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# Improvements in Walking During Subacute Stroke Rehabilitation Translate to Physical Activity at the Chronic Stage: A Sub-Analysis From the Phys Stroke Trial

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## HIGHLIGHTS

- Six months post-stroke, participants exhibited low daily step counts, averaging 5,623 steps/day.
- For every meter gained in the 6-minute walk test during the intervention period, participants increased their daily steps by 8.2 at 6 months.
- Engagement in sports activities was minimal.

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# Improvements in Walking During Subacute Stroke Rehabilitation Translate to Physical Activity at the Chronic Stage: A Sub-Analysis From the Phys Stroke Trial

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## ABSTRACT

Stroke frequently results in mobility impairments, contributing to an increased cardiovascular risk. Despite efforts to promote physical activity, stroke survivors fail to meet recommended levels. This secondary analysis of the 'Physical Fitness in Patients with Subacute Stroke' (Phys-Stroke) trial analyzes physical activity at 6 months post-stroke, and examines the effect of gains in walking capacity during the subacute phase on physical activity in the chronic stage. Phys-Stroke compared aerobic exercise vs relaxation in 200 stroke patients. Data from the 6-minute walk test (6MWT) pre and post intervention as well as accelerometry and questionnaire data at 6 months were used. Data was analyzed using mixed linear models and function-on-scalar regression. At 6 months after stroke, participants exhibited low daily step counts (5,623 ± 2,998 steps/day), with most activity occurring in the morning and midday. Per meter gained in the 6MWT during the intervention period, participants increased daily steps by 8.2 (95% confidence interval, 1.6 to 14.8, $p = 0.017$) at 6 months. Questionnaire data showed that engagement in sports activities was minimal, basic activities being the primary activity. Stroke survivors demonstrated suboptimal activity levels at 6 months but increases in walking capacity during the subacute stage did result in meaningful increases chronically.

**Trial Registration**: ClinicalTrials.gov Identifier: NCT01953549

**Keywords:** Stroke; Physical Activity; Aerobic Exercise; Circadian Rhythm; Rehabilitation

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**Conflict of Interest**
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**Author Contributions**
Conceptualization: Rackoll T; Formal analysis: Rackoll T, Hinrichs T, Neumann K; Investigation: Rackoll T, Wolfarth B, Nave AH; Project administration: Rackoll T; Writing - original draft: Rackoll T; Writing - review & editing: Rackoll T, Hinrichs T, Neumann K, Wolfarth B, Nave AH.

## INTRODUCTION

Despite intense and multidisciplinary medical care during and following the acute stage of stroke, mobility remains impaired to some degree in about one third of patients [1,2]. One goal of secondary prevention is to increase the amount of physical activity and to reduce sedentary times which are both independent risk factors for cardiovascular events [3,4]. A recent network meta-analysis confirmed the beneficial effect on cardiovascular outcomes of walking approximately 10,000 steps per day [5-7]. Still, physical activity remains below recommended amount with on average 4,078 steps taken per day [8].

Reasons for reduced mobility in stroke patients are multifactorial, with factors currently explaining it only in part [9,10]. Circadian distribution of walking can give insights into when during the day peaks occur and for example whether those are followed by longer phases of sedentary behavior. Assessment of time distribution but also type of physical activity in the chronic stage might guide identification of barriers to physical activity.

One intervention to improve physical activity is gait based aerobic exercise. Aerobic exercise has been endorsed by many clinical guidelines especially because of its many benefits across the cardiometabolic spectrum but evidence of its effectiveness in increasing physical activity in the chronic phase after stroke is conflicting [11-15]. Further, little evidence exists of its effectiveness on physical activity in the chronic stage if provided sub acutely. In particular, it is not well understood whether gains in mobility during the subacute stage translate into higher amount or frequency of physical activity in the chronic stage [16-18].

In this secondary analysis, we use data from the previously published 'Physical Fitness Training in Patients with Subacute Stroke' (Phys-Stroke) trial to describe physical activity behavior at 6 months following stroke [19]. Further, we aim to analyze the association of gains in walking endurance during the early subacute phase after stroke and steps per day, quality of life and sleep at 6 months post stroke. To summarize, this manuscript combines 3 research questions:

1. What is the amount and time distribution of walking at 6 months post moderate to severe stroke and does an early treadmill-based aerobic exercise intervention modify engagement in walking?
2. What kind of physical activity do patients engage in at 6 months post stroke and is an early aerobic exercise intervention associated with any type of physical activity at the chronic stage?
3. What is the association of gains in walking capacity during the early subacute phase on walking, sleep, quality of life and depression at 6 months?

## MATERIALS AND METHODS

We present secondary analyses of the multicenter, controlled, endpoint-blinded Phys-Stroke trial. Phys-Stroke compared a 4-week aerobic treadmill-based training with a relaxation therapy in participants with moderate to severe strokes in the early subacute phase. Primary efficacy results have been reported along with all procedures and secondary outcomes but will be summarized shortly [19]. The trial protocol was approved by the local ethics committee and registered at ClinicalTrials.gov (NCT01953549) [20]. Participants gave written informed consent. Some analyses presented here were not included in the statistical analysis plan and are therefore exploratory [21].

### Procedures

Participants were eligible if they were within 5 to 45 days post stroke, able to perform aerobic training and were disabled operationalized with a Barthel Index of ≤ 65. The Barthel Index is a measure to assess the ability to perform activities of daily living (range 0–100 with 100 being the best score). Exclusion criteria comprised among others major cardiac or orthopaedic comorbidities and bleeding from aneurysm (**Supplementary Table 1**). After screening, 200 participants were subsequently randomized to receive either aerobic training (n = 105) or relaxation therapy (n = 95). Participants in the training group received on average (± standard deviation) 16 ± 6 sessions with 21 ± 4 minutes active training on a treadmill (Functional Ambulation Category [FAC] ≥ 2) or on a mechanical gait trainer (FAC 0–2). Participants wore a parachute harness and bodyweight was supported if needed. Participants were targeted to train at 55%–65% of maximal heart rate in line with recommendations from the American College of Sports Medicine for aerobic training interventions [22]. In the relaxation group, participants received 17 ± 5 sessions with 24 ± 3 minutes per session in which they conducted progressive muscle relaxation therapy focused on the upper extremities, shoulders and head.

