BEYOND COUNTING STEPS

MEASURING PHYSICAL BEHAVIOR WITH WEARABLE TECHNOLOGY IN REHABILITATION

HANNEKE BRAAKHUIS

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Measuring physical behavior with wearable technology in rehabilitation

Hanneke Braakhuis

The studies presented in this thesis were partly funded by: Rijndam rehabilitation. Printing of this thesis was financially supported by Erasmus University Medical Center and the Hague University of Applied Sciences.

Cover design: Maartje Kuipers
Layout and design: Maartje Kuipers en Hanneke Braakhuis
Printed by: Ipskamp Printing, proefschriften.net
ISBN: 978-94-6421-767-4

BEYOND COUNTING STEPS;
Measuring physical behavior with wearable technology in rehabilitation

MEER DAN STAPPEN TELLEN;
Het meten van beweeggedrag met draagbare technologie in de revalidatie

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de
rector magnificus

Prof.dr. A.L. Bredenoord

en volgens besluit van het College voor Promoties.
De openbare verdediging zal plaatsvinden op

woensdag 6 juli 2022 om 15:30 uur

door

Hanneke Elisabeth Maria Braakhuis

geboren te Almelo

Erasmus University Rotterdam

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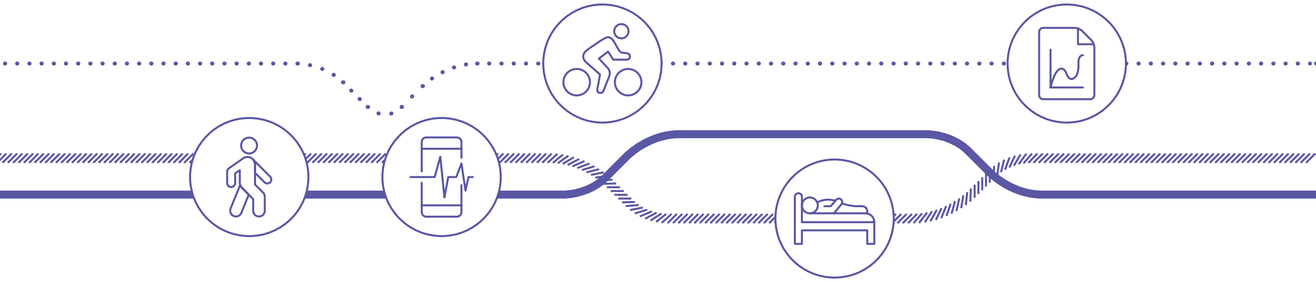
CHAPTER 1

GENERAL INTRODUCTION



Physical inactivity is marked as a global pandemic leading to an increased number of patients with lifestyle-related diseases, such as cardiovascular diseases, diabetes, and stroke, resulting in increased healthcare costs.[1, 2] Therefore, promoting an active lifestyle is imperative in primary, secondary, and tertiary prevention.[3, 4] To promote an active lifestyle, measuring physical activity objectively and reliably is pivotal. Traditional methods for measuring physical activity, such as recall questionnaires and self-report diaries, are subjective methods and socially desirable answers and recall bias lie in wait.[5, 6] In contrast, wearable sensors can measure physical activity and other lifestyle-related variables, such as sleep, heart rate, blood pressure in an objective, reliable, and non-invasive way.[7, 8] Those wearables support diagnosing, goal-setting, monitoring progress, and evaluating therapy of an individual patient.[7, 9] Besides, wearable sensors can provide continuous feedback to patients, promoting self-management and compliance.[8, 10, 11]

Already in the 1960s, objective measurements of the human physical activities were conducted.[12] Since the last decade, the development and application of motion-sensing wearables have expanded in the consumer market, clinical care and in academic research.[11, 13-15] Most of these devices rely on triaxial accelerometers[7, 16], and they are getting more user-friendly (smaller, lighter) with longer-lasting batteries, more extensive data storage capacity, smooth data extraction, and visualization.[13, 15]

Physical activity, sedentary behavior, and physical behavior

Traditionally, the term physical activity is most frequently used in research on inactive lifestyle and its consequences on health. *Physical activity* is defined as “any bodily movement produced by skeletal muscles that require energy expenditure (> 1.5 metabolic equivalents, METs)”.[17] Evidence of the health benefits of being physically active is well known. It reduces the risk of chronic diseases such as type 2 diabetes, osteoporosis, cancer, and it improves overall physical functioning, mental well-being, and quality of life for various patient populations.[12, 14, 18] Physical activity, however, does not cover all important aspects of what people physically do in their daily life. Therefore, the term *physical behavior* was introduced: an umbrella term covering all behaviors related to body postures, movements, and daily life activities.[19] Therefore physical behavior also includes sedentary behavior. *Sedentary behavior* is defined as “any waking behavior characterized by a low energy expenditure (≤1.5 METs)”.[20] Regardless of physical activity, large and uninterrupted amounts of sedentary behavior are independently associated with detrimental health outcomes such as the risk of all-cause mortality, metabolic and cardiovascular diseases.[21-24] Although physical activity and sedentary behavior seem to be the ends of a continuum, they should be regarded as two different aspects of physical behavior.[19, 25]

Measuring physical behavior in rehabilitation

People receiving rehabilitation treatment, for example people with Multiple Scleroris (MS), spinal cord injury (SCI) and stroke, have typically a less favorable physical behavior profile compared to healthy peers.[26, 27] For these patients, a healthy and active lifestyle is particularly more critical than for the general population, since it lowers the risk of secondary health problems.[18, 28] As such, to measure physical behavior over the course of clinical care and thereafter, wearable sensor technology is a promising tool in rehabilitation research and clinical practice.[15] This thesis focuses on three topics regarding sensor-based physical behavior measurement in rehabilitation: *Relationship with other domains of functioning, physical behavior outcome measures and clinical application*.

Relationship with other domains of functioning

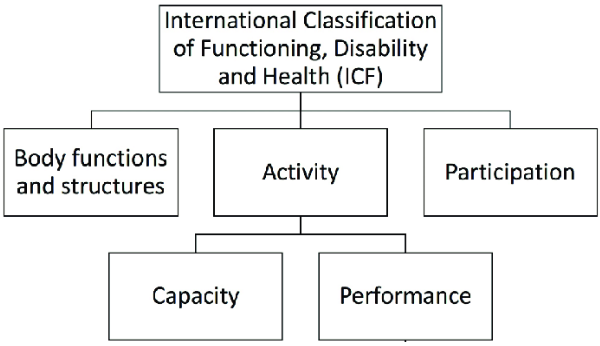


Fig. 1. The ICF domains Body Function and structures, activity and participation.

The International Classification of Functioning and Health is a standard biopsychosocial model to describe the functioning and health-related status in rehabilitation (Figure 1).[29] In the ICF model, the body functions and structures domain denote the body's physiological functions, body systems, and anatomical parts. Performance and capacity are classifiers of the "activity" domain in the ICF model representing an individual's ability to execute a task or an action.[29] Measures of body functions, such as motor performance, and capacity, such as cardiorespiratory fitness, represent what a person *can do* in a standardized or laboratory setting. Performance measures represent what a person actually does in his daily environment (*do-do*), such as a patient's physical behavior. In clinical practice, it is often assumed that performance corresponds to a patient's capacity or body functions assessed with routinely conducted clinical tests.[15] However, the literature on the relationship between body functions, capacity and performance, shows discrepancies. Some studies established a strong correlation between objectively measured performance (the ICF domain activity) and outcomes of clinical tests, such as the six-minute walking test or Berg Balance Scale (the ICF domain body functions and structures).[30] Other studies did not find such a correlation, suggesting that clinical test results reflect a snapshot of one specific moment and are inaccurate to detect physical behavior changes within a patients' environment.[31-33] More in-depth insight into the relationship between relevant clinical outcomes and objectively measured physical behavior is therefore needed, to support development of future therapy and interventions.

In addition, future interventions are preferable tailored to a patients' individual level, since the symptomology of rehabilitation populations is highly variable. It is not yet studied to what extend physical behavior outcomes measured in a patients' own context can discriminate between levels of functioning.

Physical behavior outcome measures

Using wearable technology for measuring physical behavior in rehabilitation has several challenges. One of them is selecting the appropriate outcome measures. In most commercial devices, the outcomes are energy expenditure in METs or kilocalories, or step counts, representing the number of steps walked in a specific time frame.[7] However, increasing the number of calories burned or the number of steps walked is often not the main focus of rehabilitation.[19, 34] For example, changes in the ability to transfer from sitting to standing or balance while standing may be more informative than the number of steps for monitoring recovery of functional independence.[35]

Almost every imaginable outcome can be provided by various devices and data processing algorithms.[7, 36] Over the past few years, highly variable outcomes were used in rehabilitation research, such as the number of transitions between postures, time spent in specific postures (for example sitting/lying/standing/walking), specific sports activities, but also the number and length of uninterrupted periods of physical activity or sedentary behavior (bouts).[36-38] Likewise, Mesquita[37] found 180 different ways to operationalize physical behavior in patients with COPD. To date, no consensus is reached on a single method or outcome that is most appropriate for rehabilitation purposes or specific patient populations.[34, 39, 40]

When physical behavior is captured with only one outcome, clinically meaningful information might be overlooked.[34, 41] A solution is assessing physical behavior as a multidimensional construct, represented by multiple outcomes. However, a better understanding of multidimensionality is required. A first step in establishing relevant and distinct physical behavior outcomes is compressing the numerous possible outcomes. Furthermore, a compressed set of outcomes might be valuable for identifying physical behavior profiles of patients, which can help develop tailored interventions.[42] Personalized interventions are preferred since the symptomology of rehabilitation populations is highly heterogeneous.[42, 43]

Clinical application

Wearable technology is mostly used in research for e.g. monitoring progress and assessing the effects of interventions, but can also be deployed as behavioral intervention technology.[7, 44] Creating awareness of patients' actual behavior by objective measures might result in positive behavior change in itself and support better self-awareness, enhance compliance and stimulate self-management.[45, 46] However, despite their potential, wearables are not widely clinically applied [10]. Two possible explanations will be addressed in this thesis.

First, the effectiveness of wearable monitoring as a tool to improve physical behavior of patients within the health care setting is controversial. Wearables are used as a tool in clinical research to optimize patients' physical behavior, however, so far, the results of studies were not systematically reviewed, and meta-analyses were not performed. Second, although clinicians play a significant role in successfully adopting wearable technology, it is challenging since it requires careful attention, precious time, sufficient organizational and technical infrastructure, and knowledge.[15, 47-50] So far, the perspectives rehabilitation professionals on the use of wearables were not studied. Insight in the perspectives will provide valuable information for future implementation strategies.

Aim & outline of this thesis

This thesis aims to increase the understanding of measuring physical behavior with wearable technology in rehabilitation. A better understanding may hold important implications for use in rehabilitation.

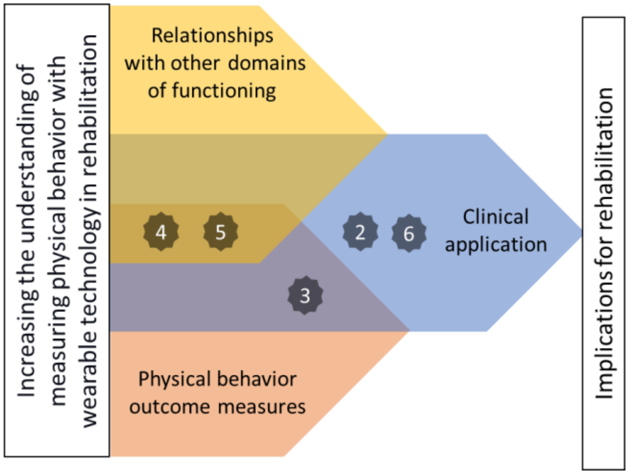


Fig. 2. The aim and outline of this thesis. Numbers represent the numbers of the different chapters.

Figure **2** shows a visualization of the outline of this thesis. The studies conducted in this thesis, represented by the different chapters are all related to one or more of the topics of this thesis (*relationships with other domains of functioning*, *physical behavior outcome measures,* and *clinical application*. It contains in-depth and exploratory studies with diverse patient populations in rehabilitation. **Chapter two** includes a meta-analysis on the effectiveness of interventions that use wearable monitoring to promote physical activity in (former) patients of health care. In addition, it provides an insight in diverse behavioral change techniques used in these interventions. In **chapter three**, data-driven techniques are applied to reduce the amount of physical behavior outcome measures. Those outcome measures are subsequently used to identify subgroups amongst fatigued patients with multiple sclerosis. In **chapter four,** the relation of multidimensional physical behavior outcomes with the ICF domain capacity is determined. In **chapter five**, the longitudinal relation of multidimensional physical behavior outcomes with the ICF domain body function is assessed. In **chapter six**, physical therapists involved in stroke care are questioned regarding using wearable technology in daily practice. The last **chapter seven** discusses the results, describes methodological considerations, recommendations for future research and clinical implications.

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CHAPTER 2

EFFECTIVENESS OF HEALTHCARE INTERVENTIONS USING OBJECTIVE FEEDBACK ON PHYSICAL ACTIVITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Monique A.M. Berger
Johannes B. J. Bussmann

Journal of Rehabilitation Medicine 2019; 51*(3)*, 151-159.

Abstract

Objective: To determine the effectiveness of health-care interventions promoting physical activity, which use objective feedback on physical activity delivered using wearable activity monitors as part of the intervention. Intervention groups are compared with control groups receiving usual care or interventions without objective feedback.

Data sources: PubMed, EMBASE, MEDLINE and Cochrane Library were searched to identify randomized controlled trials.

Study selection: Randomized controlled trials published after 2007 with (former) healthcare patients ≥ 21 years of age were included if physical activity was measured objectively using a wearable monitor for both feedback and outcome assessment. The main goal of included studies was promoting physical activity. Any concurrent strategies were related only to promoting physical activity.

Data extraction: Effect sizes were calculated using a fixed-effects model with standardized mean difference. Information on study characteristics and interventions strategies were extracted from study descriptions.

Data synthesis: Fourteen studies met the inclusion criteria (total $n = 1,902$), and 2 studies were excluded from meta-analysis. The overall effect size was in favour of the intervention groups (0.34, 95% CI 0.23–0.44, $p < 0.01$). Study characteristics and intervention strategies varied widely.

Conclusion: Healthcare interventions using feedback on objectively monitored physical activity have a moderately positive effect on levels of physical activity. Further research is needed to determine which strategies are most effective to promote physical activity in healthcare programmes.

Introduction

Physical inactivity is recognized as a worldwide problem. On the long term, active people have lower risk for disease such as cerebrovascular stroke and cardiac infarction, and frequent physical activity (PA) is beneficial for health outcomes such as mental wellbeing, physical fitness and quality of life.[1, 2] Short-term effects of PA are also well-established; for example, promoting PA in patients shortly after stroke appears to be beneficial for motor and neurological repair.[3, 4]

With increasing evidence from diverse patient populations of the benefits of being physically active, promoting PA is essential in treatment and rehabilitation.[5] Unfortunately, promotion of PA in patient populations, such as those with chronic conditions, is challenging, since they are often burdened by several health problems and encounter barriers to physical activity. Therefore, these patients are at greater risk of physical inactivity compared with their healthy peers.[6] Medical professionals, especially rehabilitation teams, can play a substantial role in improving PA with regard to patient-specific health behaviors and disease management.[5, 6] Knowledge of the most effective way to promote PA in healthcare is needed.

A progressively applied tool to support promotion of PA in healthcare is monitoring activity using wearable technology, such as pedometers and accelerometers.[7] These "wearables"' objectively measure PA and, in recent years, their accuracy and validity has increased.[7–10] Activity monitors can generate various parameters that provide information on PA, e.g. number of steps, walking distance, or energy expenditure. It is possible that providing this objective insight motivates patients to increase their levels of PA.[11.] In addition, objective insight is not only useful for increasing levels of PA, but it can help patients to regulate their behavior, e.g. by improving the distribution of activity during the day with regard to the individual's capacity. Van Achterberg *et al*.[12] support this by stating that self-monitoring contributes to successful behavior change. Thus, wearable activity monitors facilitate self-management of health behavior of patients and therefore have the potential to improve patients' functional independence.[10]

Literature reviews have shown that interventions that include objective monitoring of PA are moderately effective in healthy subjects and relatively inactive populations.[13–16] However, the methodology of these studies differs considerably. First, the types of populations included varies between reviews and between studies included in reviews. The reviews concentrated, for example, on children, adults (with and without a diagnosis of a specific disease), or, in contrast, on a specific population, such as obese adults with diabetes.[13–16] Therefore, these results cannot be transferred directly to healthcare and rehabilitation. Hence, a review that includes patient populations only is needed to support statements of the possible effectiveness of such self-management tools for the promotion of PA in healthcare interventions.[16] Another characteristic of studies included in the reviews is that PA monitoring was applied in relatively broadly defined health interventions, which targeted more aspects than PA, e.g. nutrition. Unlike previous reviews, the current review focusses on interventions in which the main goal was promoting PA using wearable monitors. Finally, another methodological issue highlighted by previous reviews is the diversity in intervention strategies applied, which makes comparison complex. In healthcare, in particular, interventions promoting PA using wearable technology are often combined with components of behavioral change techniques (BCT) targeting PA levels, e.g. behavioral counselling with goal-setting, education on the advantages of being active, or identification of barriers to PA.[13, 17] These BCT components are often already present in usual care programmes, which makes it even more complex to evaluate objective feedback on PA interventions in healthcare.[13] Another example of varying strategies is the method of feedback; interventions differ in showing real-life feedback on a display, text messages or in real-life consultations with therapists. In addition, feedback is provided by multiple types of wearable devices. Both feedback strategy and the presence and type of BCT components may influence the amount of behavior change. A more detailed insight into the presence of intervention strategies applied in healthcare, together with objective activity monitoring, such as feedback type and BCT components, is needed.

A literature review on the effectiveness of objective feedback on PA in a PA promotion intervention that focuses solely on patient populations would provide valuable knowledge to enable its effective application in healthcare. In addition, the presence of different intervention strategies should be considered. The aim of this study was to determine the effectiveness of interventions promoting PA in healthcare that use objective feedback about PA via wearable activity monitors. Interventions that use objective feedback about PA are compared either with control groups receiving usual care or with an intervention without objective feedback. Although providing objective feedback can be beneficial for either increasing or regulating PA, this study focuses on the effect of increasing PA levels and includes only those interventions in which the main goal is to promote PA. Furthermore, the influence of intervention strategies is explored by describing the type of feedback and the presence of BCT.

Methods

Data sources and searches

PubMed, Embase, MEDLINE and the Cochrane Library were searched to identify randomized controlled trials (RCTs) up to August 2017. The key words included in the literature search were: physical activity, feedback and objective device and their synonyms (see Appendix 1 for complete PubMed search strategy). The study design RCT was added to the literature search. Reference lists from the included articles were screened to check and extend the search.

Study selection

Inclusion criteria for RCTs were studies published after 2007 in which: (i) the mean age of subjects was >21 years; (ii) subjects were (former) patients treated within the healthcare system; (iii) PA was used as an outcome measure for the intervention; (iv) PA was measured objectively with a wearable monitor; (v) feedback on objectively measured PA was part of the intervention; (vi) the main goal of the intervention was promoting PA; (vii) concurrent strategies, such as behavioral change techniques, were related primarily to PA; (viii) intervention groups received feedback on objectively measured PA as part of the intervention, whereas the control group received an intervention with no feedback on objectively measured PA or usual care.

Exclusion criteria were: (i) the full text was not available in English; (ii) the document was a conference or oral session abstract, research letter or commentarial note; (iii) interventions that combined disciplines, such as nutrition and psychology, which were not primarily related to PA.

Two reviewers (HB and MB) applied the inclusion criteria to the titles and abstracts independently to select potentially relevant studies from the search results. When disagreements occurred, HB and MB resolved them by discussion. If no agreement could be achieved, a third reviewer (JB) was consulted.

Methodological quality assessment

Methodological quality was determined by the risk of bias assessment.[18] Risk of bias was scored (low risk, high risk or unclear risk) per item independently by 2 researchers (HB and MB). Random-sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases were items that were reviewed. Judgement of blinding of participants and personnel was considered as low risk when no or incomplete blinding was not likely to influence the outcome, which is expected in studies in which the work of therapists is part of the intervention. When articles were not clear about items, MB and HB discussed the item and decided the score. Any disagreements were resolved by a third researcher (JB). Scores were processed using RevMan 5.3 (Cochrane Community.

Data extraction and synthesis

The following information was extracted from the included articles:

Study characteristics: Population characteristics, intervention and control setting, duration of intervention, PA outcome measure and reported significance of the effect on PA.

Intervention strategies: Wearable monitor used for feedback, feedback parameter, frequency, visualization, therapist/coach contact and BCT components used.

Effect size calculation

Different types of PA outcome measures were allowed. Nevertheless, all measures were continuous variables, therefore a standardized measure was used to calculate effect size. The standardized mean difference (SMD) was calculated by using the weighted inverse variance approach for fixed-effects meta-analysis models in RevMan 5.3. SMDs of the included studies were combined to calculate an overall summary effect (95% confidence interval (95% CI)), SMDs of 0.2 were considered small, 0.5 moderate and 0.8 large.[18] If studies were incomplete in reporting necessary PA measures (mean and standard deviation (SD)) for calculation of the SMD, corresponding authors were emailed to request the missing measures. If SDs were still missing, the calculator in RevMan 5.3 and method of Hozo *et al*.[19] was used to estimate missing values. A leave-one-out sensitivity analysis was performed by iteratively removing one study at a time in order to confirm that the current results were not driven by any single study. Inconsistency (heterogeneity, I2) was calculated in RevMan 5.3 and was interpreted according to the method of Higgins & Green.[18] I2 was low at 25%, moderate at 50% and high at 75%. In addition, comparable with the method of Kang *et al*.[20], the contribution of mediating effects was explored by grouping different study characteristics if heterogeneity was significant ($p < 0.05$).

