# Remote Actigraphy Is Seasonally Variable with Implications for Clinical Monitoring

Alexander M K Rothman,[1,2] Jennifer Middleton,[1,2] Hamza Zafar,[1,2] Eckart M.D.D. De Bie,[3,4] Joseph Newman, [3,4] Frances Varian,[1,2] Felicity Hitchcock,[1,2] Jacob Taylor,[1] Cameron Ashraf, [1] Junaid Patel,[1] A. A. Roger Thompson,[1,2] Mark Toshner [3,4]

On behalf of ASPIRE consortium and the National Cohort Study of Idiopathic and Heritable PAH

**Affiliation:**
1. Division of Clinical Medicine, University of Sheffield, UK
2. Sheffield Pulmonary Vascular Disease Unit, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, UK
3. Victor Phillip Dahdaleh Heart and Lung Research Institute, University of Cambridge, UK
4. Royal Papworth Hospital, Papworth Rd, Trumpington, Cambridge, UK

**Corresponding author:** Prof Alexander M K Rothman
**Address:** Division of Clinical Medicine, University of Sheffield, Beech Hill Road, S102RX

**Email:** a.rothman@sheffield.ac.uk

**Words:** 937
**Tables:** 1
**Figures:** 1

Some of the results of these studies have been previously reported in the form of a preprint (medRxiv, 27 May 2025, https://doi.org/10.1101/2025.05.22.25328110).

To the Editor:

## Introduction

Remote measurement of physical activity and cardiopulmonary haemodynamics is increasingly being used in clinical practice and trials.(1) Structured exercise testing is an established clinical tool and regulatory endpoint,(3) however, passively generated activity data, potentially more reflective of real-world patient behaviour, remains investigational. Seasonal variation in passively collected physical activity has been observed in the general population and patients with chronic obstructive pulmonary disease.(4) Despite this, actigraphy has been used as a primary endpoint in regulatory trials of therapies for interstitial lung disease-associated pulmonary hypertension.(2) The seasonal variation of structured exercise testing and cardiopulmonary haemodynamics remains unexplored.

We sought to evaluate the seasonal stability of hospital-based structured exercise testing, passively collected physical activity measures and remote-monitored haemodynamics in patients with pulmonary arterial hypertension (PAH).

Some of the results have been reported in abstract form.(5)

## Methods

Patients with a confirmed diagnosis of pulmonary arterial hypertension were enrolled in the UK National Cohort Study of Idiopathic and Heritable Pulmonary Arterial Hypertension (13/EE/0203) and implanted with an insertable cardiac monitor (LinQ, Medtronic). Physical activity was measured as minutes of activities of daily living from a single-axis accelerometer within the insertable cardiac monitor between November 2018 and October 2023.(6) Activity was defined as minutes meeting a threshold of magnitude and number of deflections.(7) In sinus rhythm, heart rate variability (HRV) was calculated as the mean standard deviation of 5-minute intervals over 24 hours (Standard Deviation of Average NN intervals method).(8) A subset of patients were co-enrolled in Feasibility of Novel Clinical Trial Infrastructure, Design and Technology for Early Phase Studies in Patients with Pulmonary Hypertension (FIT-PH, NCT04078243, REC 19/YH/0354) and a pulmonary artery pressure monitor implanted (CardioMEMS, Abbott).(6)

Structured exercise testing: incremental shuttle walk tests from 5,820 patients in the ASPIRE registry (22/EE/0011) and 1001 patients in the UK National Cohort Study of Idiopathic Pulmonary Arterial Hypertension (13/EE/0203) were analysed between February 2001 and May 2019 and May 2014 and May 2023, respectively. All patients underwent systematic evaluation, including blood testing, structured exercise testing, lung function testing, multimodality imaging, and right heart catheterisation, in accordance with national standards of care.(9) No patients were lost to follow-up.

Clinical study emulation: patients with an insertable cardiac monitor were randomised into two placebo groups with January (winter) and June (summer) start dates. Activities of daily living, measured over a 14-day period, were analysed at baseline, 6-months and 12-months.

Statistics: statistical significance was determined using one-way ANOVA or the Chi-square test. Analysis was undertaken in Prism (10.0.3 MacOS).

## Results

Patient demographics are summarised in table 1. Mean daily physical activity varied throughout the year, ranging from 129.5 min/day to 155.0 min/day (Figure 1A). Physical activity was altered by season with most limitation in winter (136 ± 2.5 min/day) increased in autumn (141 ± 4.9 min/day) and spring (149 ± 2.6 min/day), and highest in summer (151 ± 2.5 min/day) (Figure 1B). No seasonal variation was observed in incremental shuttle walk test or 6-minute walk test (Figure 1C and D). Similarly, no seasonal variation was observed in heart rate, heart rate variability, pulmonary artery pressure or cardiac output (Figure 1A).