### Outcomes

Participants were assessed at baseline, post intervention, at three and at 6 months following stroke. The primary outcome in the current analysis was steps taken per day using accelerometers at 6 months post stroke. Accelerometry is an objective method to assess physical activity and allow for 24 hours recordings. Steps taken per day are a meaningful and clinically relevant measure with high relevance to the participants. There is currently no published minimal clinically important difference (MCID) for the stroke population. In patients with peripheral artery disease it was found to be 558 steps per day for a small change in health-related quality of life [23]. We attached the accelerometry devices (GT3x, RRID:SCR_008399; ActiGraph Corp, Pensacola, FL, USA) at the ankle of the paretic limb and instructed participants to wear the device for eight days and at all times except during water activities. Subsequently, we asked them to return the devices with prepaid envelops. The devices were programmed to start recording the day following the follow-up visit at 12 am. We aimed for at least 7 days of complete recording time as longer recording times are generally recommended [24,25]. Device settings are detailed in **Supplementary Table 2**. After return of the devices, data were downloaded with ActiLife software (version 6.8.2; ActiGraph Corp). To assess invalid wear time, we used more than 60 minutes of continuous zeros, with allowance of 1–2 minutes with counts between 1 and 100. Rated non-wear times were subsequently removed from the analyses. For step counts, we applied the company-made low frequency extension filter to discriminate steps of slow walkers from random noise, as suggested by Webber and St John [26] but applied the filter only to participants exhibiting a walking speed ≤ 0.4 m/s at respective visit. Step counts were chosen as it is a meaningful and easy to interpret measure for stroke survivors and clinicians [27]. Daily energy expenditure was also calculated with the ActiLife software.

Walking endurance was assessed with the 6-minute walk test (6MWT). The test was conducted within the clinical setting over 35 meters and participants were allowed any orthotic or walking aid that they also used during therapy. The level of lower limb mobility impairment was assessed using the Rivermead Mobility Index (RMI). The RMI assesses functional mobility with 15 tasks in increasing difficulty which participants are instructed to perform in subsequent order with three trials given per task. Additionally, we used questionnaire data on quality of life assessed with the EuroQol 5-Dimension 5-Level (EQ-5D-5L), sleep quality assessed with the Pittsburgh Sleep Quality Index (PSQI), depressive symptoms with the


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Center for Epidemiologic Studies Depression Scale (CES-D). We used the visual analogue scale from the EQ-5D-5L which has a reported MCID of 8.61 [28]. The CES-D questionnaire provides with a lie criteria based on four questions with flipped response options. We followed the recommendations and rated participants' answers as invalid if the lie criteria was ≤ 28 and subsequently imputed missing data. The CES-D has an anchor-based MCID of 9 points which represents a meaningful change in a clinical non-stroke population [29]. Self-reported physical activity was measured using the 'Freiburger Fragebogen zur körperlichen Aktivität' (FFKA), a validated German questionnaire to assess times spent in different household, leisure time or sport activities [30-33]. The latter includes 8 questions on whether participants engaged in a certain type of activity whilst commuting, or climbing stairs, doing grocery shopping or participate in swimming or water gymnastics during the previous week.

### Missing data

We aimed to perform an intention-to-treat analysis and therefore decided to impute missing values. In case of accelerometer data, missingness was due to lost-to-follow up of participants, and due to technical or logistic issues which were both treated as missing at random. In addition, we decided to impute data for incomplete accelerometer datasets based on our wear time validation. We imputed data if valid wear time was < 66%. Although, this cut-off is artificially set we believe that imputing low wear time data is needed to address a bias due to unexplained loss of data. Data were not imputed for the analyses of circadian activity patterns due to the high dimensionality of the data and the exploratory character of the approach which did not warrant to develop an imputation protocol for time-based data. In addition, we also did not impute FFKA data as data was in part qualitative in nature and therefore did not justify imputation.

Data were imputed using multiple imputation with chained equation with the R-package mice (version 3.16.0; R Foundation for Statistical Computing, Vienna, Austria) based on 1,000 imputed datasets and 5 iterations based on age, sex, center as well as existing values [34].

Some data was missing not at random when participants were not able to perform the 6MWT due to high functional impairment. In those cases, we imputed missing values by calculating the half of the lowest value achieved within the test of the respective visit across the cohort.

### Statistical analysis

All analyses were conducted with R Project for Statistical Computing version 4.3.2 (RRID:SCR_001905; R Foundation for Statistical Computing). Statistical tests were not adjusted for multiple comparisons due to the exploratory nature of the analysis except for the Function-on-Scalar-Regression which is detailed further down.

### Research question 1

Descriptive statistics are presented as mean (± standard deviation) or median (25%–75% percentiles), as appropriate, based on non-imputed data. Correlations were calculated using Spearman's Rho. We applied function-on-scalar regression (FoSR) to calculate temporal profiles of physical activity. The processing pipeline is detailed in **Fig. 1**. FoSR is a functional data analysis approach published by Goldsmith and colleagues which allows to calculate associations of covariates with the response variable at each point in time [35]. Compared with other forms of circadian rhythm analyses such as calculating mesor, peak and amplitude it has a high resolution in time and is easy to interpret [36]. To apply FoSR, we first extracted minute by minute data of steps taken per day with the ActiLife software. As activity exhibits high

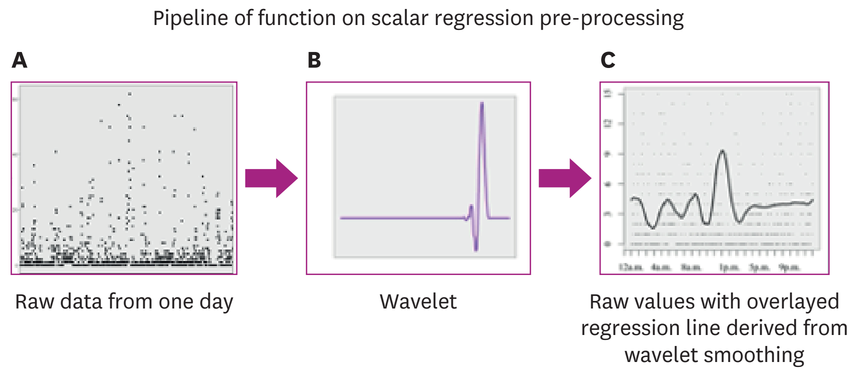


**Fig. 1.** Analysis pipeline for function-on-scalar regression.

fluctuations, the data initially required smoothing using a set of basis functions. In contrast to the approach by Goldsmith and colleagues we used Daubechies wavelets of length 10 instead of Cubic-B splines due to their harmonic nature which more appropriately resembles the 24-hour fluctuation of daily physical activity. We employed 13 basis functions, which proved sufficient for capturing relatively arbitrary temporal profiles. After the wavelet transformation FoSR was applied. FoSR is analogous with ordinary linear regression with the difference that the response is a function of time and covariates are scalars. A random intercept is added to account for the dependent structure of data as participants provided data of more than one day. We used steps as the response and treatment, sex or change in 6-minute walk distance (6MWD) as covariates. Analyses were adjusted for age and sex where appropriate. The complex data structure did not allow for additional confounders. FoSR analyses were adjusted for multiple testing using Bonferroni corrections as to not inflate a type 1 error due to the high numbers of tests within one analysis.

