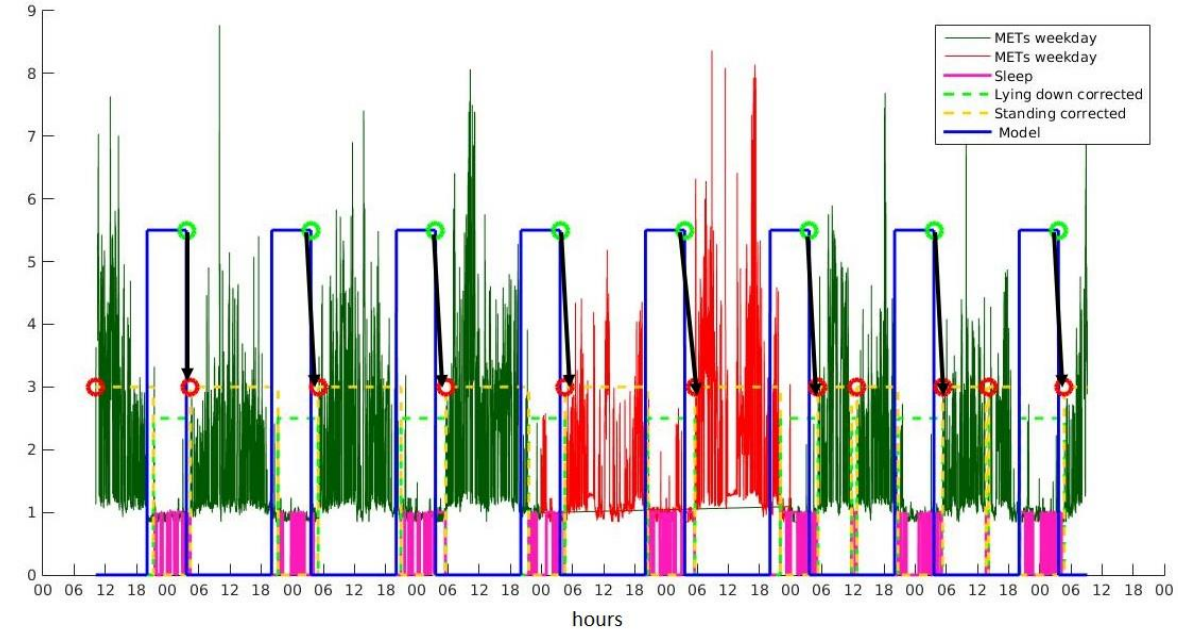
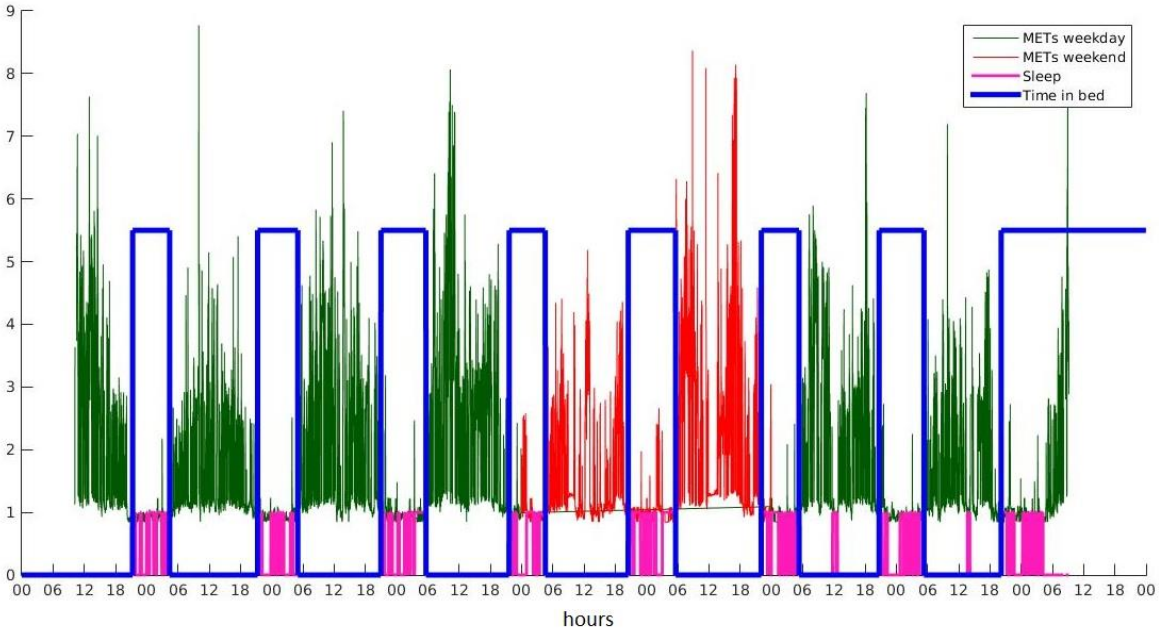

METs weekday
METs weekday
Sleep
Lying down corrected
Standing corrected
Model
hours

FIG 6


METs weekday
METs weekend
Sleep
Time in bed
hours