To simulate the effect of seasonal variation on the evaluation of physical activity in a clinical study, patients with an insertable cardiac monitor were randomised into two placebo groups with winter and summer start dates. Baseline, 6-month, and 12-month physical activity levels were 133.8 ± 2.5, 147.7 ± 0.5, and 134.9 ± 2.2 min/day int the winter group and 151.2 ± 0.9, 130.2 ± 2.7, and 153.3 ± 1.1 min/day in the summer group (Figure 1E).

## Discussion

The integration of high-dimensional physical activity and cardiopulmonary haemodynamic data from home-based monitoring has the potential to transform clinical evaluation and research. This study leveraged minimally invasive technology to assess the stability of physical activity, haemodynamic parameters, and structured exercise test results across the calendar year. While structured exercise testing and cardiopulmonary haemodynamics remained stable, passively collected physical activity showed marked seasonal variation. The absence of seasonal changes in established measures of disease severity suggests that observed activity fluctuations are attributable to external environmental factors rather than a seasonal effect on disease status.

Remote physical activity monitoring has been increasingly adopted in clinical trials due to the ease of measurement and its importance to patients(10) and regulators.
However, clinical study emulation revealed that seasonal variations in remote activity data could introduce non-differential bias. The winter group showed a +13.9 min/day increase at 6-months, while the summer group a -21.0 min/day decline, creating a 33.9 min/day difference driven by start date alone. This effect exceeds the 17.8 min/day increase observed with the addition of selexipag in patients with WHO functional class II/III PAH (vs. placebo).(11) As such, seasonal variation in physical activity introduces nondifferential error, which may bias towards the null hypothesis.

Given the global nature of clinical trial recruitment, understanding seasonal patterns is critical for selecting appropriate endpoints and mitigating biases in study design. Seasonal variation in physical activity may also complicate clinical decision-making.

Home-based monitoring offers the potential to reduce noise, provide real-world activity insights, and enhance patient engagement in disease management. However, challenges remain in quantifying activity accurately. Alternative methods, such as peak minute steps, may reduce seasonal variability compared to accelerometer-derived metrics.(12) This study highlights the need to understand and accommodate seasonal variability in passively collected physical activity data, in trials and clinical practice.

## Conclusions

Passively collected remote physical activity measures vary with season, however, cardiopulmonary haemodynamics and structured exercise testing remain stable. Clinical trials must account for this confounding effect in design and analysis. Seasonal variations in actigraphy underscore the importance of addressing these factors as remote activity monitoring becomes more prevalent in clinical care.

Funding: MRC Experimental Medicine Award (MR/W026279/1), EPSRC Project Grant (EP/Z531297/1), BHF Project Award (SP/12/12/29836). AR was supported by a Wellcome Trust Clinical Research Career Development Fellowship (206632/Z/17/Z), The research was supported by the National Institute for Health and Care Research (NIHR) Sheffield and Cambridge cardiorespiratory Biomedical Research Centres.

Disclosures: AMKR has received support from: MRC Experimental Medicine Award (MR/W026279/1), British Heart Foundation (FS/CRTF/23/24465, HI/B3/24/370100), EPSRC Project Grant (EP/Z536027/1, EP/Z531297/1), Innovate UK (TS/Y02477X/1), Novartis, Abbott, Medtronic, MSD, Gradient, Relief Cardiovascular, Jupiter. MT has received support from: NIHR Cambridge BRC, MRC Development Funding Pathway Scheme Award (MR/T025646/1), Jansen, Apollo, Merk, GSK, ComCov, FluCov.