### Research question 2

The FFKA questionnaire allows to calculate energy expenditure by multiplying the time spent in a certain activity with the product of body weight and the respective metabolic equivalent (MET) of the activity as provided by Ainsworth et al. [37] Activities are further grouped based on whether they entailed basic activities like commuting by foot or bicycle to work or for shopping, leisure time activities like gardening or sport activities. We summarized the most frequently reported sport activities and gave descriptive summaries with mean and standard deviations of the grouped energy expenditure. Energy expenditure from self-reported activities of the week prior to the 6 months visit were correlated with objectively measured energy expenditure from the ActiGraph devices which recorded 7 days after the 6 months visit.

### Research question 3

Associations of change in 6MWD on behavior at 6 months were calculated using linear mixed-effects regression analyses with steps, self-reported health (EQ-5D-5L), PSQI sum score or CES-D sum score as the response variable and change in walking distance as the predictor and shown as standardized mean differences (SMD). Analyses were adjusted for age, sex, functional impairment at baseline operationalized with the FAC, center and respective baseline values analogous to our primary endpoint analysis with the difference that center is not added as a random effect. In the Phys-Stroke trial, we found a higher risk of self-reported falls during the intervention period in participants randomized to the training group. We therefore also assessed the association of any fall during the intervention period on steps taken per day to investigate whether the experience of having fallen might influence walking at later stages.

## RESULTS

At 6 months post stroke, clinical and FFKA questionnaire data were available for 145 and 80 participants respectively. For the current analyses, we followed three research questions for which different approaches to address missing values were being used. Flow of data and number of imputed datapoints are depicted in **Fig. 2** and baseline characteristics in **Table 1**. In summary, patients were moderately to severely affected with a median National Institutes of Health Stroke Scale score of 8 (5–12) and interventions commenced on average 28 days (17–40) after stroke. Groups were comparable between intervention arms in most characteristics, but participants randomized to the relaxation group were less impaired in function as can be seen in the 6MWD. During the intervention period, participants improved on average 45.1 ± 80.6 m in their walking distance but with the training group achieving higher improvements. Participants in both groups remained approximately 2 and a half months in inpatient rehabilitation with patients from the training group staying 3 days less (95% confidence interval [CI], −8 to 14).

### Research question 1

Participants took on average 5,623 ± 2,998 steps per day. Walking in both groups displayed similar improvements with only participants in the relaxation group doing more steps per day than those from the training group but the variances in both groups were large (**Table 2**). On the contrary, participants in the training group seemed to rate their health better.
We assessed correlations of participant's functional status, quality of life, sleep quality and depressive symptoms with steps taken per day. RMI was correlated with steps per day ($\rho = 0.54$, $p < 0.001$) but neither quality of life ($\rho = -0.04$, $p = 0.692$) and sleep quality ($\rho = 0.07$, $p = 0.516$) nor depressive symptoms ($\rho = -0.01$, $p = 0.929$) were correlated at 6 months post stroke.

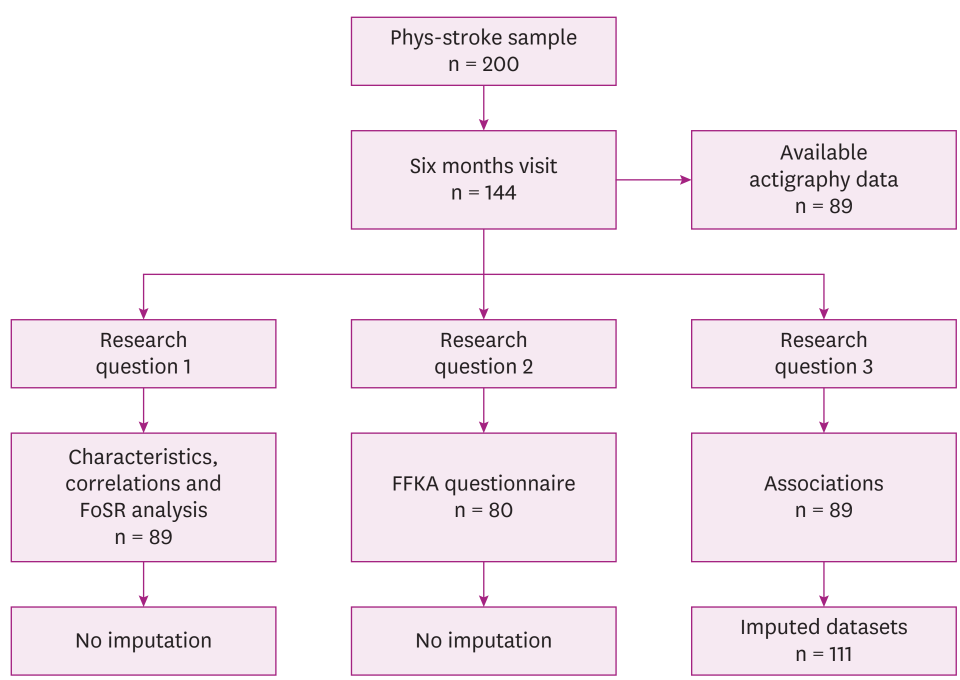


**Fig. 2.** Flow chart of accelerometer data in all three research questions.
FoSR, function-on-scalar regression; FFKA, Freiburger Fragebogen zur körperlichen Aktivität.

**Table 1.** Baseline characteristics between groups

| Baseline characteristics | Training (n = 105) | Relaxation (n = 95) |
|---|---|---|
| Age (yr) | 69 ± 12 | 70 ± 11 |
| Sex, female | 45 (42.9) | 36 (37.9) |
| Time from stroke to intervention (days) | 30 (17–39) | 27 (17–41) |
| NIHSS score* | 9 (5–12) | 7 (5–11) |
| Ischaemic stroke | 91 (86.7) | 90 (94.7) |
| Previous stroke | 27 (25.7) | 27 (28.4) |
| Barthel Index score | 50 (35–60) | 55 (35–65) |
| FAC score‡ | 2 (1–2) | 2 (1–3) |
| 6MWD (m)† | 106 ± 111 | 138 ± 114 |

Values are expressed as mean ± standard deviation, number (%), or median (interquartile range).
NIHSS, National Institute of Health Stroke Scale; FAC, Functional Ambulation Category; 6MWD, 6-minute walk distance.
*NIHSS was assessed at the acute care unit between three to 5 days after stroke.
†Participant data were imputed on the assumption of missing not at random in 16 cases in the training and 12 cases in the relaxation group.
‡FAC ranges from 0 to 5 with highest value denoting no functional impairment.