Results

The literature search yielded 2,322 relevant articles after removing duplicates from the initial search (Fig. 1). After excluding articles published before 31 December 2006 and careful screening of titles and abstracts for inclusion and exclusion criteria, the full text of 64 records were checked. After consulting the third researcher regarding 2 records, all 3 researchers agreed that 14 studies met the inclusion criteria and these were included in the full review. Inclusion and exclusion was modelled using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)(Fig. 1).[21]

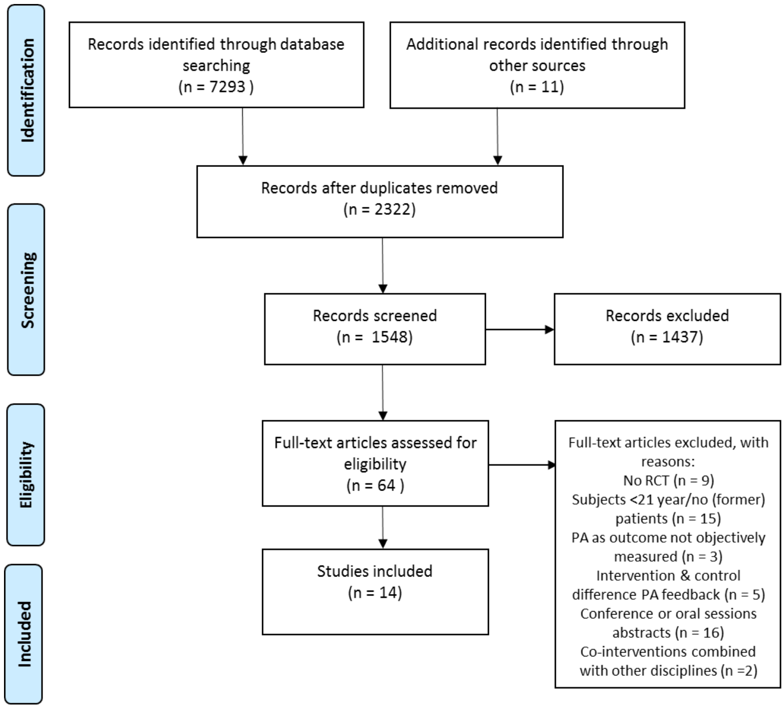

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA): flow diagram of selected studies.

Methodological quality

Full consensus was reached between researchers MB and HB on risk of bias assessment. Overall, the methodological quality of the included studies was moderate to acceptable (Fig. 2). The most frequent reason for high risk was detection[22–27] and attrition bias[22, 24, 28–30] due to lack of blinding of outcome assessors and high drop-outs, or to being unclear about incomplete outcome data. Blinding of participants and personnel was considered low risk in any study due the clinical intervention setting (Fig. 2). The randomization process was not clearly described in some studies [23, 24, 30–32]. In 7 studies, the authors had reasons to report other biases[22, 24, 27, 30–33]; for 3 studies the reason was that the RCT was a pilot RCT with a relatively small sample size[30, 31, 33]. Kaminsky *et al.*'s study had the highest methodological risk.[30]

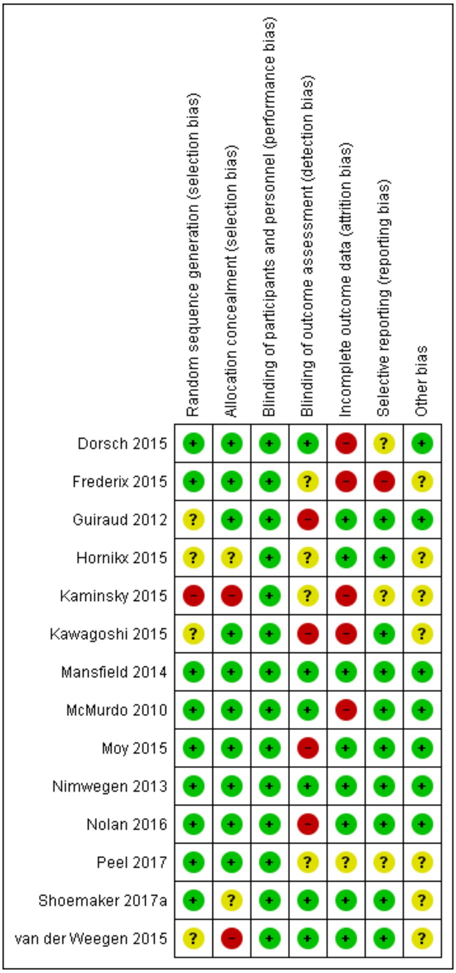

Fig. 2. Risk of bias assessment of included studies (n = 14).

Study characteristics

The studies varied with regard to the number and type of participants, duration and intervention characteristics (Table 1). The total number of participants in the included studies was 1,902, and the number of participants per study ranged from 16 to 586. Included populations were patients with chronic obstructive pulmonary disease (COPD), stroke, various cardio-vascular diseases, Parkinson's disease, and geriatric patients. The duration of interventions varied between 20 days[28] and 2 years[34]. The duration of 2 interventions was dependent on the length of inpatient rehabilitation[28, 35]. In 12 studies, all participants received usual care (UC), and the intervention group received an objective feedback PA intervention in addition to UC (Table 1). In the 2 other studies the control group received no care or wait list control[25, 29]. Five interventions were performed in an inpatient setting[22, 27, 28, 31, 35] and the other studies were outpatient- or home-based.

Outcome measures used to calculate the significance of the effect on PA were steps per day, walking time per day, energy expenditure (in kJ or kcal per day or per week), accelerometer counts per day, and time in moderate intensity PA per week. These outcomes were measured using a pedometer or accelerometer (Table 1). Steps/day was the most frequently used outcome measure. The significance of the effect on PA was calculated by the authors in 3 different ways: p-value of (i) difference in mean change between intervention and control group; (ii) difference between intervention and control group at follow-up; and (iii) difference between baseline and follow-up of the intervention and control group calculated separately (Table 1). The study by Frederix *et al*.[22] did not provide p-values of the effect on PA. Eight studies showed a significant positive effect in favour of using feedback from a wearable monitor in the intervention group ($p < 0.05$.)[23–25, 27, 29, 30, 32, 34]

Intervention strategies

Intervention strategies used in each study are shown in Table 1. Table 2 shows the frequency of intervention strategies used in the included studies. Five studies[24–26, 29, 30] used a pedometer for feedback and the others studies used accelerometers. The most frequently used feedback parameter is steps per day (Table 3). Furthermore, frequency of feedback varied between daily and monthly. In 4 studies, patients could choose when to view their PA level.[23, 25, 32, 34] In 8 studies, subjects could see their real-time PA on a display.[24–26, 29–32, 35] Four studies[22, 25, 30, 34] used no verbal interaction with a coach or therapist in real-life consultations or by telephone to provide feedback.

The following BCT components mentioned in the studies were identified: education (E), goal-setting (GS), barrier identification (BI) and/or problem-solving (PS), action planning (AP) and social support (SS) (Table 1). BCT components were used in a wide variety of combinations. Table 2 shows the frequency of BCT components present in all included studies. Five studies used 3 or more BCT components as concurrent intervention strategies.[23, 25, 29, 32, 34] GS was the most-often used BCT component (Table 2). GS and E were frequently combined with BI and/or PS. Only 1 study used social support.[25]

Effect estimates

Authors were contacted when data on PA to calculate SMD post-intervention were missing.[22, 24, 26, 29, 34, 35] SMDs of 11 studies were calculated based on original data, data sent by authors, or a combination of both. In 3 studies, the SD of the outcome measure at follow-up was estimated.[29, 31, 33] One of the intervention arms of McMurdo *et al*.[29] and Shoemaker *et al*.[33] was excluded from meta-analysis based on inclusion criteria. SMD of Frederix *et al*.[22] and Peel *et al*.[27] (respectively SMD = 4.64 and 4.73) was more than 3 times as large as SMD of other studies (SMD between –0.09 and

1.17), as shown in Fig. 3. Leave-one-out sensitivity analysis showed that after removing the study of Frederix *et al*.[22] (and Peel *et al*.)[27], the overall effect changed to SMD with a smaller confidence interval (SMD = 0.34 with 95% CI 0.23–0.44, z = 6.27, p < 0.01) and considerable less heterogeneity (I2 = 49%) (Fig. 3) compared with the overall effect size when they were included (SMD = 0.64 with 95% CI 0.52–0.73, z = 11.97, p < 0.01) and heterogeneity (I2 = 97%). Therefore, the SMD of Frederix *et al*.[22] (and Peel *et al*.)[27] were excluded from the meta-analysis and weight was reduced to 0% (Fig. 3). Heterogeneity was moderate but significant (I2 = 49%, p = 0.03, Fig. 3), which supported the exploration of the contribution of different study characteristics to the overall SMD. Pooled mean SMD per study characteristic is shown in Table 3. Outpatient- and home-based interventions had a larger effect (SMD = 0.37) on PA than inpatient interventions (SMD = 0.17). The shortest intervention durations (< 10 weeks) had the largest effect (SMD = 0.70). In populations with cardiac diseases objective feedback PA interventions had the largest effect (SMD = 0.70) on PA compared with other patient populations (SMD = 0.19–0.35).

Table 1. Overview of study characteristics, intervention strategies and reported effect on physical activity with outcome measure that was used.

Reference	Study characteristics						Intervention strategies					
	Population	*Population (n male / n female) mean age (SD)*	*Intervention & control setting*	*Duration*	*PA Outcome measure*	*Reported significane of effect*	*Wearable monitor used for feedback*	*Parameter*	*Frequency*	*Visualisa-tion*	*Thera-pist/ coach contact*	*BCT compo-nents*
Dorsch 2015	Stroke patients	**Intervention:** n = 78 (47/31) 61.8 (40.3) y **Control:** n = 73 (45/28) 65.0 (13.2) y	Inpatient RC (UC)	+/- 20 days, during inpatient rehabilitation	Walking time/day	NS (mean change IG vs. CG)	Accelerometer (Gulf Coast Data Concepts, Waveland, MS)	steps/day	3 x p/w	n/a	RLC	AP
Frederix 2015	Coronary artery disease patients	**Intervention:** n = 40 (34/6) 58 (9) y **Control:** n = 40 (32/8) 63 (10)y	Inpatient RC (UC)	18 weeks	Steps/day	n/a	Triaxial accelerometer (Yorbody company)	steps/day	weekly	WP	n/a	GS
Guiraud 2012	Non-compliant patients after a cardiac rehabilita-tion program	**Intervention:** n = 19 (17/2) 54.5 (12.6) y **Control:** n = 10 (7/3) 62.9 (10.7) y	Outpatient cardiac rehabilitation (UC)	8 weeks	EE (kcal/week)	Baseline vs. follow-up IG: P <0.01* Baseline vs. follow-up CG: NS	Accelerometer (MyWelness Key; Technogym SpA, IT)	time in moderate PA intensity	every 15 days or login by choice	WP	PC	E + GS + BI + AP
Hornikx 2015	COPD	**Intervention:** n = 15 (9/6) 68 (6) y **Control:** n = 15 (8/7) 66 (7) y	Inpatient (hospital) (UC)	4 weeks	Steps / day	Baseline vs. follow-up IG: p <0.05* Baseline vs. follow-up CG: <0.05*	Dynaport MoveMonitor (McRoberts BV, The Hague, the Netherlands)	Steps/day	3 times / week	RT	PC	GS + BI

Table 1. Continued

Reference	Study characteristics						Intervention strategies					
	Population	*Population (n male / n female) mean age (SD)*	*Intervention & control setting*	*Duration*	*PA Outcome measure*	*Reported significane of effect*	*Wearable monitor used for feedback*	*Parameter*	*Frequency*	*Visualisa-tion*	*Thera-pist/ coach contact*	*BCT compo-nents*
Kaminsky 2013	Inactive patients with cardiac diseases	**Intervention:** n = 10 (8/2) 53.3 (8.1) y **Control:** n = 8 (6/2) 59.4 (9.9) y	Home-based (UC)	8 weeks	Steps/day	Baseline vs. follow-up IG: p <0.05* Baseline vs. follow-up CG: NS	NL-1000 pedometers (New-Lifestyles, Inc. Lee's Summit,MO)	Steps/day	1 starting session	RT	n/a	GS
Kawagoshi 2014	Elderly with COPD	**Intervention:** n = 15 (14/1) 75 (9) y **Control:** n = 12 (10/2) 74 (8) y	Homebased rehabilitation (UC)	1 year	Walking time/day	p = 0.04* (mean change IG vs. CG)	Pedometer (Kens Lifecorder EX, Nagoya, Japan)	steps/day	monthly	RT	RLC	E + GS
Mansfield 2014	Stroke	**Intervention:** n = 29 (20/9) 64 (19) **Control:** n = 28 (16/12) 61.5 (13)	Inpatient RC (UC)	Based on length of inpatient rehabilitation	Steps/day	NS (mean change IG vs. CG)	Accelero-meter (Model X6-2mini, Gulf Data Concepts, LLC, Waveland, MS)	total walking time, steps/day, bout durations	daily	RT	RLC	GS
McMurdo 2010	Community dwelling elderly	**Intervention:** *pedometer + BCI:* n = 68 77.1 (4.9) y *(BCI alone group= excluded from meta-analysis)* **Control:** n = 68 77.0 (4.9) y	Home-based via primary care	6 months	Accelerometer count	Baseline vs. follow-up p = 0.02 * Baseline vs. follow-up CG: NS	Pedometer (Omron HJ-113, Healthcare UK Ltd, Milton Keynes, UK)[a]	steps/day	first month weekly, last months every 2 weeks	RT	PC	E + GS + BI + AP

Table 1. Continued

Reference	Study characteristics						Intervention strategies					
	Population	*Population (n male / n female) mean age (SD)*	*Intervention & control setting*	*Duration*	*PA Outcome measure*	*Reported significane of effect*	*Wearable monitor used for feedback*	*Parameter*	*Frequency*	*Visualisa-tion*	*Thera-pist/ coach contact*	*BCT compo-nents*
Moy 2015	COPD	**Intervention:** n = 154 (146/8) 67.0 (8.6) y **Control:** n = 84 (77/7) 66.4 (9.2) y	Home-based	4 months	Steps/day	Baseline vs. follow-up IG: p <0.01* Baseline vs. follow-up CG: NS	Pedometer (Omron HJ-720 ITC Healthcare Ltd, Milton Keynes, UK)	steps/day	1x p/w or every moment by choice	RT + WP	n/a	E + GS + SS
Nimwegen 2013	Patients with Parkinson's disease	**Intervention:** n = 299 (194/105) 65.1 (7.9) y **Control:** n = 287 (188/99) 65.9 (7.2) y	Homebased via hospital (UC)	Two years	EE (kcal/day)	P < 0.001* (mean change IG vs. CG)	Accelerometer (Directlife, Consumer Lifestyle, Philips, Amsterdam)	kcal/day	Monthly or login on website by choice	WP	RLC	E + GS + BI
Nolan 2017	COPD	**Intervention:** n = 76 (56/20) 69 (9) y **Control:** n = 76 (54/22) 68 (8) y	Outpatient PR (UC)	8 weeks	time spent expending >3METs/day	NS (mean change IG vs. CG)	Yamax Digi-walker CW700	steps/day	Every week	RT	RLC	GS + BI
Peel 2017	Elderly in geriatric rehabilita-tion	**Intervention: n = 128 (50/78) 81 (9) y Control: n = 127 (57/70) 82 (8) y**	Inpatient geriatric rehabilitation (UC)	4 weeks	minutes walking/day non-therapy hours	P = 0.001* (IG vs. CG at follow-up)	ActivPal (PAL technologies LTD, Glasgow UK)	minutes walking/day	Daily and every treatment session	n/a	RLC	GS

Table 1. Continued

Reference	Study characteristics						Intervention strategies					
	Population	*Population (n male / n female) mean age (SD)*	*Intervention & control setting*	*Duration*	*PA Outcome measure*	*Reported significane of effect*	*Wearable monitor used for feedback*	*Parameter*	*Frequency*	*Visualisa-tion*	*Thera-pist/ coach contact*	*BCT compo-nents*
Shoemaker 2017	Patients with heart failure and implantable verter defibrillator	Intervention: n = 6 62 (19) y (Exercise/health coaching group is excluded from meta-analysis) Control n = 4 63 (23) y	Home-based (UC)	3 months	Hours of activity / day	Baseline vs. follow-up IG: NS Baseline vs. follow-up CG: NS	ActiGraph GT3X triaxial accelerometer	Steps/day	Weekly	MA	RLC	E
Van der Weegen 2015	Diabetes type 2 and COPD	Intervention: n = 65 (34/31) 57.5 (7.0) y (SSP group excluded from meta-analysis) Control: n = 68 (37/31) 59.2 (7.5)	Homebased via GP (UC)	4 – 6 months	Average minutes of PA/day	P < 0.001* (mean change IG vs. CG)	Personal Activity Monitor AM300 (Pam)	average minutes of PA/day	In total 3 sessions or login by choice	RT + WP	RLC + PC	E + GS + BI + AP

*= significant effect on PA ↑ in intervention group $P<0.05$, n/a = not applicable, PA = physical activity, EE = energy expenditure, IG = intervention group, CG = control group, RC = rehabilitation center, GP = general practice, PR = pulmonary rehabilitation, (UC) = both intervention and control group received usual care, NS = not significant. Visualization: Real time display (RT) / web based portal (WP) mobile application (MA), Therapist or coach contact: Real-life-consultation, (RLC) / Phone call (PC) / text message or e-mail (TE), BCT components: Education (E)/ Goal-setting (GS)/ Barrier identification (BI) / Action planning (AP) / Social support (SS)

Table 2. Overview of frequency of specific intervention strategies that are used in the included studies

Intervention strategies		Frequency in n =14 included studies
Type of feedback monitor	Pedometer	5
	Accelerometer	9
Feedback parameter	Steps/day	9
	Energy expenditure (kcal / day)	2
	Duration of (MV)PA / day	3
Feedback frequency*	Daily	2
	≥ once per week	7
	Less than once per week	5
	Login by choice	4
Feedback visualization *	n/a	2
	Web portal or mobile application	6
	Real live display	8
Therapist/coach contact *	Real life consultation	8
	Phone call	4
	None	3
BCT components*	Education	7
	Goal-setting	12
	Barrier identification	6
	Action planning	4
	Social support	1

*multiple studies used a combination of multiple components
n/a= not applicable

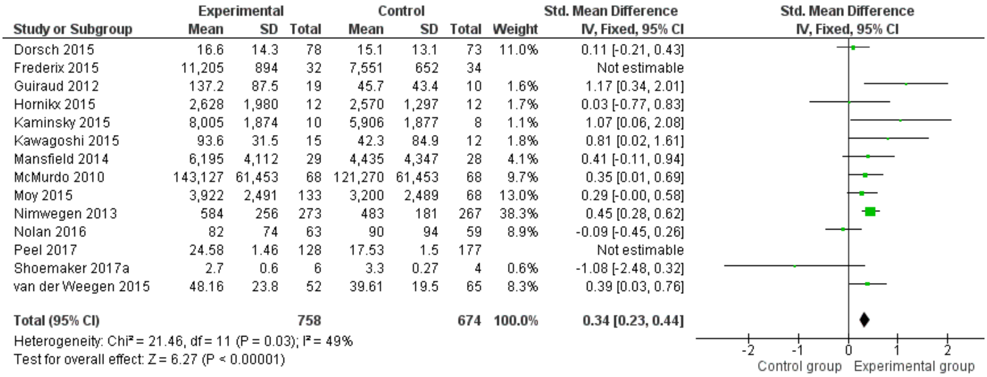

Fig. 3. Forest plots for physical activity outcome measures, overall estimate of the intervention effect.

Table 3. Pooled standardized mean differences per group of study characteristics

Study characteristics		N (total n = 14 studies)	Pooled mean SMD [CI]
Setting	Inpatient	5	0.17 [-0.08, 0.43] [a,b]
	Outpatient/home-based	9	0.37 [0.26, 0.49]
Duration	Dep. of rehabilitation length	2	0.19 [-0.08, 0.46]
	<10 weeks	4	0.70 [0.20, 1.20][b]
	10 - 20 weeks	3	0.30 [-0.06, 0.66][a]
	> 20 weeks	5	0.35 [0.23, 0.48]
Population	Stroke	2	0.19 [-0.08, 0.46]
	Cardiac patients	4	0.75 [0.16, 1.33][a]
	Geriatric	2	0.35 [0.01, 0.69] [b]
	Parkinsons	1	0.45 [0.28, 0.62]
	COPD	5	0.23 [0.05, 0.41]

[a] analyzed without Frederix 2015 based on leave-one-out sensitivity analysis
[b] analyzed without Peel 2017 based on leave-one-out sensitivity analysis

Discussion

To our knowledge, this is the first review to focus on interventions aiming at promoting PA that include feedback based on objective measurements of PA in healthcare settings. Overall, meta-analysis showed a moderately positive effect on PA, with the weight of evidence being in favour of the interventions using objective feedback on PA. Study characteristics varied widely across included studies. Pooled analysis of characteristics provided more insight into the effectiveness of setting, intervention duration, and target population. In addition, there was high variability in intervention strategies.

These results complement those of previous studies in finding that using objective feedback of PA via wearable monitors increases levels of PA. Previous meta-analyses[13, 15, 16, 20] also showed positive effects on PA in favor of the intervention groups. In contrast, the overall effect size of the current study 0.34 was lower than effect sizes of the other meta-analyses (> 0.50).[13, 15, 16] This may be explained by the type of populations included in the current study. The study focused on patients of healthcare institutions, who were mostly patients with (chronic) neurological or cardiovascular diseases. These patients may experience more barriers to increasing their PA compared with healthy individuals.[6] In addition, participants in the current study were slightly older (mostly around 65 years of age) compared with other studies. It is possible that older individuals increase their PA less because they experience difficulty using new technologies, such as activity monitors, to increase PA. Nevertheless, the overall positive results suggest that using wearable technology is also a promising tool to promote PA in healthcare settings.

Similar to other reviews[14, 16], large heterogeneity was found in the study characteristics. However, after excluding 2 studies based on leave-one-out sensitivity analyses, heterogeneity was acceptable. Mediating effects of study characteristics (setting, duration and population) were explored by calculation of pooled SMDs of grouped characteristics (Table 3). Regarding intervention setting, the effect sizes of studies were smaller in an inpatient setting compared with home-based interventions, suggesting that the difference between the intervention and control groups is smaller when both groups are situated in an inpatient setting, as stated by Dorsch *et al*.[28], who found comparable results. It can be assumed that both the intervention and control groups in inpatient populations were more dedicated to a strict treatment schedule. Thus, the chance that behavior of both the control and intervention groups was similar was higher compared with an outpatient- or home-based setting. In other words, a free-living environment allows more voluntary physical behavior. This statement may also explain the difference in magnitude of the overall effect in the current study (0.34) in comparison with, for example, the overall effect in the meta-analysis by Kang *et al*.[20] amongst mostly healthy and younger free-living populations (0.68).

Analysis of intervention duration in the current study agreed with the study of Goode *et al*.[17], since shorter intervention durations showed larger effects on PA compared with longer-lasting interventions. SMD calculation in the current study was based on post-intervention measurements. Adherence to use of wearables for a longer time in daily life may be more difficult, and thus the chance of relapsing to previous behavior is higher. Future studies should include more follow-up measurements to examine the sustainability of behavior change due to these interventions.