References


1. Rothman AMK, Villar S, Middleton J, Roussakis AA, Varian F, Zafar H, *et al.* Positioning Imatinib for Pulmonary Arterial Hypertension: A Dose Finding Phase 2 Study. *Am J Respir Crit Care Med* 2025;doi:10.1164/rccm.202410-1929OC.
2. Nathan SD, Flaherty KevinR, Glassberg MarilynK, Raghu G, Swigris J, Alvarez R, *et al.* A Randomized, Double-Blind, Placebo-Controlled Study of Pulsed, Inhaled Nitric Oxide in Subjects at Risk of Pulmonary Hypertension Associated With Pulmonary Fibrosis. *Chest* 2020;158:637–645.
3. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Carlsen J, *et al.* 2022 ESC / ERS Guidelines for the diagnosis and treatment of pulmonary hypertension Developed by the task force for the diagnosis and treatment of ( ESC ) and the European Respiratory Society ( ERS ). Endorsed by the International Society for Heart and Lu. *Eur Heart J* 2022;1–114.
4. Garriga A, Sempere-Rubio N, Molina-Prados MJ, Faubel R. Impact of seasonality on physical activity: A systematic review. *Int J Environ Res Public Health* 2022;
5. Ablott J, Roman S, Middleton J, Zafar H, Reddy A, De Bie E, *et al.* 158 Seasonal variation in remote actigraphy in patients with pulmonary arterial hypertension. *Heart* 2024;110:A170.1-A170.
6. Middleton JT, Binmahfooz S, Zafar H, Patel J, Ashraf C, Jake, *et al.* Remote monitored physiological response to therapeutic escalation and clinical worsening in patients with pulmonary arterial hypertension. *medRxiv* 2023;doi:10.1101/2023.04.27.23289153.
7. Bonnesen MP, Frodi DM, Haugan KJ, Kronborg C, Graff C, Højberg S, *et al.* Day-to-day measurement of physical activity and risk of atrial fibrillation. *Eur Heart J* 2021;42:3979.
8. Andersen MØ, Diederichsen SZ, Svendsen JH, Carlsen J. Continuous long-term heart rate variability and risk assessment in pulmonary hypertension. *Open Heart* 2023;10:.
9. Lewis RARA, Johns CSCS, Cogliano M, Capener D, Tubman E, Elliot CA, *et al.* Identification of cardiac magnetic resonance imaging thresholds for risk stratification in pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2020;201:458–466.
10. Newman J, Ghani H, Munagala S, Otter E, Fischer G, Kurzyna M, *et al.* The Pulmonary Hypertension Global Patient Survey: understanding the experiences and perspectives of patients. *ERJ Open Res* 2025;00297–02025.doi:10.1183/23120541.00297-2025.
11. Howard LS, Rosenkranz S, Frantz RP, Hemnes AR, Pfister T, Hsu Schmitz SF, *et al.* Assessing Daily Life Physical Activity by Actigraphy in Pulmonary Arterial Hypertension: Insights From the Randomized Controlled Study With Selexipag (TRACE). *Chest* 2023;163:407–418.
12. Lachant D, Light A, Lachant M, Annis J, Hemnes A, Brittain E, *et al.* Peak steps: Capacity for activity improves after adding approved therapy in pulmonary arterial hypertension. *Pulm Circ* 2023;13:e12285.

Tables

Table 1

| | Insertable Cardiac Monitor (n=87) | Insertable cardiac monitor and pulmonary artery pressure monitor (n=28) |
|---|---|---|
| Age (years, mean, SD) | 53 ± 15 | 48.9 ± 18.1 |
| Female (n, %) | 66 (75.9) | 21 (75) |
| BMI | 30 ± 7 | 28 ± 6 |
| Race (n, %)<br>Caucasian<br>Asian<br>Black | <br>79 (90.8)<br>4 (4.6)<br>4 (4.6) | <br>25 (89)<br>3 (11)<br>- |
| Years since diagnosis | 8.1 ± 5.3 | 7.2 ± 4.6 |
| Heart rate (bpm, mean, SD) | 75 ± 12 | 76 ± 11 |
| Resting $SpO_2$ (%, mean, SD) | 96 ± 3 | 95 ± 4 |
| WHO Functional class, (n, %)<br>I<br>II<br>III<br>IV | <br>5 (5.7)<br>28 (32.2)<br>39 (44.8)<br>15 (17.2) | <br>0<br><br>0<br><br>22 (79)<br><br>6 (21) |
| NT-pro BNP (g/dl, mean, SD) | 1064 ± 2474 | 1410 ± 3537 |
| Right Heart Catheter (mean, SD)<br>Mean RAP (mmHg)<br>Systolic PAP (mmHg)<br>Diastolic PAP (mmHg)<br>PCWP (mmHg)<br>Mean PAP (mmHg)<br>CO (L/min)<br>PVR (Dynes.sec.cm)<br>CI ($L/min/m^2$)<br>$SVO_2$ (%)<br>TPR (Dynes.sec.cm) | <br>9.3 ± 5.2<br>81.8 ± 23.2<br>32.4 ± 11.0<br>10.2 ± 3.1<br>50.4 ± 14.7<br>4.3 ± 1.6<br>11.3 ± 7.1<br>2.3 ± 0.8<br>65.8 ± 14.6<br>11.7 ± 7.8 | <br>9.4 ± 4.8<br>78.6 ± 25<br>33.1 ± 11.2<br>10.4 ± 4.5<br>50.8 ± 11.2<br>4.6 ± 1.6<br>10.2 ± 6.1<br>2.5 ± 0.7<br>63 ± 20.7<br>12.9 ± 7.0 |
| Pulmonary Function test<br>FEV1/ FVC ratio (mean, SD) | <br>0.70 ± 0.10 | <br>75 ± 7 |