**Table 2.** Descriptive summary of behavioral characteristics at 6 months post stroke per treatment

| Behavioral characteristics | Training (n = 79) | Relaxation (n = 65) | Treatment effect (95% CI) | p value |
|---|---|---|---|---|
| 6MWD (m) | 239 ± 152 | 233 ± 149 | 26 (−1 to 53) | 0.055 |
| RMI | 11 ± 4 | 11 ± 4 | 0.0 (−0.8 to 0.8) | 0.960 |
| Steps per day* | 4,284 (2,193–7,308) | 6,105 (3,404–7,904) | −566 (−1,497 to 365) | 0.227 |
| EQ-5D-5L index score | 0.7 ± 0.3 | 0.7 ± 0.3 | 0.0 (−0.08 to 0.08) | 0.785 |
| EQ-5D-5L visual analogue scale | 65 ± 18 | 58.8 ± 22.1 | 2.8 (−3.2 to 8.9) | 0.398 |
| PSQI sum score† | 5 ± 4 | 5 ± 3 | −1 (−1 to 0) | 0.222 |
| CES-D sum score‡ | 8 ± 7 | 9 ± 5 | 0 (−2 to 1) | 0.406 |

Treatment effects are calculated with linear mixed models adjusted for respective baseline values, age, sex, functional impairment and center. EQ-5D-5L health denotes the visual analogue rating of perceived health on the day of the visit. Values are expressed as mean ± standard deviation or median (interquartile range).
6MWD, 6-minute walk distance; RMI, Rivermead Mobility Index; EQ-5D-5L, EuroQol 5-Dimension 5-Level; PSQI, Pittsburgh Sleep Quality Index; CES-D, Center for Epidemiologic Studies Depression Scale.
*Values were not available for 34 cases in training group and 22 cases in relaxation group.
†Values were not available for 3 cases in training group and 5 cases in relaxation group.
‡Values were not available for 12 cases in training group and 7 cases in relaxation group.

We further assessed time distribution of steps at 6 months post stroke using FoSR. An actigram of a sample participant is shown in **Fig. 3**. Participants had an incline in activity over the morning hours with the highest activity during midday. The number of steps decreased afterwards constantly until the evening hours (**Fig. 4A**). Adding treatment as covariates revealed no differences between the 2 treatment groups (**Fig. 4B**). In contrast, sex as covariate did indicate differences with women moving on average 1.5 steps per minute (interquartile range [IQR], 0.0–3.0) more in the morning hours, 2.4 steps per minute (IQR, 0.9–3.9) over the midday hours and 1.8 (IQR, 0.3–3.3) in the late afternoon and evening hours. Women in our sample tended also to do more absolute daily steps than men at 6 months post stroke (6,821 [3,999–8,719] vs. 4,654 [952–6,821], p = 0.080).

## Research question 2

Data from the FFKA questionnaire were available for 80 participants (training vs. relaxation: 46 vs. 34). Summaries of energy expenditure per group can be found in **Table 3**. Energy expenditure 6 months post stroke varied substantially between participants in both groups as can be seen by the wide interquartile ranges. In both groups, most energy expenditure occurred during basic activities while engagement in sports activities contributed very little to nothing to the daily amount. Although, on average participants in the training group seemed to have spent more energy, the difference was not significant due to the large variances. We found a correlation between self-reported energy expenditure in the week prior to the 6 months visit and the objectively assessed energy expenditure during the week after the visit (ρ = 0.58, p < 0.001).