The frequency of applying different intervention strategies was explored in this study and the results emphasize the importance of combining objective PA feedback with BCT strategies (Table 2). All interventions included in this review were combined with multiple BCT components (Tables 1 and 2), assuming that researchers find BCT a substantial element for designing RCTs for promotion of PA in healthcare. In addition, Nolan *et al*.[26] explained the lack of improvement in PA by the low levels of added behavioral counselling. Nevertheless, BCT is an umbrella construct, and the BCT components in the studies included in the current review varied considerably. Not all studies described the content of the BCT sufficiently in the intervention and control groups, hence BCT could only be assessed approximately. Therefore, only careful suggestions for effect directions could be drawn regarding specific BCT components. Goal-setting, education and barrier identification are factors that are probably important, since they were often present in interventions with a relatively large positive effect size. Nevertheless, in 12 of the 14 included studies, the control group received usual care, and it can be assumed that, in most cases, BCT was also present in usual care. As Hakala *et al*.[16] have suggested previously; the effect size is influenced by the load of the control treatment. With respect to the current study, this could mean that the magnitude of the effect is relatively small because of the amount of BCT that is already present in usual care, and thereby also in control groups.

Study limitations

First, due to the heterogeneity in intervention strategies and treatments of control groups, the specific effect of the objective PA feedback component could not be determined.

Furthermore, the SMDs of PA were calculated based on post-intervention measurements assuming that the RCTs in this meta-analysis included an acceptable randomization procedure. However, baseline comparison of PA was often not taken into account in randomization procedures. Therefore, intervention and control groups may have differed in baseline PA, which might have influenced the results. Future studies should compare the intervention and control group based on mean changes between pre- and post-measurements. Another methodological limitation in the current meta-analysis concerns comparison of the intervention effects based on SMD. In the included studies, the SMDs were calculated using diverse PA outcome measures and generated by different methods of data-processing using various devices. These methodological differences between studies in accelerometer data-processing limit comparability.[36] Using a standardized version of the effect size, such as the SMD, only partly resolves the problem of comparing different PA outcomes measured using different devices.

In some studies the PA outcome parameter differed from the PA feedback parameter.[23, 24, 26, 28, 33] For example, Dorsch *et al*.[28] used the number of steps as feedback parameter and the walking time as outcome measure. Attempting to attain a goal based on a certain number of steps per day (amount of PA) is a different approach to measuring walking time (PA duration). This can lead to a mismatch between target parameters of PA promotion during the intervention and evaluation of PA.

Publication bias might have influenced the current results to some extent. Since congress abstracts, commentary articles and languages other than English were excluded, some studies with negative results regarding PA might have been missed. The methodological quality of the included studies was moderate; none of the studies scored "low risk" on all bias items. However, small sample sizes of a considerable proportion of the included studies, procedures of blinding of assessors, and incomplete data reporting limits the quality of evidence regarding intervention effects. Therefore, these results should be interpreted with caution.

Despite these limitations, this review provides useful indications for the use of wearable technology in rehabilitation programs. One of the indications is that, next to BCT, human interaction is recognized as an important feature, since contact with a coach or therapist in real life consultations or by phone calls was present in a large proportion of the included studies. Adopting innovative technologies, such as wearable monitoring, in rehabilitation therefore requires tight tuning with therapy programs. Blended interventions may offer a solution; innovative technological advancements, such as integrated goal-setting, automatic feedback functions, and real-time tele-consulting, can make human interaction and other BCT components more feasible, and less expensive, partly by reduction of the therapists' workload.[37] In addition, a systematic review by Geraedts *et al*.[38] showed that remote contact seems an acceptable-to-good alternative for real-life contact in PA interventions. A further advantage, according to Chiauzzi *et al*.[39], is that PA self-tracking has the potential to lead to positive patient engagement in healthcare interventions. Furthermore, patients are now becoming increasingly familiar with self-tracking technology.[39, 40] Overall, application of wearable technology has the potential to contribute to health behavior and self-management of patients, which may contribute to a more efficiently organized and financially attractive healthcare system. Further research is needed to determine the most effective intervention strategies, with regard to the amount and type of therapist contact and BCT components for specific patient populations. Literature studies with less heterogeneity in terms of study characteristics, intervention strategies and methodology are required.

Conclusion

Overall, healthcare interventions that provide objective feedback about PA, delivered by wearable monitors, compared with other strategies promoting PA showed a moderately positive effect on PA. Study characteristics and intervention strategies varied widely. Future research should focus on determining which intervention strategies are most effective in promoting PA in healthcare programs.

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Appendix 1:

Pubmed search strategy

#1: "motor activity" [Mesh:NoExp] OR "motor activity" OR "physical activity" OR exercise [Mesh:NoExp] OR exercise OR "exercise intensity" OR activity OR training OR swimming [Mesh:NoExp] OR swimming OR running [Mesh:NoExp] OR running OR walking [Mesh:NoExp] OR walking OR sedentary OR ''physical behavior'' OR movement OR stepcount* OR ''step count*''

#2: feedback [Mesh:NoExp] OR "feedback, Psychological" [Mesh:NoExp] OR "feedback, Physiological" [Mesh:NoExp] OR feedback OR motivat*

#3: accelerometry [Mesh:NoExp] OR accelero* OR pedomet* OR "cell phones"[Mesh:NoExp] OR ''cell phones'' OR smartphone OR telephone OR "mobile phone" OR monitor* OR microcomputer OR ambulatory OR ambulant OR device OR equipment OR sensor OR gps OR tracking OR stepcount* OR ''step count*''

#4: "Randomized Controlled Trial" [Publication Type] OR "Randomized Controlled Trials as Topic"[Mesh] OR ''randomized controlled trial'' OR RCT

CHAPTER 3

THREE DISTINCT PHYSICAL BEHAVIOR TYPES IN FATIGUED PATIENTS WITH MULTIPLE SCLEROSIS

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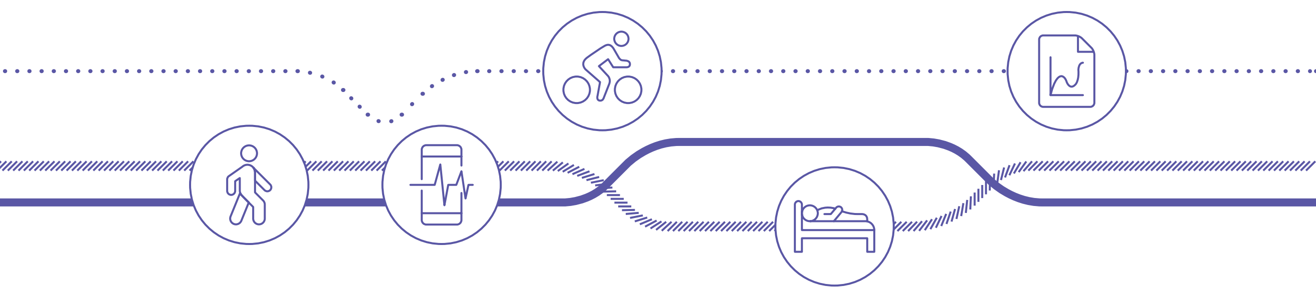
Journal of NeuroEngineering and Rehabilitation; 2019; *16*(1), 1-9.



Abstract

Background: Multiple sclerosis often leads to fatigue and changes in physical behavior (PB). Changes in PB are often assumed as a consequence of fatigue, but effects of interventions that aim to reduce fatigue by improving PB are not sufficient. Since the heterogeneous nature of MS related symptoms, levels of PB of fatigued patients at the start of interventions might vary substantially. Better understanding of the variability by identification of PB subtypes in fatigued patients may help to develop more effective personalized rehabilitation programs in the future. This study aimed to identify PB subtypes in fatigued patients with multiple sclerosis based on multidimensional PB outcome measures.

Methods: Baseline accelerometer (Actigraph) data, demographics and clinical characteristics of the TREFAMS-ACE participants (n = 212) were used for secondary analysis. All patients were ambulatory and diagnosed with severe fatigue based on a score of ≥35 on the fatigue subscale of the Checklist Individual Strength (CIS20r). Fifteen PB measures were used derived from 7 day measurements with an accelerometer. Principal component analysis was performed to define key outcome measures for PB and two-step cluster analysis was used to identify PB types.

Results: Analysis revealed five key outcome measures: percentage sedentary behavior, total time in prolonged moderate-to-vigorous physical activity, number of sedentary bouts, and two types of change scores between day parts (morning, afternoon and evening). Based on these outcomes three valid PB clusters were derived.

Conclusions: Patients with severe MS-related fatigue show three distinct and homogeneous PB subtypes. These PB subtypes, based on a unique set of PB outcome measures, may offer an opportunity to design more individually-tailored interventions in rehabilitation.

Trial registration: Clinical trial registration no ISRCTN 82353628, ISRCTN 69520623 and ISRCTN 58583714.

Keywords: Physical behavior, Multiple sclerosis, Principal component analysis, Cluster analysis

Background

Multiple sclerosis (MS) affects around 2.3 million (young) adults worldwide and leads to changes in the central nervous system that often result in impaired physical and cognitive functions.[1–3] Consequently, the majority of the patients experience fatigue and show different physical behavior (PB) compared to healthy controls.[4–6] In clinical practice, changes in PB are often assumed as a consequence of fatigue, but a number of studies show that PB and MS-related fatigue are only weakly associated.[5, 7, 8] In other words, the role of PB in MS-related fatigue is not straightforward. Several interventions, including exercise training, have been developed to reduce fatigue by improving physical behavior, but the results are insufficient [9]. One explanation for this is that in MS patients, not only the general symptomology is heterogeneous, but also the response to exercise seems highly heterogeneous.[10, 11] As a consequence, considerable variability might be present in the symptoms of fatigue, PB, and in their interaction across and within patients.[12, 13] This suggests that patients with similar levels of fatigue are likely to show varying PB, and that interventions do not match PB starting levels of all patients. More insight in the variability of PB in fatigued MS patients is needed, as better understanding will contribute to the development of more personalized interventions and improve disease management in rehabilitation.[10] To date, the heterogeneity of PB at the start of interventions for fatigued MS patients has not been considered.

To achieve a better and clinically meaningful understanding of the variability of PB in MS rehabilitation, identifying subtypes with comparable PB levels is a suitable approach. A potentially useful method therefore is data-driven clustering based on PB[14], as shown by previous studies in breast cancer patients and in patients with COPD [15]. Using PB as input for identification of subtypes is a challenge, because it is operationalized in several ways in MS.[16, 17] Often, PB is expressed with one outcome measure (e.g. number of steps, or amount of time in a certain activity level). Multiple aspects of PB, however, seem to be affected by MS compared to healthy controls[5], such as the duration and distribution of PB 'bouts', with bout defined as a uninterrupted period of a specific type of PB (e.g. sedentary behavior, moderate-to-vigorous physical activity [MVPA]). Only one outcome of physical activity (PA) might be insufficient to evaluate and effectively change a patient's PB, which makes it reasonable to quantify PB with multiple measures.[18] Assessment should take multiple dimensions such as intensity, type, duration and frequency into account, as well as temporal features, and these characteristics can all be expressed with several potentially relevant measures.[12, 16, 19, 20] Nevertheless, an overkill of measures on PB will limit the clinical interpretation and application, so it should be reduced to a set of measures with minor overlap. Literature shows that this can be realized by statistical data reduction techniques.[15]

Combining both data reduction techniques and data-driven clustering enables exploration of the variability of PB in patients based on multiple components of PB. To our knowledge, no study has identified subtypes based on PB in fatigued MS patients, taking the multidimensionality of PB into account. This study therefore aimed to identify subgroups based on PB among fatigued MS patients based on a set of multidimensional PB outcome measures. In addition, potential differences in other patient characteristics between subgroups were assessed.

Methods

Participants and data collection

This study used cross-sectional baseline data from the TREFAMS-ACE program[21] for secondary analysis (n = 266). TREFAMS is an acronym for the TReating FAtigue in MS program, and ACE refers to the ehabilitation treatment methods under study, i.e. Aerobic training, Cognitive Behavioral Therapy, and Energy Conservation Management. Data were collected from fatigued MS patients who met the following inclusion criteria: i) diagnosed with MS and severe fatigue indicated by a score of ≥35 on the fatigue subscale of the Checklist Individual Strength (CIS20r); ii) ambulatory status (i.e., Expanded Disability Status Scale (EDSS) score < 6); iii) no diagnosis of depression (i.e., Hospital Anxiety and Depression Scale score < 11); iv) no initiation or change to pharmacologic treatment for fatigue during the previous 3 months; and v) aged 18–70 years. The protocol for this study was approved by the Medical Ethics Committee of the VU University Medical Center and informed consent was provided by all participants.

Demographics, body mass index (BMI), type of MS, the disease severity score on the EDSS and fatigue with the CIS20r subscale were collected. The fatigue subscale of the CIS20r includes subjective experience of fatigue in the past 2 week based on eight items scored by a 7-point scale. The score ranges from 8 to 56 with higher scores representing more fatigue.[21] PB was assessed using a 3-dimensional accelerometer (ActiGraph GT3X+ model; 4.6 × 3.3 × 1.5 cm; 19 g) during 7 consecutive days.[8] Participants wore the accelerometer around their waist with an elastic belt during waking hours in their daily environment, except during water-related activities. The ActiGraph accelerometer has been proven valid and reliable in patients with MS.[22]

Physical behavior measures

Accelerometer pre-processing was performed as described by Blikman et al.[5] The accelerometer signals were sampled with a frequency of 30 Hz and analyzed using ActiLife (6.6.2) and MATLAB (R2011b) and the same cut-off boundaries for intensity categories (sedentary, light and MVPA) were used[5]. Accelerometer data had to be available for at least 5 days with a minimum wear time of 660 min. Since PB is approached multidimensional, PB measures were divided into three categories (amount and intensity, frequency and duration, and day patterns). Categories were based on recommendations in literature on operationalization.[5, 16, 20, 23] Each category was divided into two domains, physical activity (PA) and sedentary behavior (SB)[18], which included one or more representative outcome measures calculated by the Actigraph data (Additional file 1).

Data analysis

Principal component analysis

Operationalization of PB measures led to 15 measures in three categories and two domains (Additional file 1), standardized in Z-scores. Principal component analysis (PCA) in SPSS v24.0 was used to reduce the amount of outcome measures. The Kaiser-Meyer-Olkin (KMO) test (KMO value > 0.5) was used to verify whether the 15 measures were suitable for PCA. Before conducting PCA, outlier analysis as recommended by Hair & Black was executed[24]. Single outlier measurements were changed into missing values. PCA was performed using orthogonal direct oblimin rotation since correlations between components were expected due to some overlap between the categories and domains of PB. Selection of the amount of PB outcomes was based on the number of components with eigenvalues ≥1. Number of components was not confirmatory due to the exploratory nature of the analysis. One outcome measure was chosen per component based on high loadings. When multiple outcome measures showed high or comparable loadings, the choice of outcome measure was based on pragmatic reasons to provide a set of measures that is simple to interpret.

Cluster analysis

The Z-scores of the PB measures identified in the PCA were uses as input for cluster analysis in SPSS v24.0. Before performing cluster analysis, patients with one or more outlier measurements based on PB were removed. Due to the exploratory nature of the present study and the lack of a priori knowledge of the number of clusters, a two-step combination of a hierarchical and non-hierarchical approach was used[24]. First, agglomerative hierarchical cluster analysis (with squared Euclidian distance) was performed to identify the number of clusters. Decision regarding the number of clusters was based on the rescaled distances in the dendrogram and the percentage of change in agglomeration coefficients at each phase of clustering.[24] Hereafter, a non-hierarchical K-means cluster analysis was performed to improve the initial cluster solution and to minimize the variation within the clusters. Cluster validation was performed by a double-split cross-validation.[25] After splitting the dataset randomly into halves, hierarchical and non-hierarchical cluster analysis was repeated for both datasets. New cluster membership and the cluster centers were saved in an aggregate file. Then, k-means analysis was repeated with the cluster centers of the other random set as input for the next k-means analyses, resulting in two possible cluster solutions per set. Cluster solutions were compared for both sets separately to provide information on sensitivity with Cramer's V; Cramer's V closer to one indicates a higher level of agreement.[26]

Between-cluster differences

Between-cluster differences regarding the demographic and clinical characteristics were evaluated with ANOVA, Kruskall-Wallis and chi-square tests in SPSS v24.0. For the ANOVAs, Bonferroni's post-hoc test was performed. For the Kruskall-Wallis tests, separate Mann-Whitney U tests were conducted as post-hoc tests. A p-value of < 0.05 was considered statistically significant.

Results

Table 1 presents demographic and clinical characteristics of participants for whom Actigraph baseline measurements were available for at least 5 days (n = 212).

A small percentage (0.48%) of all data points, concerning four patients, were considered as outliers and resulted in exclusion. All outlier measurements deviated four to seven times the standard deviation of the mean for several PB measures and were removed 24.

Table 1. Characteristics of the study participants (n = 212)

Males/Females		56/156
Age in years, mean (SD)		47.9 (10.4)
Body mass index, mean (SD)		24.1 (4.6)
Type of MS, %	Relapsing - remitting	155 (73.1%)
	Primary progressive	22 (10.4%)
	Secondary progressive	21 (9.9%)
	Other/unknown	14 (6.6%)
EDSS, median (IQR)		2.5 (1.5)
Duration MS in years, median (IQR)		6.4 (7.5)
Fatigue (CIS20r), mean (SD)		43.8 (7.3)

EDSS = Expanded Disability Status Scale, CIS20r = Checklist Individual Strength

Principal component analysis

The dataset met the KMO criteria for conducting PCA (KMO = 0.708). PCA identified five key PB components; eigenvalues and explained variance per component are reported in Table 2. Total explained variance was 80.1%. Component 1 was mainly characterized by high loadings on amount and intensity measures, except for total time in sedentary bouts. Components 2 and 5 were characterized by change scores of MVPA and sedentary behavior from morning to afternoon, or afternoon to evening. All high loadings on component 4 were physical activity measures of frequency and duration, whereas high loadings on component 3 were sedentary behavior measures of frequency and duration. The percentage sedentary behavior (%SB), total time (tt) MVPA and sedentary behavior/number of bouts (SB NoB) were chosen as key outcome measures representing the amount and intensity, and the frequency and duration measures. Regarding day pattern measures,%MVPA afternoon minus %MVPA morning (dMVPA1) vs. %SB afternoon minus %SB morning (dSB1), and %MVPA evening minus %MVPA afternoon (dMVPA2) vs. %SB evening minus %SB afternoon (dSB2) showed similar loadings on components. To be consistent in choosing domains, to simplify interpretation we opted for dSB1 and dSB2 since they showed overall highest factor loadings.

Table 2. Parameters of physical behavior (i.e. physical activity and sedentary behavior) divided into categories and with their explained variance (%), eigenvalues and loading on the PCA components. For each outcome measure, the highest loading is in bold

			Component				
			1	**2**	**3**	**4**	**5**
		%Variance (total = 80.1%)	*39.59*	*13.21*	*10.53*	*9.07*	*7.68*
		Eigenvalues	*5.94*	*1.98*	*1.58*	*1.36*	*1.15*
Amount and intensity	PA	%Active	**0.97**	0.02	0.04	-0.10	-0.04
		%MVPA	**0.78**	0.07	-0.08	0.36	-0.10
		CPD	**-0.97**	-0.02	-0.04	0.10	0.03
		CPM	**0.88**	0.09	0.04	0.20	-0.09
	SB	%SB	**0.92**	0.07	-0.06	0.18	-0.08
Frequency and duration	PA	MPVA BL	-0.04	0.08	-0.09	**0.64**	0.01
		MVPA NoB	-0.04	-0.10	0.39	**0.48**	0.04
		tt MPVA	0.42	-0.06	0.04	**0.67**	-0.07
	SB	SB BL	-0.63	0.06	**-0.64**	0.15	-0.03
		SB NoB	-0.16	0.07	**0.94**	-0.01	-0.05
		tt SB	**-0.83**	0.16	0.18	0.16	-0.12
Day pattern	PA	dMVPA1	-0.07	**-0.94**	0.02	0.05	-0.02
		dMVPA2	-0.03	0.21	0.07	-0.21	**0.79**
	SB	dSB1	-0.02	**0.91**	0.05	0.08	0.04
		dSB2	0.00	0.07	0.06	-0.21	**-0.93**

PA = physical activity, MVPA = moderate to vigorous activity, CPD = counts per day, CPM = counts per minute, SB = sedentary behavior, BL = bout length, NoB = number of bouts, tt = total time, dMPVA1= %MPVA afternoon minus %MVPA morning, dMVPA 2 = %MVPA evening minus %MVPA afternoon, dSB1 = %SB afternoon minus %SB morning, dSB2 = %SB evening minus %SB afternoon

Cluster analysis

Agglomerative hierarchical and k-means clustering using%SB, tt MVPA, SB NoB, dSB1 and dSB2 as input parameters resulted in three clusters (cluster 1: n = 46, cluster 2: n = 114, cluster 3: n = 48) as shown by Z-scores in Figure 1. Cluster 1 can be characterized by a moderate%SB, a low dSB1 value and a high dSB2 value compared to the other clusters. Cluster 2 can be characterized by the highest percentage of SB. Cluster 3 is characterized by the highest value on tt MPVA. SB NoB is comparable for all clusters. Cluster validation was acceptable based on double-split cross-validation (Cramer’s V = 0.7).