6MWD - six-minute walk distance, BMI - body mass index, BP - blood pressure, CI - cardiac index, CO - cardiac output, FEV1 - Forced Expiratory Volume in 1 second, FVC - Functional Vital Capacity, ISWD - incremental shuttle walk distance, NT-pro BNP - N-terminal pro-brain natriuretic peptide, PAP - pulmonary artery pressure, PCWP - pulmonary capillary wedge pressure, PVR - pulmonary vascular resistance, RAP - right atrium pressure, $SVO_2$ - venous oxygen saturations, TPR – total pulmonary resistance, WHO - World Health Organisation

Figures

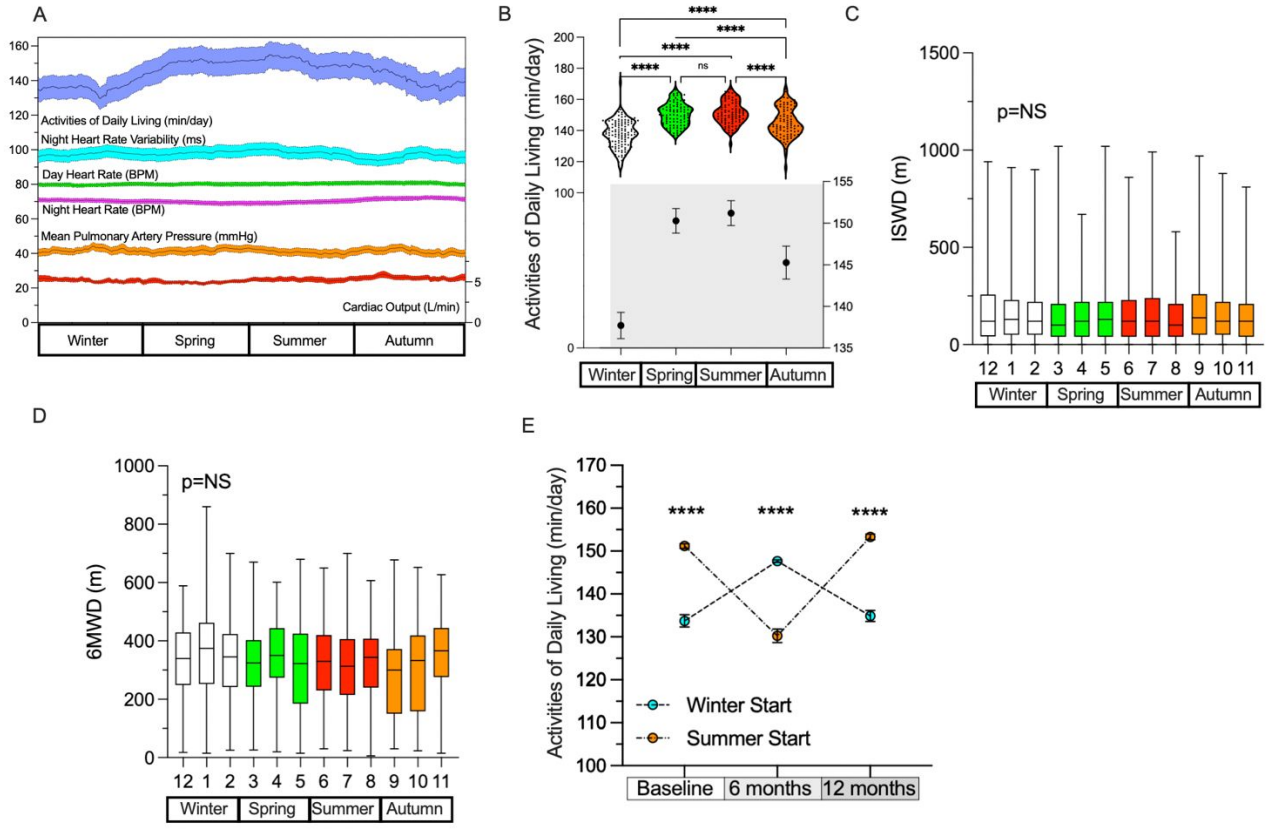



Figure 1: A - Physical activity (blue), heart rate variability (cyan), day heart rate (green), night heart rate (purple), mean pulmonary artery pressure (orange) and cardiac output (red) presented by day of the year (mean +/- SEM). B - Physical activity by calendar season (one-way ANOVA with Holm-Sidak correction, **** $p<0.0001$) with magnified inset (grey, mean +/- 95% CI). C-D - Incremental shuttle walk test (C, n=5820) and six-minute walk distance (D, n=1001) by month of the year (structured exercise test data ordered 12-december to 11-November, one-way ANOVA with Holm-Sidak correction, NS=non-significant). E – Clinical study emulation activities of daily living in two randomised placebo groups with winter and summer start dates (mean +/- 95% CI, one-way ANOVA with Holm-Sidak correction, **** $p<0.0001$).