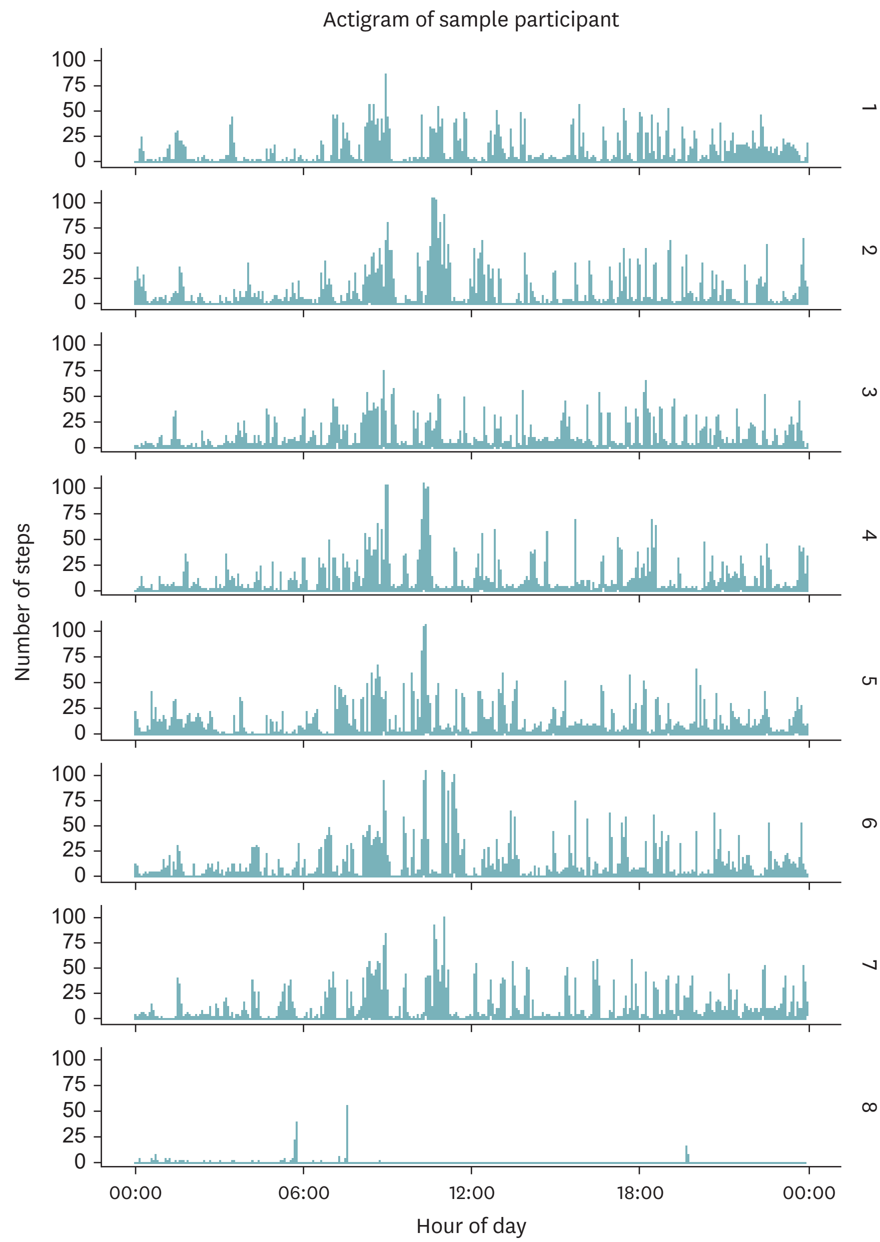


**Fig. 3.** Actigram of one sample participant.

**Table 3.** Descriptive summary of energy expenditure at 6 months post stroke per treatment

| Domain of physical activity | Training (n = 46) | Relaxation (n = 34) | SMD (p) |
|---|---|---|---|
| Energy expenditure during basic activities (kcal/week) | 5,670 (0–19,136) | 2,263 (0–9,056) | 0.45 (0.308) |
| Energy expenditure during leisure time activities (kcal/week) | 19 (0–1,002) | 97 (0–535) | 0.18 (0.898) |
| Energy expenditure during sports activities (kcal/week) | 0 (0–80) | 0 (0–61) | 0.29 (0.689) |
| Total energy expenditure (kcal/week) | 7,193 (0–19,679) | 3,028 (120–9,639) | 0.46 (0.465) |

Energy expenditure per week calculated from self-reported questionnaire ‘Freiburger Fragebogen zur körperlichen Aktivität.’ Subsample of 80 participants filled out the questionnaire. Values are expressed as median (interquartile range).
SMD, standardized mean differences.


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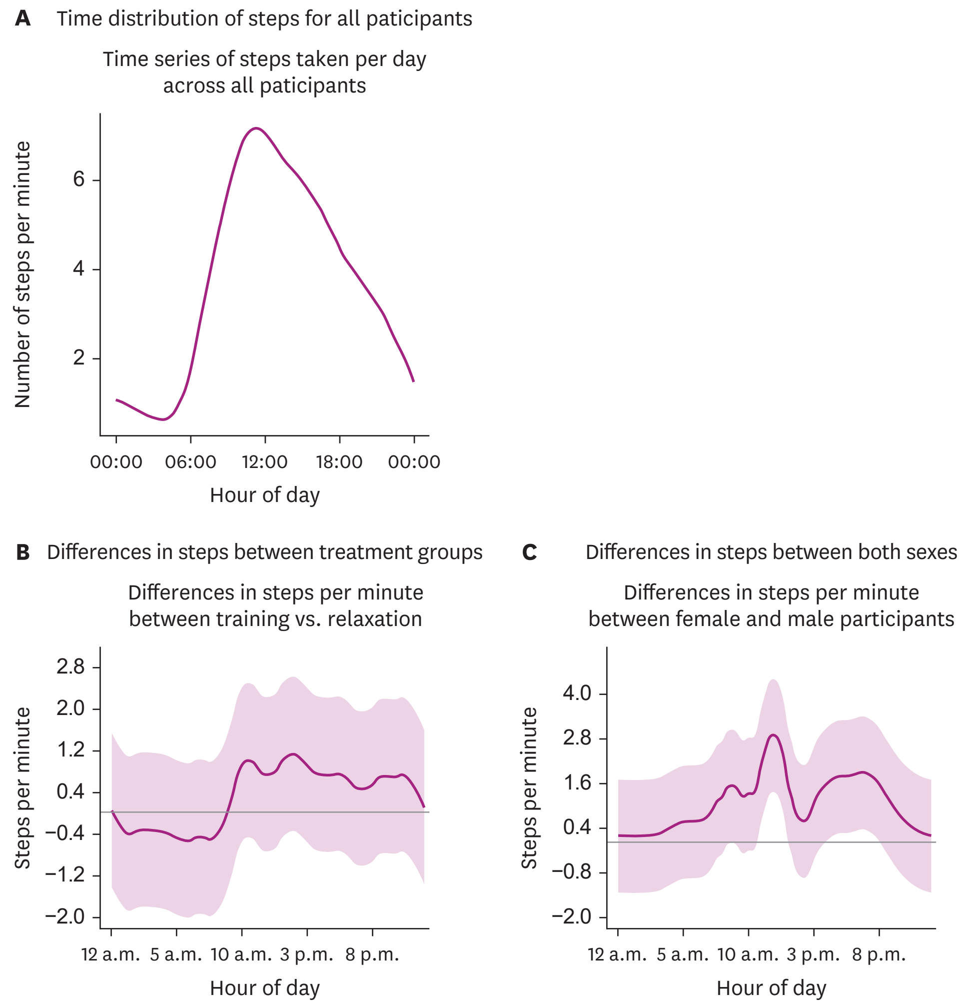


**Fig. 4.** Multiplot. (A) Time distribution across all patients, (B) Differences between both treatments, and (C) Differences between the sexes.

Twenty-one participants (26%) reported to have participated in any sorts of sport activities over the course of the month prior to the visit. Most frequently, participants reported to have engaged in physiotherapy (n = 19), fitness, cardio, or gymnastics (n = 12) or occupational therapy (n = 2). Of note, we found that male participants spent more energy in fitness related activities (SMD, 1.16; p = 0.186) while females spent more energy in dance activities (SMD, 1.19; p = 0.037) compared to the opposite gender.

## Research question 3

We assessed the associations of change in 6MWD over the intervention period with steps taken per day, quality of life and depressive symptoms using adjusted linear mixed models based on imputed data. There was a positive association of gains in 6MWD with steps taken per day at 6 months post stroke with an increase of 8.2 steps per day (95% CI, 1.6 to 14.8; p = 0.017) for every gained meter in 6MWD between baseline and post-intervention (**Fig. 5**). As a post-hoc analysis, we tested whether the found difference depended on functional impairment but could neither identify an interaction of FAC at baseline with change in 6MWD (β = −0.6; 95% CI, −5.63 to 4.42; p = 0.815) nor with treatment group (β = 201.45; 95% CI, −567.90 to 970.79; p = 0.609). We did not find effects on self-rated quality of life (β = 0.03; 95% CI, −0.00 to