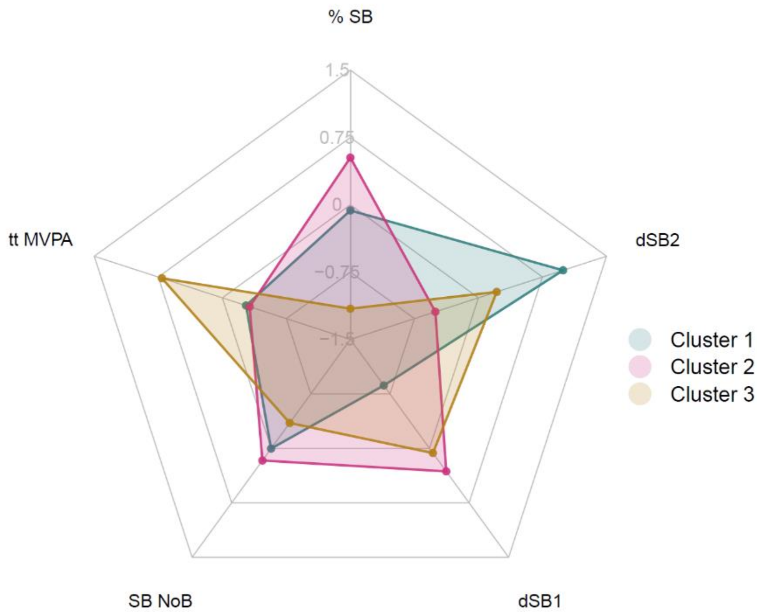


Fig. 1. Plot of Z-scores of five key outcome measures of PB per cluster

Between-cluster differences

The vast majority of PB measures showed significant differences between clusters (Table 3). Figure 2 presents the %SB per day part per cluster and provides insight into differences between dSB1 and dSB2 between clusters. Table 3 shows that dSB1 and dSB2 differ significantly between clusters. Also, Table 3 and Figure 2 show that cluster 1 is more sedentary in the afternoon compared to the morning (negative dSB1 Z-score), whereas cluster 2 is less sedentary in the afternoon compared to the morning (positive dSB1 Z-score). Cluster 1 and 2 show similar SB in the morning and evening, but cluster 2 is significantly more sedentary in the afternoon. Cluster 3 consisted of the youngest patients (44.4 ± 10.6 years), with age being significantly different compared to cluster 1 (49.8 ± 8.7 years) ($p = 0.035$) (Table 3). EDSS score showed a significant difference between cluster 1 and cluster 3 ($p < 0.001$) and cluster 2 and 3 ($p < 0.001$). Cluster 3 showed the lowest median EDSS score (2 vs. 3). There were no significant differences in BMI and CIS20r-fatigue scores between the clusters ($p = 0.166$ and $p = 0.178$, respectively).

Table 3. Between-cluster differences in patient characteristics and physical behavior measures

		Gender (%male)	TypeMS (% per type)	Age mean ± SD (min-max)	BMI mean ± SD (min-max)	EDSS median (IQR)	Fatigue (CIS20r) mean ± SD (min-max)	Years MS median (IQR)	% SB mean ± SD (min-max)	tt MVPA mean ± SD (min-max)	SB NoB mean ± SD (min-max)	dSB1 mean ± SD (min-max)	dSB2 mean ± SD (min-max)
Cluster 1 (n = 46)		30.4	RR: 80.4 PP: 8.7 SP: 8.7 E/U: 2.1	49.8 ± 8.7 (32.1 – 66.7)	25.1 ± 3.75 (18.5 – 34.8)	3 (1.9)	42.3 ± 7.2 (26 - 56)	6.9 (10.3)	63.8 ± 7.5 (50.9 - 82.6)	94.1 ± 67.5 (0.0 - 304.7)	766.6 ± 178.2 (421.0 - 208.0)	-8.8 ± 8.3 (-29.8 - 14.8)	19.5± 6.8 (4.1 - 33.3)
Cluster 2 (n= 114)		27.2	RR:68.1 PP: 11.5 SP: 12.4 E/U: 8.0	46.0 ± 10.7 (19.6 – 66.6)	25.6 ± 5.2 (17.2 – 44.8)	3 (2)	44.2 ± 7.4 (14 – 56)	6.7 (11.9)	69.0 ± 6.2 (56.7 - 84.6)	89.6 ± 62.5 (0.0 - 269.2)	794.7 ± 177.4 (373.0 - 1228.0)	2.1 ± 7.3 (-25.3 - 24.8)	6.8 ± 6.6 (-12.2 - 21.5)
Cluster 3 (n = 48)		18.8	RR: 83.3 PP: 6.3 SP: 4.2 E/U: 6.3	44.4 ± 10.6 (24.7 – 68.1)	24.1 ± 3.4 (16.7 – 43.2)	2 (1.5)	44.0 ± 6.6 (24 – 54)	4.9 (12.4)	54.2 ± 6.0 (40.5 - 70.7)	195.9 ± 97.8 (41.8 - 452.0)	706.1 ± 135.6 (292.0 - 1003.0)	-0.2 ± 8.6 (-30.4 - 24.5)	12.9 ± 7.3 (-1.7 - 28.2)
P		*0.393*	*0.501*	*0.032**	*0.166*	*<0.001**	*0.178*	*0.389*	*<0.001**	*<0.001**	*0.009**	*<0.001**	*<0.001**
Post-hoc test	***P (1 vs 2)***			*0.111*	*1.000*	*0.454*	*0.067*	*1.000*	*<0.001**	*0.809*	*0.391*	*<0.001**	*<0.001**
	P (1 vs 3)			*0.035**	*0.839*	*<0.001**	*0.168*	*0.510*	*<0.001**	*<0.001**	*0.118*	*<0.001**	*<0.001**
	P (2 vs 3)			*1.000*	*0.175*	*<0.001**	*0.741*	*1.000*	*<0.001**	*<0.001**	*0.002**	*0.063*	*<0.001**

RR = relapsing – remitting, PP = primary progressive, SP = secondary progressive, E/U = else or unknown, % SB = percentage sedentary behavior, SB no. bouts = number of bouts in sedentary behavior, tt MVPA = total time in moderate to vigorous activity, dSB1 = %SB afternoon minus %SB morning, dSB2 = %SB evening minus

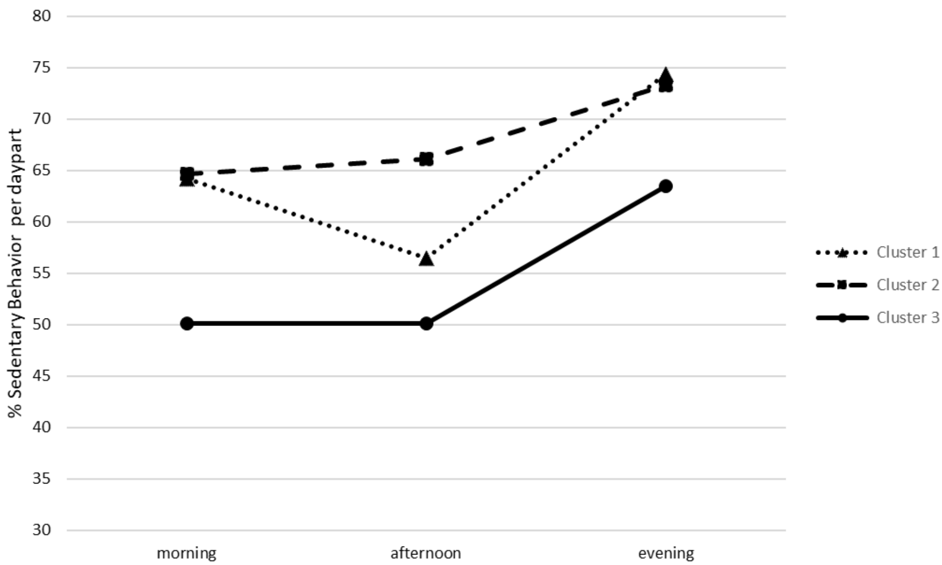


Fig. 2. Percentage of sedentary behavior of clusters in the morning, afternoon and evening

Discussion

This study aimed to identify subtypes in fatigued MS patients based on multidimensional PB measures. The results show that fatigued MS patients can be categorized in three subtypes with substantial differences in PB. The majority of the patients were classified as cluster 2 and characterized by the highest percentage of sedentary behavior. The most active patients (cluster 3) were characterized by youngest age, and lowest EDSS.

A unique aspect of the cluster analysis was that multiple objective 7-day PB measures in different dimensions specified by PCA were used as input. The main goal of the data reduction by PCA was to avoid an unnecessary number of measures that actually provide similar information and in addition, interpretation of differences between clusters based on fewer outcome measures is preferred. The five components determined by PCA accounted together for 80.1% of the total variance, which is higher than a similar study using PCA in multiple PB measures (60%).[15] The five components discriminated well but only in the category 'frequency and duration' the component loadings differentiated between the domains physical activity and sedentary behavior (Table 2). Component loadings in the categories 'amount and intensity' and 'day pattern' were more comparable between the domains physical activity and sedentary behavior.

Data-driven cluster analysis yielded three distinct PB subtypes with more homogeneous PB from a heterogeneous sample of fatigued MS patients. The number of patients in each cluster varied. Similar cluster analysis studies also showed an unequal distribution of patients in the clusters.[15, 27, 28] In contrast to similar studies using objective PB measures in other patient populations, we conducted double split cross-validation, which supports performing cluster analysis in this dataset. Even though the number of patients was not equally divided across clusters, results of the validation showed that the sensitivity of our cluster analysis was acceptable.

Comparison of PB between clusters showed that the vast majority of the five key outcome measures showed significant differences (Table 3). Cluster 2 was almost 15% more sedentary based on %SB compared to the most active cluster (cluster 3), meaning that during a day with 16 waking hours, the sedentary patients spent almost 2.5 h in more sitting or lying. Compared to cluster 1, patients in cluster 2 spent around 50 min more in sedentary behavior. However, cluster 1 (SB = 63.8%) and cluster 2 (SB = 69%) patients seem to be slightly less sedentary compared to other chronic neurological conditions, such as stroke (%SB = 74.8%)[29] and Parkinson's disease (%SB = 75%).[30] Remarkably, the %SB of cluster 1 showed a significant difference compared to cluster 2, whereas, in contrast, the number of sedentary bouts (SB NoB) was similar. Patients in cluster 2 divided their sedentary behavior into longer uninterrupted bouts and can be seen as more willingly and uninterruptedly sedentary compared to patients in cluster 1. In addition, Figure 1 shows that both day pattern measures were main causes of the distinction between cluster 1 and 2. In the afternoon, patients in cluster 1 seem to be less sedentary compared to cluster 2, however, they showed similar behavior in the morning and evening (Figure 2). A possible reason could be that patients in cluster 1, are less engaged in daytime jobs and have more time to be active during the day. Conversely, it is also possible that patients in cluster have more need for an afternoon nap. These findings support earlier studies[20, 31] reporting that the temporal feature of PB is useful to understand patients' PB. Noteworthy is that dSB1 and dSB2 are relative change scores and they are not completely independent of each other, since both include SB in the afternoon. Nevertheless, component loadings show minor interrelatedness (Table 2). Although challenging, only one easy-to-interpret outcome measure that represents day pattern is recommended in future studies.

In cluster 1 and 2, the minimum of tt MVPA was zero and the standard deviations were relatively high, meaning that several patients did not, or barely met the intensity threshold for MVPA. As a result, a substantial part of these patients did not perform activities with intensities > 3 METs in daily life, such as heavy household activities or sporting activities like brisk walking and cycling. Nevertheless, it can be considered that tt MVPA was the most distinctive measure for cluster 3 compared to the other clusters (Figure 1). Every patient in cluster 3 met the threshold for at least 41 min per week. Since these active patients even showed slightly less %SB (54.2 ± 6.0%) compared to their healthy peers (57.5 ± 9.4%)[5], it can be concluded that their PB is not affected by MS-related fatigue. In addition, cluster 3 consisted of the youngest patients. Similar results regarding age were found in studies with healthy subjects.[32] In general, older adults are less active than young adults because of e.g. sports and commuting activities.[32] Also other cluster analysis studies showed similar results regarding age.[15, 27, 28]

The most important finding was that patients with similar fatigue levels showed large differences in PB. Magnitudes of differences (e.g. 2.5 h more sedentary per day divided into long uninterrupted bouts) can be considered as clinically relevant. Patients who are willingly and mostly uninterruptedly sedentary, like patients in cluster 2, require a different approach compared to patients with similar PB as healthy controls (cluster 3). Other studies support the idea of tailoring intervention approaches, since they showed that sedentary patients are often not willing to change behavior and have low awareness of their personal physical activity levels.[33, 34] In contrast, active patients seem to cope better with their feeling of fatigue since their PA levels are not affected. In other words, fatigue is apparently not a reason to be sedentary for every patient. Likely, motivating patients in cluster 3 to increase their levels of PA even more will not decrease the feeling of fatigue. This supports the thought that the relation between fatigue and PB is not straightforward and as a reason, targeting primarily on PB, even when personalized, will not lead to reduced levels of fatigue for every patient. Still, it is important to maintain a healthy lifestyle including appropriate levels of PA in order to improve other symptoms than fatigue, such as disability, quality of life and incidence of comorbidity.[35, 36] Insight in the PB profile with multiple PB measures therefore has potential as a starting point during counseling sessions to further interrogate the underlying causes of a patients affected PB. Nevertheless, future interventions that target at PB should also consider baseline PB levels since it is highly variable in fatigued MS patients.

Study limitations

Several limitations of this study need to be addressed. First, since we were restricted to outcome measures that could be calculated from the Actigraph, our selection of PB outcome measures might not be completely comprehensive, we did not measure specific movements or postures like sitting, walking, cycling or running. Comparison with other MS studies is thereby limited since they used other devices and settings.[16] Besides, comparing PB outcomes of different studies and devices should be done with caution, since different operationalization of PB can result in systematic differences in outcomes.[37] Second, since cross-sectional baseline data of the TREFAMS-ACE study were used, no causal associations between PB and fatigue can be drawn. Nevertheless, all participants in this sample 'approved' the TREFAMS-ACE interventions and our results support that the PB starting levels were considerably different. Also, the inclusion criterion of severe fatigue was determined with the CIS20r which resulted in no differences in fatigue between clusters. Subsequently fatigue was not heterogeneous in our study sample and generalizability to the total MS population might be limited. Finally, removing outliers from the dataset was rather based on highly exceptional PB and not on technical errors. In four patients, one or more PB measures deviated four to seven times a SD from the mean. In order to maintain generalizability to the fatigued MS population and to successfully conduct our statistical techniques it was decided to exclude four patients.

Conclusion

This is the first study that explored identification of sub-types based on multidimensional PB in severely fatigued MS patients. Three distinct PB subtypes could be distinguished. The PB subtypes, based on a unique set of PB outcome measures are promising for the design of more individually-tailored PB interventions in rehabilitation. Further research should focus on the clinical feasibility of PB subtypes in the design of interventions.

Abbreviations:

MS: Multiple Sclerosis
PB: Physical behavior
CIS20r: fatigue domain of the Checklist Individual Strength
EDSS: Expanded Disability Status Scale
BMI: body mass index
MVPA: moderate-to-vigorous-physical-activity
PCA: principal component analysis
KMO: Kaiser-Meyer-Olkin
PA: physical activity
SB: sedentary behavior
NoB: number of bouts,
tt: total time
TREFAMS-ACE: TREating FAtigue in Multiple Sclerosi - Aerobic training, Cognitive Behavioral Therapy

Acknowledgements

This study was performed on behalf of the Treating Fatigue in Multiple Sclerosis: Aerobic Training, Cognitive Behavioral Therapy, Energy Conservation management (TREFAMS-ACE) Study Group: V de Groot and H Beckerman (program coordination), A Malekzadeh, LE van den Akker, M Looijmans (until September 2013), SA Sanches (until February 2012), J Dekker, EH Collette, BW van Oosten, CE Teunissen, MA Blankenstein, ICJM Eijssen, M Rietberg. VU University Medical Center, Amsterdam;
M Heine, O Verschuren, G Kwakkel, JMA Visser-Meily, IGL van de Port (until February 2012), E Lindeman (until September 2012), Center of Excellence for Rehabilitation Medicine, University Medical Centre Utrecht and Rehabilitation Centre, De Hoogstraat, Utrecht;
LJM Blikman, J van Meeteren, JBJ Bussmann, HJ Stam, RQ Hintzen. Erasmus MC, University Medical Center, Rotterdam;
HGA Hacking, EL Hoogervorst, STFM Frequin. St Antonius Hospital, Nieuwegein;
H Knoop, BA de Jong (until January 2014), G Bleijenberg (until April 2012). University Medical Center St Radboud, Nijmegen;
FAJ de Laat, Libra Rehabilitation Medicine & Audiology - location Leijpark, Tilburg;
MC Verhulsdonck, Rehabilitation Center, Sint Maartenskliniek, Nijmegen;
EThL van Munster, Jeroen Bosch Hospital, Den Bosch;
CJ Oosterwijk, GJ Aarts (until March 2013). Dutch Patient Organisation, Multiple Sclerosis Vereniging Nederland (MSVN), The Hague.
The authors would like to thank Lyan Blikman PhD, Martin Heine PhD and Lizanne van den Akker PhD, for sharing their baseline TREFAMS RCT data.

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Additional file 1: Operationalization of physical behavior measures.

Amount & intensity categories:

- *Mean counts per day (CPD):* the total counts per day based on wear time.
- *Mean counts per minute (CPM):* the mean number of counts per minute per day based on wear time.
- *% active per day (% Active):* percentages of wear time when patients spend time active. 'Active' was defined as PA spent above 150 CPM.
- *% MVPA per day (%MVPA):* percentages of wear time when patients spend time moderately to vigorously active. MVPA was defined as PA spent equal or above 2691 CPM.
- *% SB per day (%SB):* percentages of wear time when patients spend time sedentary. SB was defined as SB spent equal or below 150 CPM.

- Frequency & duration:
  Frequency and duration measures were assessed according to the method of Chastin & Granat (2010). A MVPA bout was defined as at least 1 minute of CPM ≥ 2691. A SB bout was defined as at least 1 minute of CPM below ≤ 150.

- *MVPA bout length (MVPA BL):* mean bout length of MVPA bouts per day.
- *MVPA number of bouts (MVPA NoB):* mean number of MVPA bouts per day.
- *Total time in MVPA bouts (tt MVPA):* total time spent in MVPA more than 1 minute consecutive.
- *SB bout length (SB BL):* mean bout length of SB bouts per day.
- *SB number of bouts (SB NoB):* mean number of SB bouts per day.
- *Total time in SB bouts (tt SB):* total time spent in SB more than 1 minute consecutive.

Day patterns

Day patterns were analyzed by method of Wolvers et al. (2018). Day pattern parameters represent the change score of percentages MVPA and SB between day parts. Day parts were divided based on time of the day: morning (5:00 AM to 12:00 M), afternoon (12:00 M to 6:00PM), and evening (6:00 PM to 12:00 AM).

- *Change score MVPA morning vs. afternoon (dMVPA1):* dMPVA1 = $MVPA_{afternoon}$ - $MVPA_{morning}$
- *Change score MVPA evening vs. afternoon (dMVPA2):* dMVPA2 = $MVPA_{evening}$ – $MVPA_{afternoon}$
- *Change score SB morning vs. afternoon (dSB1):* dSB1 = $SB_{afternoon}$ - $SB_{morning}$
- *Change score SB evening vs. afternoon (dSB2):* dSB2 = $SB_{evening}$ - $SB_{afternoon}$

CHAPTER 3

CHAPTER 4

INTENSITY OF DAILY PHYSICAL ACTIVITY A KEY COMPONENT FOR IMPROVING PHYSICAL CAPACITY AFTER MINOR STROKE?

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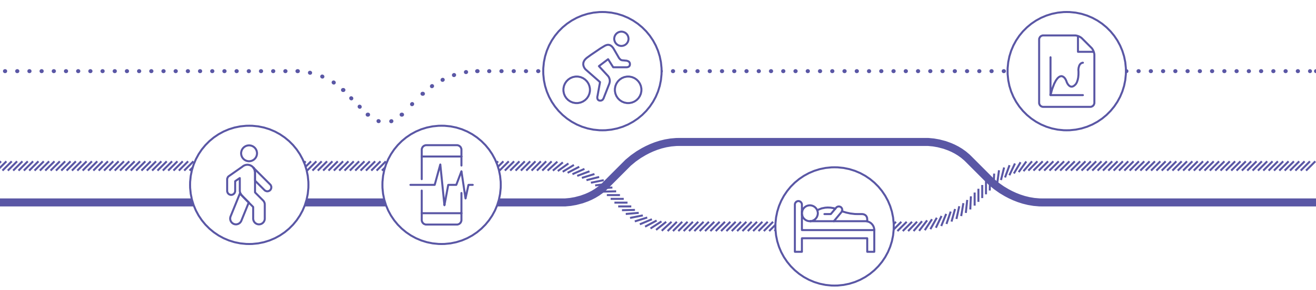
Disability and Rehabilitation 2020; *Advance online publication*, 1-6.



Abstract

Purpose: Elucidating the complex interactions between physical activity (PA), a multidimensional concept, and physical capacity (PC) may reveal ways to improve rehabilitation interventions. This cross-sectional study aimed to explore which PA dimensions are related to PC in people after minor stroke.

Materials and methods: Community dwelling individuals >6 months after minor stroke were evaluated with a 10-Meter-Walking-Test (10MWT), Timed-Up & Go, and the Mini Balance Evaluation System Test. The following PA outcomes were measured with an Activ8 accelerometer: counts per minute during walking ($CPM_{walking}$; a measure of intensity), number of active bouts (frequency), mean length of active bouts (distribution), and percentage of waking hours in upright positions (duration). Multivariable linear regression models, adjusted for age, sex and BMI, were used to assess the relationships between PC and PA outcomes.

Results: Sixty-nine participants [62.2 ± 9.8 years, 61% male, 20 months post onset (IQR 13.0–53.5)] were included in the analysis. $CPM_{walking}$ was significantly associated to PC in the 10MWT (std. ß = 0.409, p = 0.002), whereas other associations between PA and PC were not significant.

Conclusions: The PA dimension intensity of walking is significantly associated with PC, and appears to be an important tool for future interventions in rehabilitation after minor stroke.

Introduction

Worldwide, stroke is one of the leading causes of death and disability [1.] In the Netherlands, around 56% of stroke survivors, the majority diagnosed with "minor stroke", do not participate in a rehabilitation program (whether community based, outpatient or inpatient) because they recuperate relatively quickly and experience almost no visible motor symptoms.[2,3]

Although these individuals are all screened for cardiovascular risk factors, reductions in physical capacity (PC) — defined as what an individual can do in a standardized environment [4,5] —may go unnoticed.[6,7] Indeed, significantly reduced levels of PC after minor stroke may be observed more than six months post-onset.[8] This an important finding, as PC is related to functioning, overall health, well-being, and reduction of cardiovascular risk factors for recurrent strokes.[9–14]

Optimizing PC is therefore a major target of stroke rehabilitation whether it involves aerobic exercise or strength training.[15,16] Another applied strategy to improve PC is to enhance a person's daily physical activity (PA) by stimulating an active lifestyle.[13,17] PA and PC are intertwined constructs. Research has shown that higher levels of daily PA are correlated to higher PC.[17] Therefore, maintaining or regaining a physically active lifestyle might be an accessible and affordable way to optimize PC.[13,18]

PA is an umbrella construct covering multiple dimensions such as frequency, intensity, duration and distribution of PA.[19–21] Therefore, to evaluate PA sufficiently, PA after minor stroke should be expressed using more than one dimension.[19] However, given this multidimensionality, it is expected that not all PA dimensions will be similarly related to PC outcomes. For example, the review by Wiener *et al*.[22] indicates that being physically active at a high intensity has a more substantial effect on diverse capacity measures (for example, the 10MWT, Berg Balance Scale, Timed Up & GO) compared to moderate intensity. Further, more prolonged PA bouts (e.g., >10 min) have a more positive effect on PC compared to shorter bouts.[23] In the present study, in accordance with Wiener *et al*.[22], we considered PC to be a comprehensive term represented by independent validated tests so as to obtain insight into several PC components.[4] Unraveling the complex interactions between PA and PC outcomes will aid in improving the effectiveness of interventions and guidelines.[24] Therefore, this cross-sectional study aimed to explore which dimensions of PA are related to PC in individuals who experienced a minor stroke more than six months prior.