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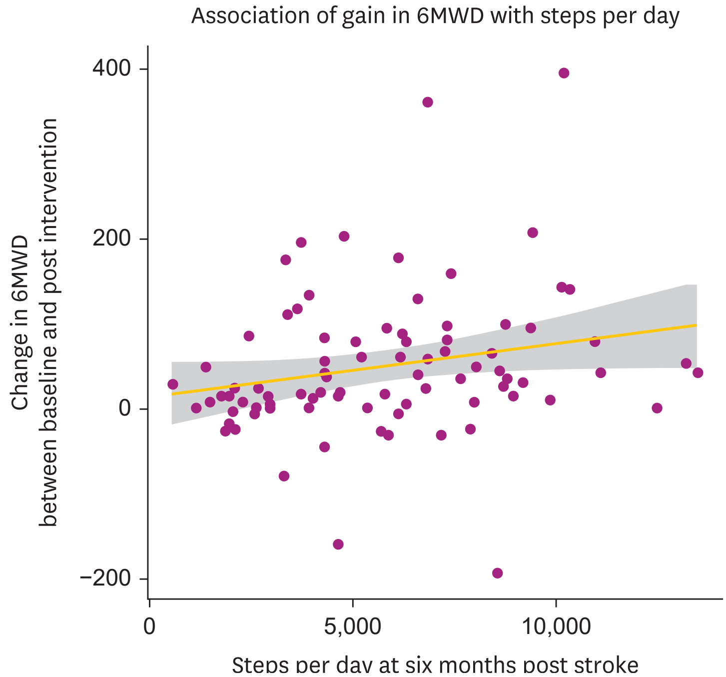


**Fig. 5.** Association of gain in 6MWD with steps per day.
6MWD, 6-minute walk distance.

0.08; p = 0.073), depressive symptoms (β = −0.01; 95% CI, −0.02 to 0.01; p = 0.07) or on sleep quality (β = −0.00; 95% CI, −0.01 to 0.00; p = 0.575).

In addition, we assessed whether we could identify any association of self-reported falls occurring over the course of the intervention period and steps taken per day at 6 months but could not find any association (β = −136 steps; 95% CI, −1,387 to 1,115; p = 0.832).

## DISCUSSION

In this secondary analysis of the Phys-Stroke trial comparing aerobic training to relaxation in moderate to severely affected subacute stroke patients, we assessed activity patterns at 6 months post stroke. Overall, we see a comparable behavioral progression in both treatment arms with only neglectable differences. Participants do less steps per day as recommended in current guidelines with most activity occurring during the morning and midday hours with daily energy expenditure mostly derived from basic activities such as grocery shopping. Women took more steps compared to men.

Participation in physical activity has been identified several times as a key element of secondary prevention, while adherence to recommendations remains poor [38]. Monitoring physical activity with objective measurements and providing information with high relevance for stroke survivors were recently identified as key elements to increase physical activity [27]. Here, we provide information on amount, type and patterns of physical activity 6 months after stroke as well as indications on what contribution an aerobic exercise intervention within the inpatient clinic has on walking in the chronic stage.


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Daily step counts within our sample resemble reports from previous studies with participants reaching about half of the recommended daily steps but were also below the suggested threshold for people with chronic diseases [39]. In the systematic review by Fini et al, daily step counts varied from 4,047 to 6,407 which is in line with our findings [8]. Of note, in this systematic review step counts were even lower when only data from devices with high test-retest reliability were used. The accelerometers used in our study fall within this category.

Despite amount of physical activity, intensity plays an important role in secondary prevention. Only one fourth of our questionnaire data indicated that participants were engaged in any sports activity. Sports activities are more likely to provide with higher intensities than other kinds of activities. Two of the most often reported activities were either physio or occupational therapy. While these activities fall outside of many definitions of sports activities, the fact that they are mentioned most often might give an indication that those activities belong to the more strenuous activities participants from our sample were involved in. In another study, walking has been reported to be the most frequent type of activity followed by fitness [40]. Similar to our study, involvement in other sports activities were generally low.

Our FoSR provided insights on the distribution of activity throughout a 24-hour cycle. Participants were found to be more active in the morning and midday hours with declining mobility until the evening. This is in line with a study from English et al. [16] in which participants were reported to be more active in the morning hours and to be engaged in more sedentary behavior towards the afternoon and evening hours. In this study, authors reported the relative contribution of different intensities of activity within every hour which is different from our approach in which we provide an overview of steps taken in more granularity throughout the day. In another study, authors investigated net time spent in sedentary behavior, light or moderate to vigorous activity [17]. Here, the majority of the day was spent in sedentary behavior but time distribution of activity was not analyzed. Higher amounts of time spent in sedentary behavior has been identified as an independent risk factor for stroke besides low levels of physical activity [41,42]. Therefore, the goal of future interventions should aim for disrupting prolonged phases of sedentary behavior. A cohort study of 92,139 participants from the UK Biobank associated timing of moderate to vigorous activity with all-cause mortality and found most reductions in midday to afternoon hours (11 am to 5 pm) [43]. Here, no specific analyses for participants with cardiovascular diseases were undertaken. Of note, protective effects were strongest among elderly, male, less physically active participants. In our analysis we found higher step counts in females especially during the midday hours highlighting an activity dependent sex difference.

So far, we could not identify any study looking at the associations of increases in walking capacity during the subacute stage after stroke with physical activity assessed at the chronic stage. Here, we found that clinically meaningful effects in walking capacity in the subacute stage did result in meaningful increases in activity in the chronic stage which highlights the beneficial effects of improvements in capacity gained early after stroke. Given the effect size found in our analyses, an increase of walking distance of 71 m during early rehabilitation as has been identified as a clinically meaningful difference could translate up to 582 extra steps in the chronic phase highlighting the effect that a focus on aerobic exercise in the rehabilitation during the early subacute phase could have on daily physical activity in the chronic stage [44]. In line with our findings, Brown and colleagues [15] investigated whether participation in a structured aerobic exercise program during inpatient rehabilitation increased physical activity up to 6 months after discharge and found no difference in behavior compared to patients not being referred to the exercise program. Walking capacity seems to be one factor important for engagement in physical activity but most likely other factors need to be considered. Further replications are needed with in-depths analyses of moderators to effectively guide training prescriptions and behavior change interventions. Identification of responders to aerobic exercise might help successful translation of improvements during rehabilitation to meaningful increases in physical activity in the chronic stage.

This secondary analysis extends the breadth of evidence derived from the Phys-Stroke trial. The following limitations need to be discussed. Less than 4% of screened participants were included in Phys-Stroke. Here, 2 additional subsamples of participants – one with valid accelerometer or FFKA data each were created, limiting the generalizability of our findings. We used multiple imputation methods whenever feasible to minimize bias. Energy expenditure values were calculated from questionnaire data and a compendium of metabolic equivalents validated on healthy participants which might have biased our calculation. Our findings are comparable with values reported in the literature. Because of our sample size, FoSR analyses with only one covariate were calculated. Direction of effects can therefore be influenced by unaccounted confounders. Similarly, we were not able to model interaction effects of gains in 6MWD with treatment allocation due to the limited participant number.