Materials and methods

Participants

Individuals with minor stroke were recruited via neurologists and rehabilitation physicians of Radboud University Medical Center Nijmegen, Rijnstate Hospital Arnhem, Reinier de Graaf Gasthuis Delft, and through advertisements in local newspapers in the Netherlands between February 2017 and February 2019. Participants were eligible if they were in the chronic phase (>6 months) after minor stroke. Participants were screened by diagnosis of minor stroke at stroke onset, which was defined in this study as having a unilateral supratentorial transient ischemic attack (TIA) or having motor and/or sensory loss in the contralesional leg at stroke onset, with (near) complete clinical motor recovery of the paretic leg (Fugl-Meyer Assessment score of the lower extremity >24 at the time of inclusion).[25] Participants were excluded if they were receiving inpatient rehabilitation at the time of inclusion, experiencing other neurological or musculoskeletal problems, having severe cognitive problems (Montreal Cognitive Assessment <24)[26], using psychotropic medication or having persistent unilateral spatial neglect (Behavioral Inattention Test – Star Cancellation Test <44)[27]. This study was approved by the Medical Ethics Committee of the Arnhem-Nijmegen region, and all the participants gave written informed consent prior to the measurements.

Measures

Physical capacity

Participants were invited to Radboud University Medical Center for assessments. PC was assessed by three different tests: comfortable walking speed (10-Meter-Walking-Test, 10MWT), mobility capacity (Timed-Up & Go, TUG) and static and dynamic balance control (Mini Balance Evaluation Systems Test, Mini-BESTest). The 10MWT (duration of walking ten meters at a comfortable speed[4]) was performed three times and the average duration was recorded. The average duration was transformed to walking speed in m/s. Comfortable walking speed is an important aspect of walking capacity and is able to distinguish between different post-stroke ambulation levels.[28] The TUG determines the duration of standing up from a chair, walking three meters, turning around, walking back to the chair and sitting down again.[29] The duration of the TUG was reported. The Mini-BESTest determines balance by assessing tasks such as push and release, standing on toes or one leg, and assesses gait quality during changes in gait speed while avoiding obstacles and turning around.[30] The higher the Mini-BESTest score (maximum of 28) the better the dynamic balance control. PC tests were conducted by two trained assessors. All tests show excellent inter- and intra-rater reliability.[31–35]

Physical activity

After the PC assessment, participants wore an Activ8 physical activity monitor at home for seven consecutive days and 24 h per day. The Activ8 is a small (30 x 32 x 10 mm) and light-weight (20 g) triaxial accelerometer that has been validated to continuously measure daily PA in individuals after stroke.[36] The Activ8 was set to record data using a 30-s epoch length. The Activ8 was attached to the front of the thigh of the non-affected leg with TegadermTM skin tape. This waterproof attachment allowed participants to swim and shower while wearing the device. In addition, the participants were asked to report waking hours each day in a logbook in order to check whether those hours corresponded with the registration of activity by the Activ8. Since this study focuses on PA, sleep was cut out of the data based on the waking hours reported in the paper logbooks. PA assessments were considered valid if data from at least 10 waking hours per day were available for 5 days.

The output of the Activ8 monitor consists of the time spent in six categories of body postures and movements (lying, sitting, standing, walking, running and cycling) within an epoch length of 30 s. In addition, in each epoch the number of movement counts is calculated for each category, representing the amount of movement within that epoch. By dividing the movement counts by the time spent in a category, the movement intensity can be calculated for each category. Standing, walking, running and cycling were merged into upright activities, while the same activities minus standing were classified as active activities. If a 30-s epoch showed activity for >24 s (80%), then the epoch was classified as active. If at least four sequential active epochs occurred (i.e., 2-min period), such a period was classified as an active bout. Matlab R2014b was used to process the time and counts of the postures and movements into different outcomes representing four distinct dimensions of PA:

- Counts per minute during walking ($CPM_{walking}$), representing the *intensity* of walking.[37] Walking is the most common and important movement for stroke survivors in daily activities and participation in society.[11,38,39]
- The number of active bouts ($N\ Bout_{active}$), representing the *frequency* of PA.
- The mean length of active bouts ($ML\ Bout_{active}$), representing the distribution of PA, calculated as the sum of the length of all active bouts divided by the number of active bouts.[40,41]
- The relative time (% Upright) spent in upright postures and movements, representing the duration of PA, calculated by the sum of the duration in upright movements divided by the total waking hours multiplied by 100%.

All outcome measures were averaged per day by dividing by the number of days that contained valid measurements.

Statistical analysis

Descriptive statistics were acquired for all participants, and Kolmogorov–Smirnov tests were used to test for normality of the participant characteristics and the PC and PA measures. The results of the 10MWT, TUG, and Mini-BESTest were tested for associations with participant characteristics and PA measures using Pearson's or Spearman's correlation coefficients. The association of PC with the dichotomous variable sex was assessed using a t-test or Mann–Whitney U test. Stepwise multivariable linear regression analyses were conducted, with the 10MWT, TUG and Mini-BESTest results as dependent variables and PA outcomes ($CPM_{walking}$,$N\ Bout_{active}$, $ML\ Bout_{active}$,%Upright) as independent variables, adjusted for potential confounders (age, sex and BMI). With seven independent variables in each model, we aimed to include at least 70 participants.[42] Assumptions for linear regression were checked: homoscedasticity was tested by plotting the residuals versus the fitted values, presence of multicollinearity was determined by a variance inflation factor (VIF) larger than 3, and influential points were inspected with Cook's distance. To correct for multiple testing in the regression models, the significance level was set at a < 0.05/3 = 0.017. For the t-test, Mann–Whitney U test and correlations, a significance level of a < 0.05 was used. All analyses were performed using Rstudio version 1.1.456.

Results

Seventy-four patients were included in this study. Five participants were lost to follow-up, because the Activ8 was not returned (n = 1), there was an invalid number of measurement days (n = 1) or there were technical problems with the Activ8 (n = 3). Therefore, 69 patients were included in the analysis. Patient characteristics are shown in Table 1. The majority of the participants were male (61%). The mean age of all participants was 65.2 (SD 9.8) years, and age was significantly different between males mean (SD): 67.0 (9.1) and females mean (SD): 62.3 (10.2), p = 0.047. All other patient characteristics were not significantly different between males and females. The median time since occurrence of the minor stroke event was 20 months (IQR 13.0 - 53.5) and the majority of the participants had sustained an ischemic stroke.

Table 1. Characteristics of the participants (n=69)

Participant characteristic	
Sex (male/female) ***(% male)***	42/27 (61%)
Age (years)	65.2 (9.8)
Body Mass Index (BMI)	26.1 (23.6 – 28.3)
Type of stroke (ischemic/hemorrhagic/unknown)	62/6/1
Affected body side (left/right)***(% left)***	36/33 (52%)
Time since stroke (months)	20 (13.0 – 53.5)

NOTE: values are mean (SD), median (IQR) or n

Table 2 presents the PC (10MWT, TUG and Mini-BESTest) and PA outcomes ($CPM_{walking}$, N $Bout_{active}$, ML $Bout_{active}$ and %Upright) of the participants. The mean number of waking hours measured with the Activ8 accelerometer was 15 h 35 min (SD 1 h 23 min) per day.

Table 2. Physical capacity (PC) and physical activity (PA) outcomes of participants (n=69)

PC test or PA outcome	Participant outcomes *mean (SD)*
Physical capacity	
10MWT (m/s)	1.3 (0.2)
TUG (seconds)	10.2 (2.0)
Mini-BESTest (score)	24.0 (2.6)
Physical activity	
$CPM_{walking}$	1447.9 (169.9)
N $Bout_{active}$	8.9 (5.0)
ML $Bout_{active}$	6.9 (3.7)
% Upright	34.8 (10.3)

NOTE: values are mean (SD), 10MWT = 10-Meter-Walking-Test, TUG = Timed-Up&Go, Mini-BESTest = Mini Balance Evaluation Systems Test, CPM $_{walking}$ = counts per minute during walking, N $Bout_{active}$ = number of active bouts, ML $Bout_{active}$ = mean length of active bouts, % Upright = percentage in upright postures and movements relative to the waking hours. Physical activity outcomes are expressed as mean per waking hours a day. Mean waking hours were 15h 35min (SD 1h 23min).

Table 3 shows the correlation coefficients between the PC tests (10MWT, TUG and Mini-BESTest), participant characteristics (age, BMI) and the four different PA outcomes ($CPM_{walking}$, N $Bout_{active}$, ML $Bout_{active}$, % Upright). All correlation coefficients were low to moderate ($r < 0.5$).

Table 3. Correlation coefficients of physical capacity tests (10MWT, TUG, Mini-BESTest) vs. participant characteristics and physical activity outcomes

	10MWT	TUG	Mini-BESTest
Characteristics			
Age	0.440**	0.369**	-0.488**
BMI	-0.090	0.175	-0.253*
Physical activity			
CPM $_{walking}$	0.428**	-0.160	0.155
N $Bout_{active}$	-0.170	-0.219	0.280*
ML $Bout_{active}$	-0.179	-0.108	-0.019
% Upright	-0.073	-0.188	0.042

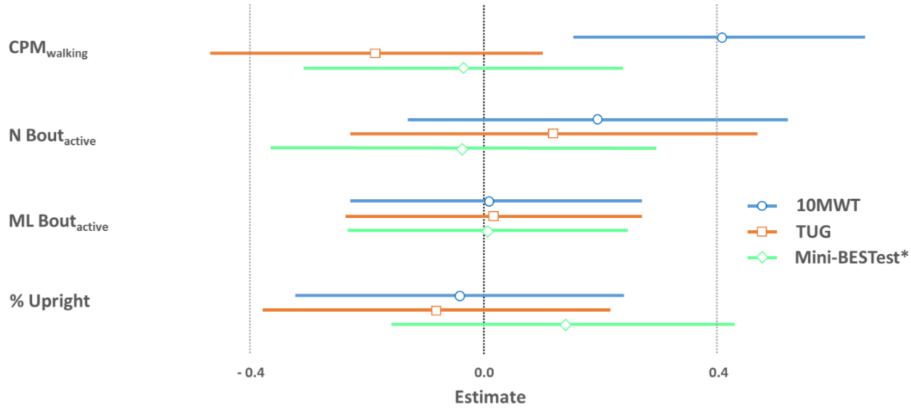
*=p<0.05, **=p<0.01, 10MWT = 10-Meter-Walking-Test, TUG = Timed-Up&Go, Mini-BESTest = Mini Balance Evaluation Systems Test, CPM $_{walking}$ = counts per minute during walking, N $Bout_{active}$ = number of active bouts, ML $Bout_{active}$ = mean length of active bouts, % Upright = percentage in upright postures and movements relative to the waking hours.

Table 4 shows the results of the multivariable linear regression models with the three PC tests as dependent variables and the PA outcomes as independent variables. All models were adjusted for age, sex and BMI. The only PA outcome that correlated significantly to PC was $CPM_{walking}$ in the 10MWT model (std. b = 0.409, p = 0.002). The other PA outcomes did not show significant associations with the PC tests.

Table 4. Multivariable linear regression models representing the relation between physical capacity tests and physical activity outcomes

	R^2	ß (SE)	95% CI	Std. ß	p
10MWT	0.331				
$CPM_{walking}$		0.001 (0.003)	[-0.000, -0.001]	0.409	0.002*
N $Bout_{active}$		-0.011 (0.007)	[-0.025, 0.002]	-0.261	0.107
ML $Bout_{active}$		0.002 (0.007)	[-0.017, 0.015]	0.030	0.794
% Upright		0.002 (0.003)	[-0.004, 0.001]	0.099	0.475
TUG	0.205				
$CPM_{walking}$		-0.002 (0.002)	[-0.005, 0.001]	-0.183	0.205
N $Bout_{active}$		0.049 (0.071)	[-0.092, 0.190]	0.122	0.488
ML $Bout_{active}$		0.009 (0.069)	[-0.129, 0.147]	0.017	0.895
% Upright		-0.016 (0.029)	[-0.073, 0.045]	-0.074	0.679
Mini-BESTest	0.293				
$CPM_{walking}$		0.001 (0.036)	[-0.003, 0.005]	0.035	0.796
N $Bout_{active}$		0.018 (0.085)	[-0.152, 0.188]	0.035	0.843
ML $Bout_{active}$		-0.004 (0.083)	[-0.170, 0.162]	-0.003	0.960
% Upright		-0.035 (0.036)	[-0.108, 0.038]	-0.140	0.339

All models were adjusted for age, sex and BMI. * = P<0.017, 10MWT = 10-Meter-Walking-Test, TUG = Timed-Up&Go, Mini-BESTest = Mini Balance Evaluation Systems Test, $CPM_{walking}$ = counts per minute during walking, N $Bout_{active}$ = number of active bouts, ML $Bout_{active}$ = mean length of active bouts, % Upright = percentage in upright postures and movements relative to the waking hours.



*NOTE; in order to compare the direction of the association between physical activity and physical capacity, the scores of the TUG were inverted. Circles, squares and deltoids are standardized estimates with 95% CI. 10MWT = 10-Meter-Walking-Test, TUG = Timed-Up&Go, Mini-BESTest = Mini Balance Evaluation Systems Test, CPM $_{walking}$ = counts per minute during walking, N Bout$_{active}$ = number of active bouts, ML Bout$_{active}$ = mean length of active bouts, % Upright = percentage in upright postures and movements relative to the waking hours.

Fig. 1. Summary of standardized estimates with 95% confidence intervals of the association between multiple physical activity outcomes and physical capacity tests.

Figure 1 presents a visual summary of the standardized estimates of the PA outcomes in the three PC regression models. To improve visual comparison with the other outcomes, the scores of the TUG were inverted, so that the direction of all outcomes is the same.

CHAPTER 4

Discussion

This study examined relationships between PA and PC, more than six months after minor stroke. The intensity of daily walking was significantly associated with PC, as determined by the 10MWT. No other PA dimension (frequency, duration or distribution) was related to any of the PC outcomes (10MWT, TUG, Mini-BESTest).

Our findings are in line with those of earlier studies in which PA intensity was correlated to PC. Both Mudge *et al*.[43] and van de Port *et al*.[44] also found a moderate to strong relationship between measures of PA intensity during walking and comfortable walking speed in more severe stroke patients. However, they did not examine multiple outcomes of PA in relationship to walking tests concurrently, thus limiting further comparison with our results. Wolff-Hughes *et al*.[45] found a relationship between movement intensity and cardiometabolic biomarkers, which was stronger than the relationship between the distribution outcome accumulation of PA in long bouts and the same biomarkers. Therefore, we suggest including a measure of intensity when evaluating PA, to avoid missing important information about a person's PA that might signify a risk for health issues.

Our finding that intensity showed the strongest association with PC might be explained by the fact that the 10MWT and the intensity outcome $CPM_{walking}$ are indicators of walking speed.[37] $CPM_{walking}$ has a strong conceptual or theoretical linkage with walking speed as measured during the 10MWT.[46] The different environments between the 10MWT and $CPM_{walking}$ during free-living conditions do not seem to play a significant role. The link between daily CPM walking is weaker with the TUG and the Mini-BESTest. They require more complex coordination and control skills due to transitions between postures and movements, whereas the 10MWT involves only walking.

The TUG and the Mini-BESTest show weak or nearly absent associations with PA frequency, distribution and duration. Possibly, the more complex tasks required during these tests are not representative of the activities performed in daily life, although in the latter, people are also confronted by diverse challenges.[47] Another explanation for the absence of association might be related to the type of PA outcomes measured in our study. For example, if rising time from a chair was quantified in daily life, relationships with TUG may have been found. This supports the importance of measuring not only each person's capacity with standardized tests, but also the actual performance in daily life, and disentangling the relationships between the different outcomes of these domains.

Although we found a statistically significant and strong association between the self-selected walking speed during the 10MWT and daily life accelerometer counts during walking ($CPM_{walking}$), the explained variance of this regression model was low. This could be because walking in a free-living environment incorporates a broader range of walking activities compared to the self-selected walking speed on a flat surface in a straight line during the 10MWT, as shown by previous research.[43] However, self-selected walking speed is a relevant measure in individuals after minor stroke since it is associated with several health outcomes, including functional decline, mobility disability, and clinically relevant changes in quality of life.[48,49] Future research should focus on exploring the causal relationships between walking capacity tests and intensity of walking in daily life as well as related health outcomes in minor stroke patients. Other PC models also showed a low explained variance and wide confidence intervals of the standardized estimates. This suggests high intra-individual variability in the association between daily life PA and PC. One possible explanation is that other factors involved in community PA, such as the physical and social environment or levels of mental and social functioning, contribute to variability between individuals.[17,50]

Nevertheless, our findings suggest the importance of performing activities beyond a certain intensity, speed, or energy expenditure threshold when one aims to improve PC. Especially in minor stroke cases, secondary prevention is essential, and targeting the intensity of PA seems opportune, since this parameter is lowered compared to healthy peers.[8,51] Moreover, previous studies showed that when persons who suffered from a stroke exercise at high intensities, their quality of life improves and the likelihood of stroke recurrence is reduced.[39,52,53] Future studies should seek to determine the intensity threshold that improves PC most effectively, so it can be used to set targets in interventions.

Some limitations need to be addressed. First, the cross-sectional design of this study limits conclusions on causal inference. Second, although PA operationalization and data processing were developed carefully, our results may still depend on the selection of PA outcomes that were included. However, we chose distinct and uncorrelated measures representing theoretically different dimensions of PA. Third, previous studies often used other types of accelerometers to measure objective outcomes of PA of stroke patients, such as the Stepwatch Activity Monitor or the ActivPAL.[19] The use of those different accelerometers might limit comparisons to our results, obtained with the Activ8 accelerometer. We note that the Activ8 has been shown to provide relevant and valid information on postures and movement to map the daily PA of stroke patients.[36] Lastly, the generalizability of our findings is limited by the relatively young age of our study sample and the wide range of times after stroke occurrence.

In conclusion, the present study provides insight into the relationship between multidimensional PA and PC in individuals after minor stroke. The intensity of walking, measured by accelerometer counts during walking, appears to be a useful tool to increase the effectiveness of interventions that aim to improve PC after minor stroke. Future studies could evaluate if and how augmenting PA intensity leads to increased PC, ultimately to improve overall health and quality of life.

Acknowledgements

The authors thank Sanne Beurskens for her help with data collection and analysis.

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CHAPTER 5

PHYSICAL ACTIVITY DIMENSIONS AFTER STROKE: PATTERNS AND RELATION WITH LOWER LIMB MOTOR FUNCTION

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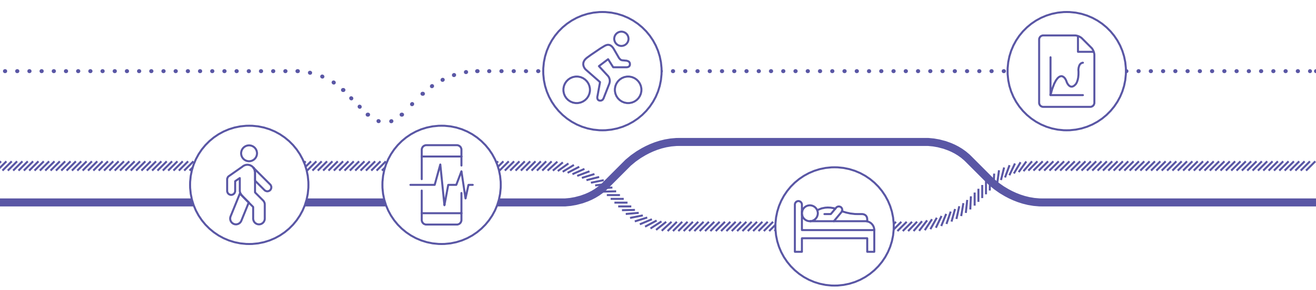
Journal of NeuroEngineering and Rehabilitation, *18*(1), 1-9.



Abstract

Background: Stroke survivors show deteriorated physical functioning and physical activity levels. Physical activity levels of stroke survivors are generally low. It is increasingly recognized that physical activity is a multidimensional construct that cannot be captured in a single outcome. In-depth insight into multidimensional physical activity patterns may guide the development and timing of targeted rehabilitation interventions. This longitudinal cohort study explored how multidimensional physical activity outcomes develop during recovery in the subacute phase after stroke and if changes in physical activity were correlated to recovery of lower limb motor function.

Methods: Patients were recruited during inpatient rehabilitation. At 3, 12, and 26 weeks post-onset, motor function was measured by the Fugl-Meyer Lower Extremity Assessment (FMA-LE). Physical activity was measured with the Activ8 accelerometer in multiple outcomes: counts per minute during walking ($CPM_{walking}$; a measure of Intensity), number of active bouts (Frequency), mean length of active bouts (Distribution) and % of waking time in upright positions (Duration). Generalized estimating equations (GEE) were used to study changes in physical activity over time and the relation with the change in lower limb motor recovery.

Results: 39 patients (age 56 ± 9, 77% male, 89% ischemic stroke) were included. GEE models showed a significant main effect of time for PA Intensity (+ 13 %, $p=0.007$) and Duration (+ 64%, $p=0.012$) between 3 and 12 weeks. Motor function did not show a significant effect in all PA models across the 3 timepoints ($p>0.020$). A significant interaction effect of time × motor function was observed ($p<0.001$).

Conclusions: Patterns of PA recovery depend on the PA dimensions: PA Intensity and Duration increased mostly between 3 and 12 weeks post-stroke, whereas Frequency and Distribution did not show substantial changes. Further, no strong associations with motor recovery and high inter-individual variability were documented, which underlies the need to consider factors specific to the disease, the individual patient and the context.