Stroke patients in our cohort exhibited daily step counts below endorsed recommendations at 6 months post stroke. Meaningful improvements in walking capacity during the subacute stage after stroke were associated with relevant increases in daily step counts at the chronic stage. Replication of this finding as well as investigations of variances in physical activity after stroke are needed to adapt therapies during and after rehabilitation to individual needs.

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## SUPPLEMENTARY MATERIALS

### Supplementary Table 1
Inclusion and exclusion criteria

### Supplementary Table 2
Device setting of actigraph devices

## REFERENCES

1. Platz T. Clinical pathways in stroke rehabilitation: evidence-based clinical practice recommendations. Available at http://www.ncbi.nlm.nih.gov/books/NBK585587/. [accessed on 23 March 2024].
2. Jönsson AC, Delavaran H, Iwarsson S, Ståhl A, Norrving B, Lindgren A. Functional status and patient-reported outcome 10 years after stroke: the Lund Stroke Register. Stroke 2014;45:1784-1790. PUBMED | CROSSREF
3. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, Lennon O, Meschia JF, Nguyen TN, Pollak PM, Santangeli P, Sharrief AZ, Smith SC Jr, Turan TN, Williams LS. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. Stroke 2021;52:e364-e467. PUBMED | CROSSREF

4. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, Benetos A, Biffi A, Boavida JM, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, Di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Jankowska EA, Michal M, Sacco S, Sattar N, Tokgozoglu L, Tonstad S, Tsioufis KP, van Dis I, van Gelder IC, Wanner C, Williams B; ESC National Cardiac Societies; ESC Scientific Document Group. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2021;42:3227-3337. PUBMED | CROSSREF
5. Sheng M, Yang J, Bao M, Chen T, Cai R, Zhang N, Chen H, Liu M, Wu X, Zhang B, Liu Y, Chao J. The relationships between step count and all-cause mortality and cardiovascular events: a dose-response meta-analysis. J Sport Health Sci 2021;10:620-628. PUBMED | CROSSREF
6. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, Carty C, Chaput JP, Chastin S, Chou R, Dempsey PC, DiPietro L, Ekelund U, Firth J, Friedenreich CM, Garcia L, Gichu M, Jago R, Katzmarzyk PT, Lambert E, Leitzmann M, Milton K, Ortega FB, Ranasinghe C, Stamatakis E, Tiedemann A, Troiano RP, van der Ploeg HP, Wari V, Willumsen JF. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med 2020;54:1451-1462. PUBMED | CROSSREF
7. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, George SM, Olson RD. The physical activity guidelines for Americans. JAMA 2018;320:2020-2028. PUBMED | CROSSREF
8. Fini NA, Holland AE, Keating J, Simek J, Bernhardt J. How physically active are people following stroke? Systematic review and quantitative synthesis. Phys Ther 2017;97:707-717. PUBMED | CROSSREF
9. Hendrickx W, Riveros C, Askim T, Bussmann JBJ, Callisaya ML, Chastin SFM, Dean CM, Ezeugwu VE, Jones TM, Kuys SS, Mahendran N, Manns TJ, Mead G, Moore SA, Paul L, Pisters MF, Saunders DH, Simpson DB, Tieges Z, Verschuren O, English C. Identifying factors associated with sedentary time after stroke. Secondary analysis of pooled data from nine primary studies. Top Stroke Rehabil 2019;26:327-334. PUBMED | CROSSREF
10. Guzek Z, Dziubek W, Stefańska M, Kowalska J. Evaluation of the functional outcome and mobility of patients after stroke depending on their cognitive state. Sci Rep 2024;14:1515. PUBMED | CROSSREF
11. Billinger SA, Arena R, Bernhardt J, Eng JJ, Franklin BA, Johnson CM, MacKay-Lyons M, Macko RF, Mead GE, Roth EJ, Shaughnessy M, Tang A; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Lifestyle and Cardiometabolic Health; Council on Epidemiology and Prevention; Council on Clinical Cardiology. Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014;45:2532-2553. PUBMED | CROSSREF
12. National Clinical Guideline for Stroke for the UK and Ireland. Available at https://www.strokeguideline.org/. [accessed on 23 March 2024].
13. MacKay-Lyons M, Billinger SA, Eng JJ, Dromerick A, Giacomantonio N, Hafer-Macko C, Macko R, Nguyen E, Prior P, Suskin N, Tang A, Thornton M, Unsworth K. Aerobic exercise recommendations to optimize best practices in care after stroke: AEROBICS 2019 update. Phys Ther 2020;100:149-156. PUBMED | CROSSREF
14. Brouwer R, Wondergem R, Otten C, Pisters MF. Effect of aerobic training on vascular and metabolic risk factors for recurrent stroke: a meta-analysis. Disabil Rehabil 2021;43:2084-2091. PUBMED | CROSSREF
15. Brown C, Fraser JE, Inness EL, Wong JS, Middleton LE, Poon V, McIlroy WE, Mansfield A. Does participation in standardized aerobic fitness training during inpatient stroke rehabilitation promote engagement in aerobic exercise after discharge? A cohort study. Top Stroke Rehabil 2014;21 Suppl 1:S42-S51. PUBMED | CROSSREF
16. English C, Wondergem R, Hendrickx W, Pisters MF. People with stroke are most sedentary in the afternoon and evening. Cerebrovasc Dis 2022;51:511-516. PUBMED | CROSSREF
17. Wondergem R, Veenhof C, Wouters EM, de Bie RA, Visser-Meily JM, Pisters MF. Movement behavior patterns in people with first-ever stroke. Stroke 2019;50:3553-3560. PUBMED | CROSSREF
18. Cavalcanti P, Campos T, Araujo J. Actigraphic analysis of the sleep-wake cycle and physical activity level in patients with stroke: implications for clinical practice. Chronobiol Int 2012;29:1267-1272. PUBMED | CROSSREF
19. Nave AH, Rackoll T, Grittner U, Bläsing H, Gorsler A, Nabavi DG, Audebert HJ, Klostermann F, Müller-Werdan U, Steinhagen-Thiessen E, Meisel A, Endres M, Hesse S, Ebinger M, Flöel A. Physical Fitness Training in Patients with Subacute Stroke (Phys-Stroke): multicentre, randomised controlled, endpoint blinded trial. BMJ 2019;366:l5101. PUBMED | CROSSREF
20. Flöel A, Werner C, Grittner U, Hesse S, Jöbges M, Knauss J, Seifert M, Steinhagen-Thiessen E, Gövercin M, Dohle C, Fischer W, Schlieder R, Nave AH, Meisel A, Ebinger M, Wellwood I. Physical Fitness Training in Subacute Stroke (Phys-Stroke)--study protocol for a randomised controlled trial. Trials 2014;15:45. PUBMED | CROSSREF