Introduction

Approximately two-thirds of stroke survivors experience physical functioning problems, resulting in low levels of participation in physical activity (PA).[1, 2] Pursuing a physically active lifestyle is important because it reduces the risk for recurrent strokes, and it is linked to better functional capacity, quality of life, and overall life satisfaction.[3, 4] Therefore, from very early on post-stroke, one of the rehabilitation targets is optimizing patients' levels of PA.[5-7]

In the last decade, objective measurement of PA is increasingly used in stroke studies, with accelerometry as the dominant technology.[8] Although accelerometry is relatively simple in itself, the interpretation and comparison of data are complex due to variable methods and devices. In addition, multiple outcome measures are reported, affecting the conclusions.[8-10] For example, Sanchez et al.[11] reported the mean duration of walking bouts after stroke and showed that it did not differ from healthy controls. In contrast, other studies showed that the average walking time and the daily number of steps were significantly lower in stroke survivors.[11-13] It is increasingly recognized that PA is multidimensional, including dimensions such as Intensity, Frequency, Duration and Distribution.[8, 10, 14] Therefore, clinically relevant information on PA cannot be captured in one outcome and reporting multiple outcomes concurrently preferred.[8, 10, 15]

Longitudinal studies describing changes in multiple dimensions of PA post-stroke are scarce. Two longitudinal studies found different patterns of multiple dimensions, for example; frequency and time in short, long, low and moderate intensity bouts.[16, 17] Both studies started their measurements after discharge from rehabilitation, between 3 weeks and 4 months post-stroke. However, especially in the subacute phase (between seven days and six months), measurements at fixed time points post-stroke are recommended due to the timing of several biological recovery processes.[18] Insight into the multidimensional PA patterns within the subacute phase is needed since it may guide appropriate timing and development of targeted interventions in rehabilitation.[19-21]

PA patterns after stroke may be influenced by the level of motor recovery of a patient, since the performance of daily activities, such as walking, requires sufficient motor function, which is dependent on synergies.[22] However, a cross-sectional study showed no association between motor function and self-reported PA.[23] To date, it is unknown what the longitudinal relation is between motor function and PA measured in multiple dimensions with accelerometry. This longitudinal cohort study explored how multidimensional physical activity outcomes develop during recovery in the early and late subacute phase after stroke and how this related to changes in motor recovery.

Methods

Study design & Participants

This is a longitudinal observational cohort study. Patients were included <3 weeks post stroke in this sub-study from Rijndam Rehabilitation (Rotterdam, The Netherlands) if they suffered from an ischemic or hemorrhagic stroke with a paretic arm or leg (defined as NIHSS 5A/B or 6A/B 4 ≥ score > 0). Other inclusion criteria were i) 18 years or older, ii) a Mini Mental State Examination (MMSE) score >19, and iii) ability to sit at least 30 min with back support. Patients were screened by a trained research assistant between September 2016 and June 2019. All patients included in this study received the usual inpatient rehabilitation care program at Rijndam Rehabilitation. All patients gave their written informed consent, and the study was approved by the Medical Ethics Committee of Erasmus MC University Medical Center Rotterdam, The Netherlands (MEC-2015-687).

Procedures

Measurements were conducted at three fixed time points post-stroke; 3 (T1), 12 (T2) and 26 weeks (T3).[24] Demographic and clinical characteristics were collected at the time of inclusion. At each time point, a trained assessor conducted all tests. During the first measurement (T1), patients were visited during inpatient rehabilitation; The measurements at 12 and 26 weeks took place during either inpatient or outpatient rehabilitation or at home. If a patient was discharged from inpatient services, the patient was visited at home.

Measures

Motor function

Motor function was determined by the Fugl Meyer Lower Extremity Assessment (FMA-LE) administered at 3, 12, and 26 weeks post-stroke.[25] The FMA-LE assesses motor function of the lower extremity based on diverse tasks, concerning reflex activity, movement within and outside synergy patterns, speed and coordination. The FMA-LE consists of 17 items, with a maximum score of 34 points. Each item was scored on a 3-point scale (0 = cannot perform, 1 = can partially perform, 2 = can fully perform). A higher score represents a higher level of motor function.

Physical activity

PA was measured by the Activ8, which is a small (30*32*10 mm) and light-weight (20 gr) triaxial accelerometer that can validly and continuously measure daily PA of individuals after stroke.[26] The Activ8 was attached to the front of the thigh of the non-affected leg of the patient with TegadermTM skin tape. This waterproof attachment allowed patients to swim and shower while wearing the device. The patients wore the Activ8 for 7 consecutive days. In addition to the PA monitoring, the participants were asked to report waking hours each day in a logbook to check whether this corresponded with the registration by the Activ8. PA assessments were considered valid if data from at least 10 hours of waking hours per day were available over 5 days.[27]

The output of the Activ8 monitor consists of time spent in six categories of body postures and movements (lying, sitting, standing, walking, running and cycling) within an epoch length of 30 seconds.[14] In each epoch, the number of movement counts is calculated for each category, representing the amount of movement within that epoch. The movement intensity van be calculated for each category, by dividing the number of movement counts by the time spent in a category. Standing, walking, running and cycling were merged into upright activities, while the same activities minus standing were classified as active activities. If a 30-sec epoch consisted of >80% of active activities, such an epoch was classified as active. If a time period of at least 4 subsequent active epochs occurred (i.e. a 2-min period at least), such a period was classified as an active bout.

Matlab R2014b was used to process the time and counts of the postures and movements into different outcomes representing four distinct dimensions of PA:

- *Intensity*: counts per minute during walking ($CPM_{walking}$).[28] Walking is the most common and important movement for stroke survivors in daily activities and participation in society.[29-31]
- *Frequency;* the number of active bouts (N $Bout_{active}$).
- *Distribution:* the mean length of active bouts (ML $Bout_{active}$) represented the distribution of PA and was calculated by the sum of the length of all active bouts divided by the number of active bouts.
- *Duration:* the relative time (% Upright) in upright postures and movements represented duration of PA and was calculated by the sum of the duration in upright movements, divided by the total waking time multiplied by 100%.

All outcome measures were averaged per day by dividing by the number of days that contained valid measurements.

Statistical analyses

Statistical analyses were performed in RStudio (version 1.2.50001, Rstudio, Inc.). Baseline characteristics, motor function and PA outcomes were described by means and standard deviations with minimal and maximal values for continuous variables and frequencies and percentages for categorical variables.

Marginal modelling with Generalized Estimating Equations (GEE) was used to detect longitudinal changes since it controls for correlations between repeated measurements.[32] All four PA outcomes were used as dependent variables in the GEE models. Time was set as an independent factor with three levels (3, 12, 26 weeks). For all models, an identity link function was used according to the distribution of the PA outcomes. The choice of the most suitable working correlation matrix was based on the lowest quasi-likelihood under the independence model criteria (QIC).[32]

First, to detect changes in multidimensional PA over time, a univariate GEE model with only time as a predictor was developed for each PA outcome. After that, to investigate the relation with motor recovery, other multivariate GEE models, including time, motor function and an interaction between time and motor function were developed. The interaction term assessed the association between PA outcomes and changes in motor function over time. These GEE models were conducted with stepwise approach; first, a full model was developed with time, motor function and the interaction between time and motor function. Second, if the interaction term showed no added value, it was deleted from the model.

Since PA is measured in four domains, we used Bonferroni for correcting for multiple testing, considering $p < 0.0125$ as significant. If a significant main effect of time was observed, post-hoc comparisons with a Bonferroni correction was conducted. Post-hoc analyses were considered significant at $p<0.05$

Results

Participants

Figure 1 shows the flow of inclusion of patients. Sixty-two patients accepted informed consent. Twenty three patients withdrew before or during the first measurement (T1) and were excluded. Reasons for withdrawing were amongst others; withrew from study due personal reasons, wrong diagnosis, hospitalization, and early discharge. Thirty-nine patients were included in further analyses. The number of valid measurements that were included in the analysis was n = 30 at T1, n = 28 at T2 and n = 24 at T3. Baseline characteristics of the patients within the study sample at baseline (n=39) are shown in Table 1.

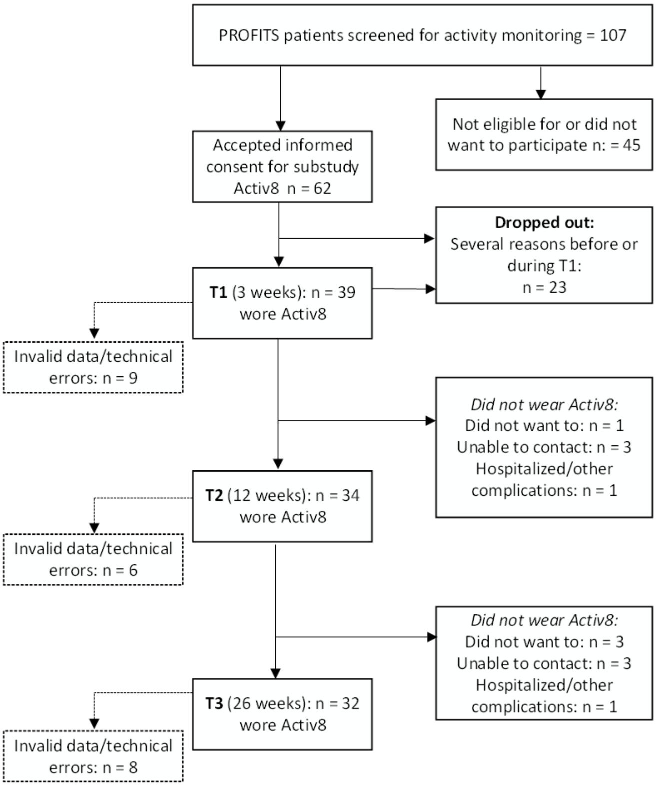


Fig. 1. Flowchart of inclusion of patients

Table 1. Baseline characteristics of patients included in Activ8 measurements (N = 39)

Age (years, mean ± SD, min-max)	56 ± 9 (37-75)
Sex (male n, %)	30, 77%
Type of stroke (hemorrhagic/ischemic, n, %ischemic)	4/35, 90%
Time between stroke and admission to inpatient rehabilitation (days mean ± SD, min-max)	11 ± 6 (0 – 22)
Length of inpatient rehabilitation (days, mean ± SD, min-max)	59 ± 34 (9 – 120)
Barthel Index (mean ± SD, min-max)	15 ± 4 (7 – 20)
Motricity Index Lower Extremity (mean ± SD, min-max)	64 ± 29 (0 – 100)
Berg Balance Scale (mean ± SD, min-max)	36 ± 16 (4 – 56)
Fugl Meyer Lower Extremity (mean ± SD, min-max)	22 ± 10 (4 – 33)

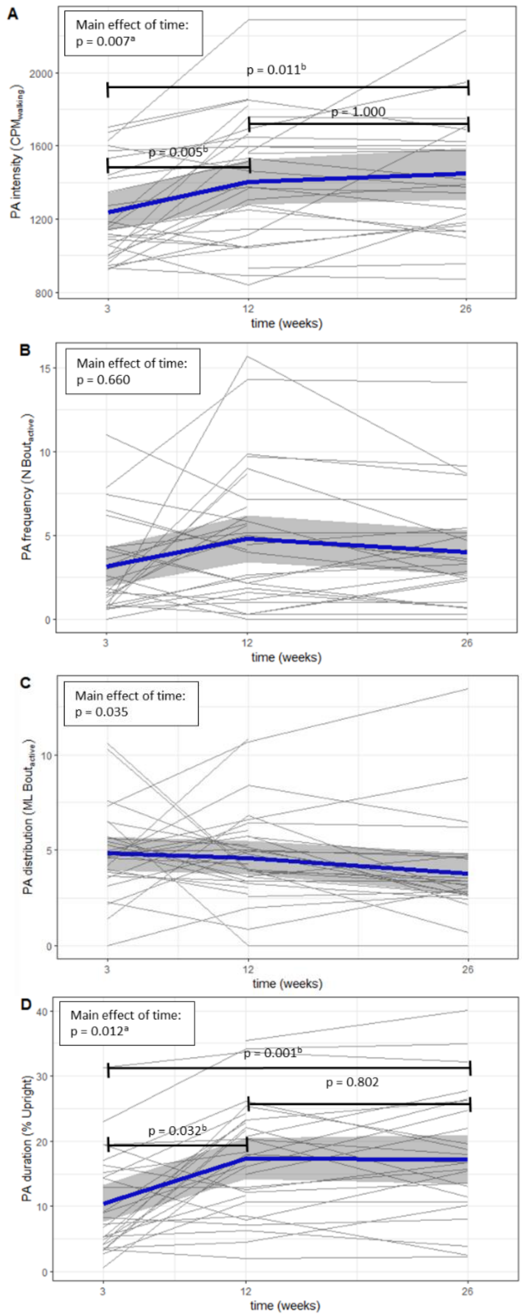
CHAPTER 5

Longitudinal changes of physical activity

The mean waking time used for Activ8 measurements was 14h19min ± 1h6min per day. Figure 2 shows PA changes per individual and mean change of the sample. Additionally, Figure 2 shows the results of the univariate GEE models with only time as a predictor. After Bonferroni correction, a main effect of time was observed for PA intensity ($p = 0.007$) and PA duration ($p = 0.001$) but not for PA frequency ($p=0.660$) and distribution ($p =0.035$). Post-hoc analyses showed a significant increase (+ 13%) of PA intensity between 3 weeks and 12 weeks ($p=0.005$) and significant increase (+ 64%) of PA duration between 3 weeks and 12 weeks ($p = 0.032$).

Longitudinal relation between physical activity and motor function

Average FMA-LE at 3 weeks was 22 ± 10, at 12 weeks 27 ± 7 and at 26 weeks 27 ± 6. Table 2 shows the results of the four multivariate GEE models, including time, motor function and time × motor function. In the multivariate GEE analyses, main effects of time were observed in the PA intensity ($p =0.007$) and duration ($p=0.001$) model (Table 2). Post-hoc analyses between time points showed a significant effect for duration between 3 vs. 26 weeks ($p<0.021$). No effect ($p < 0.013$) for motor function was observed in all PA models (PA Intensity; $p = 0.032$, Frequency; $p = 0.020$, Distribution; $p = 0.021$, Duration; $p = 0.121$)



NOTE: Grey lines represent PA of individuals, blue lines represent mean PA and grey band represent 95%CI, a p < 0.0125 for main effect, b p < 0.050 for post-hoc analyses between time points

Fig. 2. Individual and mean changes of physical activity (PA) intensity, frequency, distribution and duration from 3 to 26 weeks post-stroke with p-values of of post-hoc analyses between time points from the univariate generalized estimating equations (GEE) models.

CHAPTER 5

Table 2. Results of multidimensional physical activity (PA) in the multivariate generalized estimating equations (GEE) models with post hoc analyses between 3 vs. 12. 3 vs. 26 and 12 vs. 26 weeks post-stroke.

	B	**SE**	**p-value**	**p-value of the main effect of time**	**Post-hoc between time points, p-value**		
					3 vs. 12 weeks	*3 vs. 26 weeks*	*12 vs. 26 weeks*
PA Intensity ($CPM_{walking}*10^3$)							
time *(12 weeks)*	176	853	0.040	0.007[a]	0.118	0.254	1.000
time *(26 weeks)*	153	887	0.085				
FMA-LE	10.7	498	0.032				
PA Frequency (N $Bout_{active}$)							
time *(12 weeks)*	-0.51	1.55	0.744	0.032	-	-	-
time *(26 weeks)*	-1.21	1.21	0.318				
FMA-LE	0.17	0.07	0.020				
PA Distribution (ML $Bout_{active}$)							
time *(12 weeks)*	-5.88	1.78	0.001[a]	0.035	-	-	-
time *(26 weeks)*	-7.12	1.80	<0.001[a]				
FMA-LE	-0.11	0.05	0.021				
time *(12 weeks)* × FMA-LE	0.22	0.07	0.001[a]				
time *(26 weeks)* × FMA-LE	0.23	0.07	0.001[a]				
PA Duration (% Upright)							
time *(12 weeks)*	4.83	2.47	0.051	0.001[a]	0.153	0.021[b]	1.000
time *(26 weeks)*	5.91	2.20	0.007[a]				
FMA-LE	0.24	0.15	0.121				

NOTE: PA = physical activity, FMA-LE, Fugl Meyer Assessment Lower Extremity as a measure of motor function, n/a = not applicable

[a] p < 0.013 for main effect, b p < 0.050 for post-hoc analyses between time points

Discussion

This study showed that PA Intensity and Duration improved between three and twelve weeks post stroke whereas PA Frequency and Distribution did not show significant change during the subacute phase after stroke. Overall, the relation with motor recovery was absent or weak. In all PA dimensions, high inter-individual variability, both cross-sectional and over time was observed.

It is generally known that the most considerable improvement in post-stroke physical functioning is by spontaneous recovery occurring most strongly within the first five to six weeks, and by intensive rehabilitation therapy within the first three months post stroke.[5, 19] Our study showed significant improvements in PA Intensity and PA Duration from three to twelve weeks post-stroke, with a plateau thereafter. In other words, patients increased spending time upright and walked more intensively. PA Intensity, measured by accelerometer counts during walking, indicates walking speed, and has been shown a sensitive measure for detecting clinically important changes.[28, 33] In contrast, no increase was observed in the bout-specific outcomes of PA Frequency (bout number) or PA Distribution (bout length), suggesting that the passage of time after stroke did not lead to more persistent and prolonged physical activities of two minutes or more. Therefore, it seems that the evaluation of temporal PA changes is sensitive to the selected outcome measure, which is in line with the results of Mahendran *et al*.[16] Since until now, no consensus on the best post-stroke PA measures has been recommended[8], we recommend measuring and reporting multiple dimensions of PA. Besides giving a complete overview of patients' PA, it will also contribute to a better understanding and a well-grounded selection of future outcomes that are sensitive to change post stroke.

Only the PA Distribution model showed significant interaction effects between motor function and time at 12 weeks and 26 weeks after stroke, meaning that patients with increasing motor function seem to be more persistent in uninterrupted activity as time progresses. However in general, no or at best weak associations between PA and motor function were found in the multivariate GEE models. One explanation is that overall, the FMA-LE scores in our study sample were relatively high, and the changes over time relatively small. At three weeks, mean FMA-LE was 22 ± 10. According to Kwong *et al*. [34], a score of 21 or higher represents a high level of motor function in stroke survivors. It is possible that for these patients, substantial spontaneous recovery occurred before the first measurement and no large nor clinically relevant FMA-LE changes were taken into account in our longitudinal analysis. FMA-LE may not be sensitive enough to detect small increments in motor function in patients with a relatively high level of motor function. Also, learned compensatory strategies to overcome motor impairments might have distorted the relationship [35]. The weak relationship between physical activity and motor recovery supports the importance of collecting objective information on a patients' performance in their own context, such as accelerometer-based PA, is relevant in addition to other clinical tests.

Another remarkable finding was large within and between-subject variability that was observed in our study (Figure 2). To illustrate, the relative time spent in upright positions at 26 weeks after stroke ranged from 1% to 40% of the day, representing eight minutes a day to more than five hours. Comparable ranges were found in PA intensity, frequency and distribution. This variability might be the result of the varying demographics, functional level (Table 1), and other factors such as cognitive impairments, and pre-stroke lifestyle, physical and social environment.[23] The high intra-individual variability underscores the urge for an individual approach in rehabilitation research and practice.[5, 36]

Unique in our study was the measurements at fixed time points post onset aligned with the underlying recovery mechanisms of body structures and functions.[24] In contrast, other longitudinal PA studies[16, 17] measured at time points relative to time of admission to or discharge from rehabilitation, reflecting a process of care.[18] Future research should reveal if measurements of PA changes based on both approaches differ and what is most informative for appropriate timing of interventions. To date, optimal timing of interventions after stroke is still a challenge.[18, 21]

Although similar to earlier studies on post-stroke PA[16, 37, 38], a limitation of this study was the relatively small sample size. Therefore, the results of the regression models should be interpreted with caution. Another limitation was the amount of missing data resulting from device failures and subject compliance. Future developments – e.g., smaller sensors, body posture and movement detection from wrist-worn devices – might improve compliance in future studies. Nevertheless, GEE analyses appropriately handles at-random missing data. Also, the choice of outcome measures may have influenced our results. To the best of our knowledge, we chose four theoretically different physical activity measures that are still easy to interpret from many available possibilities.

Conclusion

Our study showed that patterns of PA recovery depend on the PA dimensions: PA Intensity and Duration increased mostly between three and twelve weeks post-stroke, whereas Frequency and Distribution did not show substantial changes. Further, we observed high inter-individual variability and no, or at best weak associations between PA dimensions and motor recovery. The observed differences in PA patterns underline the importance of capturing multiple PA dimensions and considering factors specific to the disease, the individual patient and the context.

Acknowledgements

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CHAPTER 6

WEARABLE ACTIVITY MONITORING IN DAY-TO-DAY STROKE CARE; A PROMISING TOOL BUT NOT WIDELY USED

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Sensors 2021; 21(12), 4066.

Abstract:

Physical activity monitoring with wearable technology has the potential to support stroke rehabilitation. Little is known about how physical therapists use and value the use of wearable activity monitors. This cross-sectional study explores the use, perspectives, and barriers to wearable activity monitoring in day-to-day stroke care routines amongst physical therapists. Over 300 physical therapists in primary and geriatric care and rehabilitation centers in the Netherlands were invited to fill in an online survey that was developed based on previous studies and interviews with experts. In total, 103 complete surveys were analyzed. Out of the 103 surveys, 27% of the respondents were already using activity monitoring. Of the suggested treatment purposes of activity monitoring, 86%were perceived as useful by more than 55% of the therapists. The most recognized barriers to clinical implementation were lack of skills and knowledge of patients (65%) and not knowing what brand and type of monitor to choose (54%). Of the non-users, 79% were willing to use it in the future. In conclusion, although the concept of remote activity monitoring was perceived as useful, it was not widely adopted by physical therapists involved in stroke care. To date, skills, beliefs, and attitudes of individual therapists determine the current use of wearable technology.

Introduction

Stroke is a major cause of disability and is an age-dependent problem.[1] With an aging society and improved acute care, the number of stroke survivors living with long-term stroke consequences is increasing beyond the level of increase of professional capacity.[2,3] Many stroke survivors show deteriorated levels of functioning, with low levels of physical activity.[4,5] Being physically active is an important determinant of social participation and is a major target of stroke rehabilitation[6]. Furthermore, being physically active is related to physical and psychosocial functioning, quality of life, and reduction of cardiovascular risk factors.[7–10]

Physical activity is one of the components of physical behavior, that covers all movements, postures, and activities of a person's during their daily life[11]. Another component is sedentary behavior, which is associated with cardiovascular disease incidence and mortality and depressive symptoms. [12,13] Targeting stroke rehabilitation by increasing physical activity and decreasing sedentary behaviors may help to suppress the burden of stroke.