21. Rackoll T, Grittner U, Nave A, Flöel A, Ebinger M. Physical Fitness in Subacute Stroke (Phys-Stroke) - statistical analysis plan, version 1.0 (September 1st, 2017). Available at https://figshare.com/articles/journal_contribution/Physical_Fitness_in_Subacute_Stroke_PHYS-Stroke_-_Statistical_Analysis_Plan/5375026?file=9246310. [accessed on 30 May 2024].
22. Thompson PD, Arena R, Riebe D, Pescatello LS; American College of Sports Medicine. ACSM's new preparticipation health screening recommendations from ACSM's guidelines for exercise testing and prescription, ninth edition. Curr Sports Med Rep 2013;12:215-217. PUBMED | CROSSREF
23. Gardner AW, Montgomery PS, Wang M, Shen B. Minimal clinically important differences in daily physical activity outcomes following supervised and home-based exercise in peripheral artery disease. Vasc Med 2022;27:142-149. PUBMED | CROSSREF
24. Fini NA, Burge AT, Bernhardt J, Holland AE. Two days of measurement provides reliable estimates of physical activity poststroke: an observational study. Arch Phys Med Rehabil 2019;100:883-890. PUBMED | CROSSREF
25. Fini NA, Holland AE, Bernhardt J, Burge AT. How many hours of device wear time are required to accurately measure physical activity post stroke? Int J Environ Res Public Health 2022;19:1191. PUBMED | CROSSREF
26. Webber SC, St John PD. Comparison of ActiGraph GT3X+ and StepWatch step count accuracy in geriatric rehabilitation patients. J Aging Phys Act 2016;24:451-458. PUBMED | CROSSREF
27. Fini NA, Simpson D, Moore SA, Mahendran N, Eng JJ, Borschmann K, Moulaee Conradsson D, Chastin S, Churilov L, English C. How should we measure physical activity after stroke? An international consensus. Int J Stroke 2023;18:1132-1142. PUBMED | CROSSREF
28. Chen P, Lin KC, Liing RJ, Wu CY, Chen CL, Chang KC. Validity, responsiveness, and minimal clinically important difference of EQ-5D-5L in stroke patients undergoing rehabilitation. Qual Life Res 2016;25:1585-1596. PUBMED | CROSSREF
29. Haase I, Winkeler M, Imgart H. Anchor-based ascertaining of meaningful changes in depressive symptoms using the example of the German short form of the CES-D. Neuropsychiatr 2016;30:82-91. PUBMED | CROSSREF
30. Ludwig K, Graf von der Schulenburg JM, Greiner W. German value set for the EQ-5D-5L. Pharmacoeconomics 2018;36:663-674. PUBMED | CROSSREF
31. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213. PUBMED | CROSSREF
32. Shinar D, Gross CR, Price TR, Banko M, Bolduc PL, Robinson RG. Screening for depression in stroke patients: the reliability and validity of the Center for Epidemiologic Studies Depression Scale. Stroke 1986;17:241-245. PUBMED | CROSSREF
33. Frey I, Berg A, Grathwohl D, Keul J. Freiburg Questionnaire of physical activity--development, evaluation and application. Soz Praventivmed 1999;44:55-64. PUBMED | CROSSREF
34. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate imputation by chained equations in R. J Stat Softw 2011;45:1-67. CROSSREF
35. Goldsmith J, Liu X, Jacobson JS, Rundle A. New insights into activity patterns in children, found using functional data analyses. Med Sci Sports Exerc 2016;48:1723-1729. PUBMED | CROSSREF
36. Rackoll T, Neumann K, Passmann S, Grittner U, Külzow N, Ladenbauer J, Flöel A. Applying time series analyses on continuous accelerometry data-a clinical example in older adults with and without cognitive impairment. PLoS One 2021;16:e0251544. PUBMED | CROSSREF
37. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR Jr, Tudor-Locke C, Greer JL, Vezina J, Whitt-Glover MC, Leon AS. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc 2011;43:1575-1581. PUBMED | CROSSREF
38. Fini NA, Bernhardt J, Churilov L, Clark R, Holland AE. Adherence to physical activity and cardiovascular recommendations during the 2years after stroke rehabilitation discharge. Ann Phys Rehabil Med 2021;64:101455. PUBMED | CROSSREF
39. Tudor-Locke C, Craig CL, Aoyagi Y, Bell RC, Croteau KA, De Bourdeaudhuij I, Ewald B, Gardner AW, Hatano Y, Lutes LD, Matsudo SM, Ramirez-Marrero FA, Rogers LQ, Rowe DA, Schmidt MD, Tully MA, Blair SN. How many steps/day are enough? For older adults and special populations. Int J Behav Nutr Phys Act 2011;8:80. PUBMED | CROSSREF
40. Fini NA, Bernhardt J, Holland AE. Types of physical activity performed pre and post stroke. Braz J Phys Ther 2022;26:100412. PUBMED | CROSSREF
41. Wang Z, Jin X, Liu Y, Wang C, Li J, Tian L, Teng W. Sedentary behavior and the risk of stroke: a systematic review and dose-response meta-analysis. Nutr Metab Cardiovasc Dis 2022;32:2705-2713. PUBMED | CROSSREF

42. Hooker SP, Diaz KM, Blair SN, Colabianchi N, Hutto B, McDonnell MN, Vena JE, Howard VJ. Association of accelerometer-measured sedentary time and physical activity with risk of stroke among US adults. JAMA Netw Open 2022;5:e2215385. PUBMED | CROSSREF

43. Feng H, Yang L, Liang YY, Ai S, Liu Y, Liu Y, Jin X, Lei B, Wang J, Zheng N, Chen X, Chan JW, Sum RK, Chan NY, Tan X, Benedict C, Wing YK, Zhang J. Associations of timing of physical activity with all-cause and cause-specific mortality in a prospective cohort study. Nat Commun 2023;14:930. PUBMED | CROSSREF

44. Mishra B, Sudheer P, Agarwal A, Nilima N, Srivastava MV, Vishnu VY. Minimal clinically important difference of scales reported in stroke trials: a review. Brain Sci 2024;14:80. PUBMED | CROSSREF