Stroke rehabilitation could benefit from remote monitoring of physical behavior with wearable sensor technology[14]. The development of wearable activity monitors has rapidly evolved over the last decades in academic research and the consumer market.[15,16] They provide an objective insight into behavior in a non-invasive and continuous way and can be applied in the home environments as well as in in- and outpatient settings to patients and therapists.[17] In addition, increased patient involvement by providing feedback on physical activity may enhance compliance and stimulate self-management[18]. The objective insights also allow therapists to set tailored therapy goals, guide patients towards them, and evaluate progress.[19,20]

Although the body of evidence of remote monitoring of physical activity is growing in academic research, its clinical implementation lags behind.[21,22] Adopting technologies in day-to-day care routines seems challenging for therapists, who are key players in adopting remote monitoring of physical activity[22], since it requires careful attention, precious time, sufficient organizational and technical infrastructure, and knowledge.[23–27] Studies indicate that physical therapists acknowledge the potential benefits and practical purposes of wearable activity monitoring in rehabilitation therapy.[28–30] However, so far these studies have applied individual interviews and small focus groups. To provide an extensive insight into the current uses and clues on how to push the clinical implementation of this technology in stroke care forward, a study with a wide group of physical therapists involved in stroke care is needed. Therefore, the current study aimed to explore the use, perspectives, and barriers to potential applications of wearable activity monitoring in day-to-day stroke care amongst physical therapists in the Netherlands.

Materials and Methods

Participants and Data Collection

This cross-sectional study used an online survey (LimeSurvey®) among physical therapists in the Netherlands involved in post-stroke rehabilitation. Therapists were included if they were involved in the treatment of at least one stroke patient in the last month in a rehabilitation center, geriatric care center, or in primary care in the Netherlands. Participants were invited by e-mail with a web link via contact persons of seven primary care stroke networks in the Netherlands and ten Dutch rehabilitation centers and via a newsletter of the special interest group “rehabilitation” of the Royal Dutch Society of Physical therapy (KNGF: Koninklijk Nederlands Genootschap voor Fysiotherapie). After three weeks, a reminder for filling in the questionnaire was sent. Surveys were filled in anonymously.

Survey Development

A research team of physical therapists, human movement scientists, and researchers developed the survey based on literature and interviews. The survey included questions on demographic and occupational characteristics. Literature was used to formulate questions on the following topics: innovativeness (multiple choice answers to the question on innovativeness were based on the descriptions of the adoption categories of Rogers[31]), health care technology, activity monitoring outcome measures, perceived usefulness, barriers, and willingness to use it in the future[15,16,27,29,32] (See Supplementary Materials for the complete survey). To measure the attitudes of the participants regarding these questions, a 5-point Likert scale was used[33]. Participants were also asked if they were familiar with activity monitoring, if they use it for tracking their own activities, and if they already use it in stroke care. If a participant answered “yes” to the question concerning use in stroke care, they were defined as a user, and otherwise as a non-user. The users received additional questions about the use in day-to-day practice. They were asked how long they have been applying it, for how many patients per week, for what purpose, and what outcome of physical behavior they were interested in. Additionally, with an open-ended question, the reason for use was questioned. At the end of the survey, all participants were asked by an open-ended question if they wanted to share anything else on activity monitoring in stroke care.

To ensure common understanding, definitions were explained in between the questions (see Supplementary Materials). Experts and physical therapists checked the initial survey for face validity, comprehensibility, vocabulary, and layout. The survey was pilot-tested by five physical therapists in primary care before distribution.

Data Analysis

Rstudio (version 1.2.50001, Rstudio, Inc., Boston, MA, USA) was used for the data analyses. Descriptive analysis was provided for all questions with means (SD), frequencies, and percentages. The Likert package[34] was used to visualize the questions answered with a Likert scale. Differences between users and non-users were carried out with Chi2 and Mann–Whitney U tests. The significance was set at α = 0.05.

All individual answers to the open-ended question were collected in Microsoft Excel for qualitative analysis. All answers were divided into emergent themes. The most frequent, remarkable, or important issues that were relevant to this study were extracted and reported in the results.

Results

Participants

Over 300 physical therapists received the e-mail with the invitation to fill in the online questionnaire. Of them, approximately 100 therapists were recruited via a primary care stroke network and approximately 200 therapists were recruited via a contact person within their rehabilitation center. The survey was available from 1 March till 1 June 2020. N = 132 started the survey via the web link and n = 103 completed the questionnaire (78%). Only complete surveys were used for further analysis.

Table 1 shows the demographic characteristics of the participants. The mean age of the study sample was 42.2 (SD 12.1) years. Most of the participants worked in a rehabilitation center as a physical therapist (n = 58). Nine participants were employed in two or three different settings. All therapists were involved in the treatment of stroke patients. Other patient groups treated by the therapists were congenital and acquired brain injuries, (inactive) elderly, chronic diseases, orthopedic conditions, and sports injuries.

Twenty-seven percent used activity monitoring in the treatment of stroke patients and were defined as users. Characteristics of both groups and differences between them are presented in Table 1.

Table 1. Demographic characteristics of respondents.

		Total (n = 103)	Users (n = 28) (27%)	Non-Users (n = 75) (73%)	*p*-Value
Age, mean (SD)		42.2 (12.06)	41.70 (13.24)	45.30 (12.11)	0.212
Gender (m/f)		26/76	8/20	18/56	0.420
Years of work Experience, n (%)	<5	9 (8.7%)	2 (7.1%)	7 (9.3%)	0.331
	5–10	18 (17.5%)	8 (28.6%)	10 (13.3%)	
	10–15	22 (21.4%)	7 (25.0%)	15 (20.0%)	
	15–20	7 (6.8%)	2 (7.1%)	5 (6.7%)	
	>20 years	47 (45.6%)	9 (32.1%)	38 (50.7%)	
Setting [a] (n)	Primary care	34	7	27	
	Rehabilitation	59	21	38	
	Geriatric care	20	2	18	

[a] = participants were allowed to fill in multiple answers; user is defined by answering "yes" on the question if they already use activity monitoring during their work as a physical therapist.

More than half of the non-users (59%) were familiar with activity monitoring before filling in this questionnaire. Similar percentages of users (54%) and non-users (53%) used a smartphone app or consumer-grade activity tracker for monitoring their own lifestyle and sports activities. Two participants (1.9%) considered themselves as people who were initially reluctant to use new healthcare technology and innovations. Most of the therapists in the total study sample described themselves as a person who had no problem going along with pioneers in healthcare technology and innovation but who did not initiate it themselves (60%). Only one (0.9%) of the therapists described himself as someone who invented and designed new healthcare technology and innovations and 18% of the total sample said they were someone who followed the latest developments in healthcare technology and innovation and looked for applications in practice. The most often used health care technologies in the total study sample, other than activity monitoring, were applications and websites supporting the patient with practicing (21% often, 5% very often). The least often used was technology that supported diagnostics (15% often, 0% very often). Users of activity monitoring used significantly more other health care technologies (apps/websites, $p = 0.036$; online consulting (expert) colleagues, $p = 0.023$; technology that supports diagnostics, $p = 0.009$; and technology that supports treatment, $p = 0.026$) compared to non-users (Figure 1).

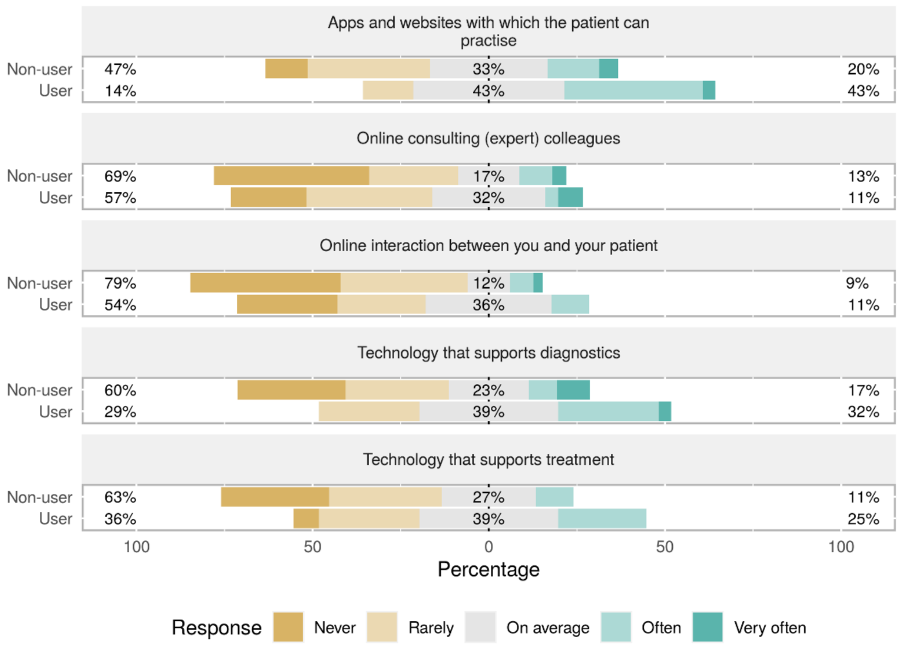

Fig. 1. Other health technology used by participants, with differences between users and non-users.

Users

Most users (54%) have been applying activity monitoring between six months and two years. Thirty-six percent have been applying activity monitoring shorter than six months, and eleven percent longer than two years. Most of the users applied activity monitoring between one and five patients per month (61%). Thirty-two percent applied activity monitoring in one patient per month or less, and seven percent in more than five patients per month.

Figure 2A shows the treatment purposes of activity monitoring of the users. Almost all therapists used the monitor to create awareness for the patient with regard to their physical behavior (96%). Giving feedback about their physical behavior (82%) was also often recognized as a useful activity monitoring purpose. Figure 2B shows the activity monitor outcomes of interest during treatment. Most of them were interested in the number of steps. Additional outcomes of interest reported by users were heart rate and demands vs. capability, or in other words, the relation between what a patient did compared to what the patient was capable of.

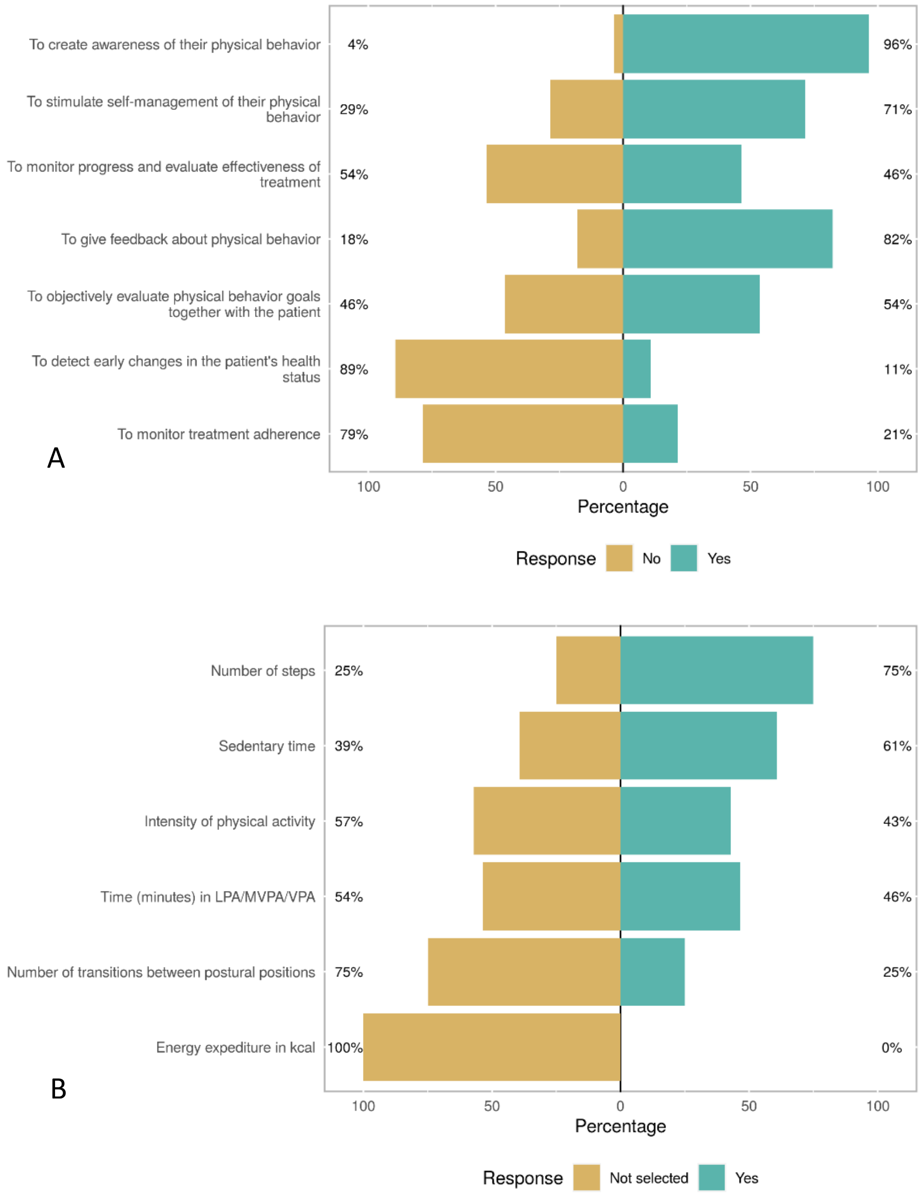

Fig. 2. Treatment purposes (A) evaluated by users and outcome of interest of users (**B**). LPA= low physical activity, MVPA = moderate to vigorous physical activity, VPA = vigorous physical activity.

In addition to the purposes in Figure 2A, users filled in for what reason they applied activity monitoring. Some of them reported new purposes compared to the ones provided in the answers; that they were instructed or motivated by external factors such as other colleagues who were already working with activity monitors or research/projects initiated by their organizations.

Perceived Usefulness

All participants (users and non-users) were asked for their opinion about the usefulness of activity monitoring for stroke patients. Six out of seven suggested purposes were considered useful by more than half of the study sample (Figure 3).

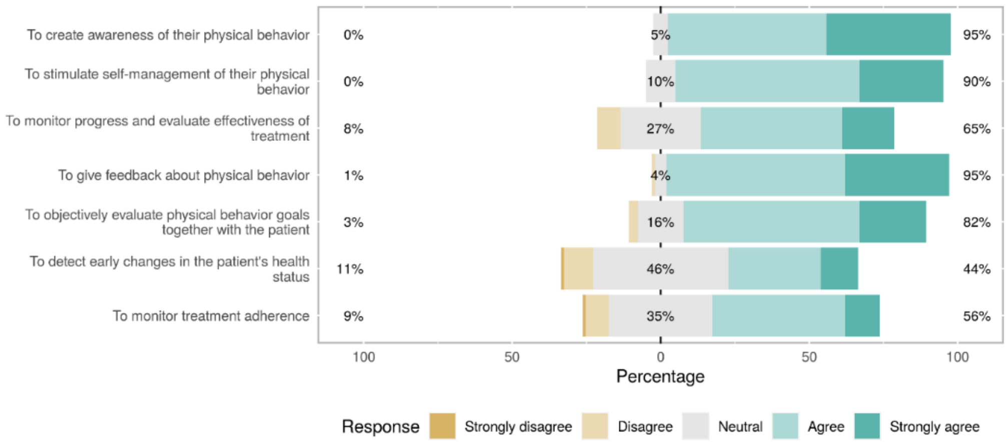

Fig. 3. Perceived usefulness for eight different activity monitor purposes.

One significant difference was found between users and non-users: the users perceived creating awareness as more useful than non-users (p =0.031). The participants were asked if they could come up with useful purposes other than noted in the question. Sixteen participants (16%) filled in the open-ended question on useful purposes other than mentioned in the question (Figure 3). Providing insight into a patients' demands vs. their capabilities (n = 6) was the most common purpose. Two mentioned heart rate and one mentioned arm/hand use.

Barriers

The most present barriers reported by the whole sample were lack of skills and knowledge of patients (65%), not being sure what monitor to purchase (54%), finding it too expensive (47%), and taking too much time (27%). Overall, seeing no added value for their patients and their work as physical therapists was not recognized as a barrier by participants (Figure 4).

Non-users agreed more strongly with the following barriers compared to users: not knowing much about the effectiveness (p = 0.015), lacking knowledge and ability to apply the technology themselves (p = 0.013), finding it too expensive (p = 0.043), and not being sure what monitor to purchase (p = 0.035). Other barriers did not show significant differences between users and non-users.

Additional Thoughts

The survey's last question asked all participants if they wanted to share anything else on activity monitoring. Thirty-two participants (31%) filled in this question. Several positive and enthusiastic thoughts on activity monitoring were provided. Participants report that activity monitoring offers valuable insight into a patients' behavior. About half of the 32 participants added some critical notes; they had doubts about the added value to the standard care relative to the effort. A few stated that applying technology was not always a holy grail and could not define therapy. Multiple participants mentioned that the usefulness was highly dependent on the age and stroke severity of the population.

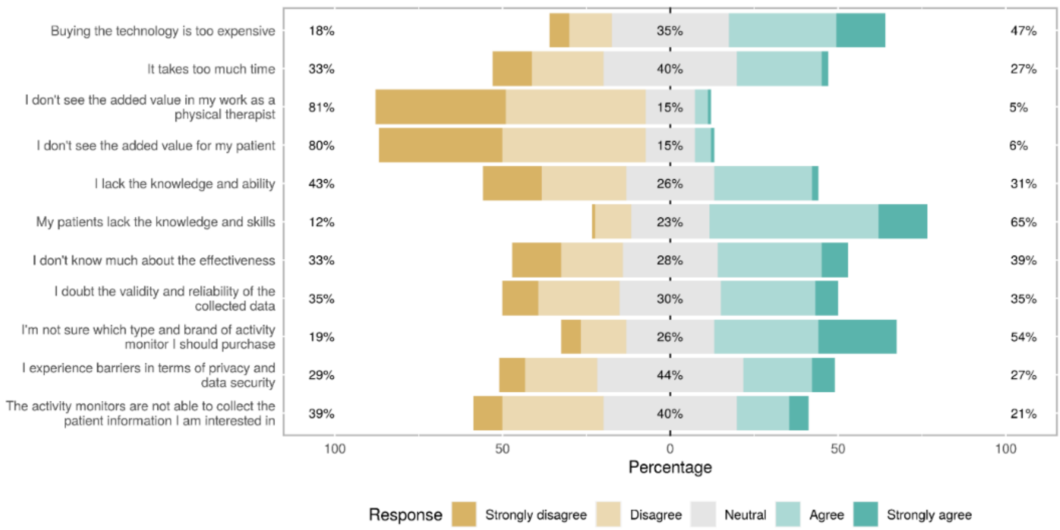

Fig. 4. Barriers of using activity monitoring as a physical therapist.

Discussion

This study showed that, although physical therapists perceived wearable monitoring as potentially useful in stroke rehabilitation, only a minority of 25% actually used it in clinical care. Therapists that already used activity monitoring during treatment of stroke patients used it more often than other health care technologies and described themselves as being more innovative compared to non-users. The most recognized barriers were lack of knowledge and skills of patients, financial constraints, and not being sure what monitor to purchase.

The vast majority of our sample had not yet adopted the use of activity monitoring in day-to-day stroke care. The low numbers of technology used in treatment amongst physical therapists were in accordance with other studies that focused on technology use in rehabilitation practice.[21,22] A majority of 80% of therapists not using remote monitoring technology (non-users) did see value in the concept of objective physical behavior measurements with wearable technology, such as raising the patients' awareness of their behavior and the ability of providing objective feedback in order to promote physical activity and were willing to use it in the future. Correspondingly, a majority disagreed with seeing no added value for their work as a therapist and for their patients as a barrier. Other studies also found positive attitudes and excitement of therapists towards the concept of objective physical behavior data collection in clinical practice.[28,35]

The discrepancy between the levels of adoption of activity monitoring and its perceived potential value suggests the presence of barriers. Potential barriers to adoption were indeed identified. The most frequently recognized barrier (65%) was perceived lack of skills and knowledge to use wearable monitoring technology in patients. Obviously, cognitive problems and generally older age might complicate the use of technological devices in daily life in stroke patients.[36] Especially for this group of patients, a user-friendly design of technology is desirable.[14,28] Issues with older and more severely affected patients were also explicitly stressed by the therapists in the open-ended questions. It should be noted that these results represent a perception of the therapists and are not confirmed by the patients themselves. Mercer *et al*.[37] found that older patients with chronic conditions also saw meaningful potential for wearable activity trackers but acknowledged that help from health professionals was desired to integrate the use in their daily life. In addition, caregivers who know the patient and his circumstances can play a crucial role in successful adoption.[38,39] Their support and encouragement might help patients to learn how to use wearable technology in their daily lives. To further improve the adoption of remote monitoring of physical behavior, collaboration with end-users, both therapists, patients, and their caregivers is to be recommended[28]. Whether the device matches the needs of end-users seems a critical factor for successful use.[40]

Another frequently recognized barrier, especially by the non-users, is the lack of skills in selecting and using the appropriate wearable activity monitor suitable for the patient. This might be aggravated by the increasing amount of available consumer and research-grade wearable monitors and their different specifications.[23,41] Research-grade devices are generally accurate and reliable but are not easy to use in clinical practice, whereas consumer-grade devices have limited accuracy in rehabilitation populations.[23] A clear overview of best practices and skill training for therapists may help to overcome this barrier. The non-users also expressed significant doubts about the effectiveness of wearable monitoring for stroke patients' treatment. The field of research on the effectiveness for stroke patients is still evolving, more high-quality evidence might be a positive stimulus for use in the future.[40,42] Another critical concern physical therapists shared in the open-ended questions was that using technology can not define the course of therapy. Using technology should address the clinical need and the interaction between a patient and professional should not be forgotten.[40]

Next to the individual skills and knowledge, successful, sustainable, and widespread adoption of technology is likely to be dependent on beliefs and attitudes of health care professionals.[25,43,44] Only one percent of the therapists in our study explicitly indicated being a person designing health care technologies and only 18% indicate that they are up-to-date and are looking for ways to adopt technology in daily practice. This low or absent innovative attitude might hamper the wide adoption in clinical practice. Therefore, if it is not widely accepted and fully integrated within organizations or the health care system, the use of wearable monitors will depend on the individual professional. Other stakeholders that have the potential to support and facilitate wider adoption of wearable technology are, for example, the policymakers of health care organizations, activity monitor companies, educational programs, and post-graduate training of professionals.

Our study has some limitations. As common in electronic surveys[21,27], non-response bias might have influenced our results. Respondents were probably more interested in contributing to a study on innovative technology than non-respondents, which may have overestimated the results. Since our respondents were selected based on being a physical therapist involved in stroke care, caution against generalizing our results to other health care occupations and patient populations is at its place. In addition, generalizability to other countries is limited since health care can be organized in a different way. We do not expect that geographical differences within the Netherlands have influenced our results since we tried to attempt diverse regions. No validated questionnaire that met our study purpose was available in the literature, and therefore to the best of our knowledge, we developed a survey with experts from the field and based on sufficient previous literature. The survey was pilot-tested amongst therapists and showed to be understandable and feasible. In addition, due to our study's narrative and exploratory nature, we could not establish in-depth and underlying thoughts regarding the use of wearable technology for stroke patients. From our results, no extensive requirements or (sensor) features of wearable monitors for clinical practice could be derived. Future studies should provoke a more profound discussion with therapists about the need and requirements for wearable monitors and relevant datasets for clinical use. However, together with qualitative studies[28,29], our study contributed to a comprehensive understanding of physical therapists' perspectives who, in the present years, are key stakeholders in adopting wearable technology in stroke care.

Conclusions

Our explorative study showed that despite physical behavior monitoring with wearable technology becoming commonplace in the consumer market and in academic research, it is not widely used by physical therapists involved in treatment of stroke patients. The concept of quantifying physical behavior with wearable monitors was perceived as useful by therapists, however, several barriers were identified. In current stroke care, physical therapists' skills, beliefs, and attitudes determine the current use of wearable technology.

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Supplementary Materials; Questionnaire

1. **What is your gender?**
    - Male
    - Female

2. **What is your age?**
    (open-ended question)

3. **For how many years have you been working as a (BIG-registered) physical therapist?**

- > 5 years
- 5-10 years
- 10-15 years
- 15-20 years
- < 20 years

4. **In which setting are you working as a physical therapist?**

- Primary health care
- Rehabilitation centre
- Nursing home
- Other... *(please complete)*

5. **Which patient group do you primarily work with?**

- Stroke patients
- Other congenital and non-congenital neurologic conditions
- (inactive) elderly
- Patients with chronic diseases
- Orthopedic conditions
- Sports injuries
- Other.. *(please complete)*

6. **What is your highest level of education in the field of physiotherapy or another relevant field?**

- Bachelor physical therapy
- Master manual, sports or geriatric physical therapy
- Master neurorehabilitation or musculoskeletal rehabilitation
- Master human movement sciences, health sciences or comparable
- Master innovation in health care
- PhD
- Other .. *(please complete)*

The next two questions are about healthcare technology, also known as E-health, in general. Healthcare technology is a collective term for all digital and electronic means that help us to improve healthcare.

7. **When it comes to new healthcare technology and innovations, I would describe myself as...**

- Someone who invents and designs new healthcare technology and innovations
- Someone who is at the forefront, someone who follows the latest developments in healthcare technology and innovation and looks for applications in practice
- Someone who has no problem going along with pioneers in healthcare technology and innovation, but someone who doesn't initiate it themselves
- Someone who needs some time to get used to new healthcare technology and innovations, but ultimately participates in their deployment
- Someone who is initially reluctant to use new healthcare technology and innovations

8. **Do you already use the following healthcare technologies in your work as a physical therapist?**

- Apps and websites with which the patient can practise and/or have more control over their condition
- Interaction between you and your patient, such as making appointments online, e-consults
- Consulting (expert) colleagues, for example via videocalling or applications such as Siilo
- Technology that supports diagnostics, such as the use of applications to perform a gait analysis or to measure the range of motion
- Technology that supports treatment, such as exercises at home, monitoring and measuring instruments with sensors

The following questions are about a specific part of healthcare technology; objective measuring, also known as 'tracking', patients' exercise behavior by means of activity monitors. By exercise we mean all physical activities, but also the sedentary behavior of patients. Activity monitors, also called 'wearables' or 'activity trackers', are very promising tools for physiotherapy because they give you and your patient an objective insight into, for example, how much, how often and how intensively a patient exercises. In addition, the activity monitors also offer the possibility of automatically providing feedback on physical behavior. Examples of activity monitors are a Fitbit, the AppleWatch, but also step counter apps on your smartphone.

9. **Were you familiar with activity monitors as described above prior to taking this survey?**

- Yes
- No

10. **Do you use activity monitors to measure your own exercise behavior, such as sports activities, in your daily life?**
- Yes, …. *(please fill what you use)*
- No

The following questions are about the use of activity monitors during your work as a physical therapist. Although you may treat various patient groups, the questions below are specifically about the application of activity monitors in the treatment of stroke patients.

11. **Are you already using activity monitors as part of the treatment of your patients?**

* QUESTIONS 12 TO 17 WERE ASKED ONLY TO PARTICIPANTS WHO ANSWERED "YES" TO QUESTION 11 **

12. **For how long have you been applying activity monitoring as part of the treatment?**
- < 6 months
- 6 months – 2 years
- > 2 years

13. **For how many patients do you apply activity monitoring as part of the treatment on a weekly basis?**
- < 1 patient per month
- 1-5 patients per month
- > 5 per month

14. **What outcomes of physical behavior of your patients are you interested in**
- Number of steps
- Sedentary time
- Intensity of physical activity
- Time (minutes) in low, moderate or vigorous physical activity
- Number of transitions between postural positions
- Energy expenditure in kcal
- Other .. *(please complete)*

15. **For what treatment purposes do you use activity monitoring?**
- To create awareness for the patient with regard to their physical behavior
- To stimulate the patient to take control of their own physical behavior

- To monitor the progress in the physical behavior of patients and thereby evaluate the effectiveness of the treatment
- To give the patient objective feedback about their physical behavior
- To objectively evaluate physical behavior goals together with the patient
- To detect early changes in the patient's health status
- To monitor treatment adherence
- Other purposes, namely...

16. What prompted you to apply activity monitoring?
(open-ended question)

17. To what extent do you think activity monitoring can be used for the treatment purposes mentioned above within physiotherapy?

Per treatment purpose:

5-point Likert scale: 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree

- To create awareness for the patient with regard to their physical behavior
- To stimulate the patient to take control of their own physical behavior
- To monitor the progress in the physical behavior of patients and thereby evaluate the effectiveness of the treatment
- To give the patient objective feedback about their physical behavior
- To objectively evaluate physical behavior goals together with the patient
- To detect early changes in the patient's health status
- To monitor treatment adherence

18. In addition to the treatment purposes mentioned above, are there any other purposes for which you think activity monitoring would be useful within physiotherapy?
(open-ended question)

19. What barriers have prevented you/could prevent you from using activity monitors in treatment?

Per barrier:

5-point Likert scale: 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree

- Buying the technology is too expensive
- It takes too much time
- I don't see the added value of using the technology in my work as a physical therapist
- I don't see the added value for my patient

- I lack the knowledge and ability necessary to apply such technology
- My patients lack the knowledge and skills necessary to use the technology
- I don’t know much about the effectiveness of using activity monitors
- I doubt the validity and reliability of the collected data
- I’m not sure which type and brand of activity monitor I should purchase
- I experience barriers in terms of privacy and data security
- The activity monitors are not able to collect the patient information I am interested in

20. To what extent are you open to using activity monitors in your work as a physical therapist?

5-point Likert scale: 1 = Not at all, 2 = a little, 3 = neutral, 4 = open, 5 = very open

21. How likely do you think it is that you will use activity monitors in the next 5 years in your work as a physical therapist?

5-point Likert scale: 1 = very small, 2 = small, 3 = neutral, 4 = big, 5 = very big

22. Is there anything else you would like to mention about the use of activity monitoring as a physical therapist?

(open-ended question)

CHAPTER 7

GENERAL DISCUSSION

The aim of this thesis is to increase the understanding of measuring physical behavior with wearable technology in rehabilitation. Wearable technology provides a promising, non-invasive, and objective method for measuring physical behavior in rehabilitation research and clinical practice. However, despite the potential benefits, there are still several unresolved fundamental questions which limit the use and relevance of this technology in rehabilitation. In this thesis we focus on three of those unresolved topics related to physical behavior measurement;

(1) Relationships with other domains of functioning *(**chapters 4 & 5**)*
(2) Physical behavior outcome measures *(**chapters 3, 4 & 5**)*, and
(3) Clinical application *(**chapters 2, 3, 4, 5 & 6**)*.

This chapter summarizes the main findings of the studies presented in this thesis (figure 1) and discusses how these outcomes compare to the literature and clinical practice. Furthermore, it suggests directions for future research and rehabilitation practice.

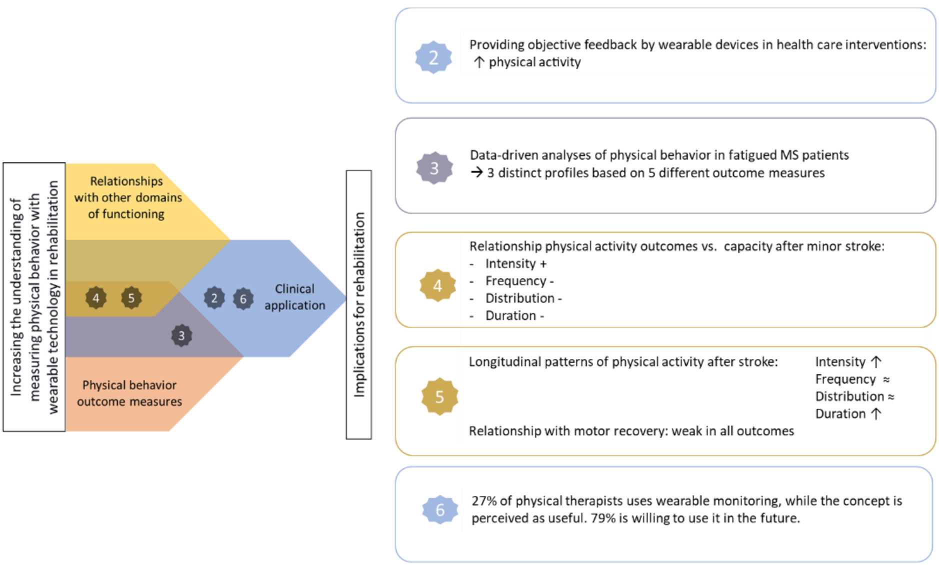

Fig. 1: Main aim and outline of this thesis, with the most important results per chapter.

Main findings

Chapter 2 presents a systematic literature review, which reveals that providing objective feedback on physical activity moderately increases physical activity levels of (former) patients of health care institutes. The effect of such feedback depends on several factors, such as the population receiving the feedback and whether behavioral change techniques are provided next to objective feedback, for example, goal-setting, education, and action planning.
Chapters 3, 4 and 5 focus on the various outcome measures generated by wearable monitors that objectively measure physical behavior. In these chapters, multiple physical behavior outcomes are described and compared, since physical behavior is reported with different outcome measures and there is no consensus on the selection and application of appropriate outcome measures. **Chapter 3** identifies physical behavior subtypes in patients with multiple sclerosis (MS), based on multidimensional physical behavior outcome measures. From an a priori set of fifteen physical behavior outcomes, data-driven techniques lead to a set of five indicative physical behavior measures. These five multidimensional measures allow to identify three distinct physical behavior subtypes (sedentary, moderately sedentary and active patients).
Chapters 4 & 5 study the cross-sectional and longitudinal relationships of physical behavior outcomes with measures representing other domains of functioning, such as body function and structures, and capacity, in patients with minor and severe stroke. Four physical behavior outcomes are selected, representing the dimensions: intensity, frequency, duration and distribution. Overall, weak relations are found with low explained variance. The strength of the relationship differs per outcome measure, with intensity of physical activity showing the strongest relationship.
Chapter 6 documents the perspectives of physical therapists on the use of wearable monitors in day-to-day stroke care routines. Although only 27% of the physical therapists uses wearable monitors, a majority (79%) of the non-users believes in the concept and its added value, and is open to using wearables in the future. The therapists mostly value the possibility to provide feedback objectively, creating awareness, and stimulating self-management.
The following sections discuss the above findings in the context of this thesis, current literature and clinical practice.

Relationships with other domains of functioning

The results described in this thesis reveal overall weak relationships between objectively measured physical behavior and outcomes of clinical tests. This suggests that physical behavior is a construct of performance that is independent of, and cannot be exchanged with, the outcomes of clinical tests. This corresponds with the

International Classification of Functioning and Health (ICF) model[1], in which clinical tests generally represent the domains of body functions & structures and capacities, while physical behavior outcomes represent performance under the activities domain. In clinical practice, however, it is often assumed that what someone *can do* corresponds to what someone *actually does* in reality.[2] The results of our studies are in contrast to that assumption.

Several factors may contribute to the observed weak relationships. First, there is a conceptual gap between clinical test outcomes and physical behavior outcomes. The strength of this relationship seems to depend on what type of physical behavior is compared with what type of capacity measure.[3, 4] While data collected with wearables express performance in terms of the *quantity* of movements, clinical tests often target the *quality* of movements and therefore include some form of judgement.[5] For example, Rand *et al*. (2012)[6] found a gap between the recovery of motor function and improvement of performance measured with accelerometry in stroke patients during inpatient rehabilitation. Furthermore, it has been suggested that the strength of the relationship is affected by pre-existing physical impairments.[7] The range of body functions & structures and capacities is larger in individuals without severe impairments, and it seems easier for these individuals to fully use their abilities to be active in daily life.

The findings in this thesis also support the existence of a conceptual gap. It is hypothesized that the relationship between clinical test outcomes and physical behavior outcomes is stronger when the movement performed during the clinical test is equivalent to the activities performed during daily life, and assessed on the same aspect. The section “physical behavior outcome measures” below addresses the choice of the type of outcome measure to correctly express physical behavior. Further, routinely conducted clinical tests often have limited ecological validity since they do not incorporate the environmental challenges a patient is facing, whereas wearable monitors perform measurements in a real-life setting.[7] Finally, social environment, self-efficacy, motivation, and psychosocial well-being are potential determinants of physical behavior predictors of explaining variability between patients independent of physical capacity.[8, 9] To deal with such variability, prolonged and uninterrupted (e.g. 24h cycle) measurement periods may provide a more accurate and reliable reflection of physical behavior, which is less affected by temporary factors. Moreover, the high variability implies that more individually tailored interventions are needed in rehabilitation.[10]

Physical behavior outcome measures

Physical behavior monitored with wearable monitors is often expressed with only one outcome measure. As it is possible to score high on one aspect of physical behavior and low on another, essential findings are easily overlooked.[11, 12] Therefore, in this thesis, physical behavior is considered a construct consisting of multiple dimensions, expressed in multiple outcomes. In our explorative study (Chapter 3), we performed a data-driven analysis and showed that 15 *a priori* outcomes can be reduced to five specific and distinct physical behavior measures, confirming the preconceived idea of multidimensionality. However, selecting the appropriate (set of) multidimensional outcome measures comes with several challenges:

Instruments

Comparing studies on objective physical behavior outcome measures is complicated, as the high variability of available measurement instruments on the market is accompanied by high variability in reported outcome measures.[13] Also, algorithms to calculate outcome measures and analytical approaches vary widely.[14, 15] Therefore, standardization on physical behavior measurement in rehabilitation should be a topic in future research.

Target population

Different rehabilitation populations likely require different outcome measures.[16] For example, in MS patients (Chapter 3) the change score ratio between day parts is relevant in terms of energy management.[17] The time spent upright (Chapters 4 and 5) may be relevant in stroke patients in whom immobility contributes to decline of functioning.[18] In contrast to the importance of a population-specific approach, the selected outcome measure in literature is often the one that is easily generated by the available measurement instrument. Further, instruments should be validated for the rehabilitation populations they are used for.[14] For example, severely affected stroke patients typically have a slower gait speed, which cannot be detected by devices designed for healthy persons.[19] The measurement instrument selected in Chapters 4 and 5 of this thesis was specifically validated for stroke patients.[20]

Interpretation

Besides reliability and validity, interpretability is one of the clinimetric criteria of instruments.[21] This means the data should be presented in an easy to interpret format, such as for example the existing Dutch physical activity guidelines.[22] Many wearables can quickly generate simple time-based outcome measures. However, in clinical populations other measures may be more relevant: non-time-based, such as

accelerometer counts; a measure closely reflecting the accelerations of the wearable device that is attached to the body. Measures directly reflecting accelerations may have stronger links to health outcomes than time-based outcomes (Chapter 4).[14] For example, in this thesis we look at the intensity of physical activity, as expressed with accelerometer counts. Measures like these are however more difficult to envision and interpret for health care professionals compared to time-based measures. Application in clinical care will therefore require a balance between interpretability on the one hand, and relevance for health and functioning on the other. It is crucial that clinical professionals understand the information obtained from wearable monitors, and understand the differences between various outcome measures.
Obviously, using an overly large set of different outcomes will be too complex and time-consuming to interpret, as confirmed by health care professionals.[23] Therefore, intelligent and low-threshold solutions are needed to be able to apply the multidimensional aspect of physical behavior in clinical practice. A possible solution could be a simplified presentation of various outcome measures, such as the physical behavior profiles visualized in the spider plots in Chapter 3 of this thesis.

Clinical application

Potential for rehabilitation

Objectively measured physical behavior data represent a specific and independent measure of functioning captured under the ICF domain "activities". The potential of wearable technology for performing diagnostics, measuring treatment effects, and monitoring progress and decline, is widely known.[24, 25] Objectively measured physical behavior adds new and relevant information for clinical management; it allows physicians to evaluate the impact of rehabilitation interventions in daily life, thus supporting clinical decision-making.[2, 5, 26] Also, wearable monitors offer opportunities for at-home management of diseases.[27] Wearable monitors can passively and effortlessly gather physical behavior data for days or even weeks.[26, 27]

Wearable monitors can further be deployed as behavioral change tools by generating objective feedback to patients. In Chapter 2 and comparable reviews[26, 28-33], overall positive results on physical behavior were observed in cardiac patients, oncology patients, and patients with COPD. A crucial aspect for effectively applying wearable monitors is to combine them with other behavioral change techniques (Chapter 2). These could include techniques such as goal setting, education, and barrier identification. Such methods are already frequently used in usual care by professionals.[34] Wearable technology therefore offers an excellent opportunity to catalyze behavioral change. However, as described in Chapter 6, providing objective physical behavior feedback may not suit every patient or patient group. For example elderly patients may not have the skills to use modern technology.[35] Additionally, severely affected patients residing in rehabilitation likely focus on other more fundamental aspects of their recovery instead of being physically active.

Barriers for use

The use of wearable technology in clinical practice still lags behind due to several reasons.[2, 36, 37] For example consumer-grade devices are not yet designed for specific patients and care processes in rehabilitation.[23] Ideally, the technology should be tailored to the individual patient's health status and context in order to achieve more significant health gains.[38] End-users such as therapists and patients should be involved in the development of new wearable technologies for clinical practice as co-designing technology may result in quicker adoption in real-world care routines.[39]
Another fundamental prerequisite for successful uptake of wearable monitors in clinical practice is that health care professionals acknowledge the value of physical behavior monitoring with wearable technology.[2] For this thesis, physical therapists were questioned about the use of and perspectives regarding wearable monitors. In general, despite the positive perspectives towards using wearable technology in daily practice, it is only sparsely applied. Common barriers amongst the health care professionals are a lack of skills and knowledge (for example; not knowing what type of monitor to choose or how to interpret the data), lack of skills and knowledge of patients, design flaws and lack of support from the health care organization.[23, 36, 40] Hilty *et al.* (2021)[37] also found that the current clinical, technological, and administrative workflows are not designed to include easy-to-use technology.

Additional perspectives for future research and rehabilitation practice

The above discussion provides several perspectives and recommendations for future research and clinical application of wearable technology, such as more prolonged and uninterrupted measurements, the multidimensionality of outcomes, awareness of conceptual differences between physical behavior outcomes and involving patients and health care professionals in designing new technology. Additional recommendations and future perspectives on physical behavior measurement in research and rehabilitation practice are described below.

- External factors that affect physical behavior, such as physical and social environment, and personal characteristics such as motivation and psychosocial well-being should be taken into account in future studies towards developing personalized interventions and guidelines to improve patients' health. For example, the behavioral change wheel, including different sources of behavior as capability, opportunity, and motivation, may be a helpful framework for developing personalized interventions that promote physical behavior.[41]

- Standardization in the use of outcome measures in research is needed. Recently, Migueles *et al.*[14] developed a draft of a decision tree to assist researchers in making decisions on outcome measures, including multiple steps with questions regarding conceptual and analytical choices for measuring physical behavior, which may support the development of using standardized outcome measures in research. From large (pooled) datasets, physical behavior patterns can be detected, and normative values can be developed using machine learning techniques.
- Multi-sensor devices, allowing integration of physiological and non-physiological variables such as heart rate, sleep (24h cycle), blood pressure, global position system (GPS) and respiration rate, are increasingly available on the market. Future research on the relevance and usefulness of these other variables in combination with physical behavior is recommended.
- Currently, health care professionals lack time and support to adopt rehabilitation technologies.[42] Engaging the entire system may lead to more centralized and routine data collection, supporting clinical decision-making.[23] Therefore, future studies on how to effectively implement wearable technology in clinical practice should consider the entire organizational context.
- The current use of wearable monitors seems to depend on enthusiasm of individual health care professionals. Motivating health care professionals who are not naturally front-runners in using (novel) technology requires tailored education strategies that target both competencies and attitudes. The latter should not be forgotten as clinicians may prefer their professional acumen over data provided by wearables, hampering widespread use.[43] Education should also cover the similarities between standard and innovative technological tools to measure clinically relevant outcomes.[21]
- Professionals who are thinking about using wearable technology should be very precise in identifying what it is they want to know and which device is most suitable for that specific purpose and patient population. In the current pioneering age, with new technologies and features continuously emerging, there are no standard protocols to rely on for such decisions. This means that professionals should keep themselves up to date with policy-related and technological developments in their field. Also, graduate and post-graduate education will have to pay attention to innovative technologies.
- In the meantime, more and more patients are using wearables to self-measure their daily health situation. Therefore, health professionals should

expect patients arriving to consultations carrying their own data.[26] Kos *et al.* (2021)[5] even state that, given current developments in artificial intelligence and machine learning, it is highly conceivable that the data collected by various wearable sensors will prove superior to assessing performance by professionals.

Concluding remark

This thesis zooms in on three aspects of objective measurement of activity in rehabilitation; relationships with other domains of functioning, physical behavior outcome measures, and clinical application. There is considerable potential and added value in applying wearable technology in rehabilitation. However, our results reveal that there is still a world to win regarding the practical and meaningful use of wearable technology for physical behavior measurement in rehabilitation research and clinical practice. The gains to be made will have to come from many different areas, such as the (establishment of) outcome measures and their analysis, technology-oriented and clinically oriented research, health care, education, and commercial development of wearable technology. This requires a collective effort with the ultimate goal to establish technology that is easily accessible, easy to use in rehabilitation practice, beneficial to health care, and contributing to healthier lives of patients.

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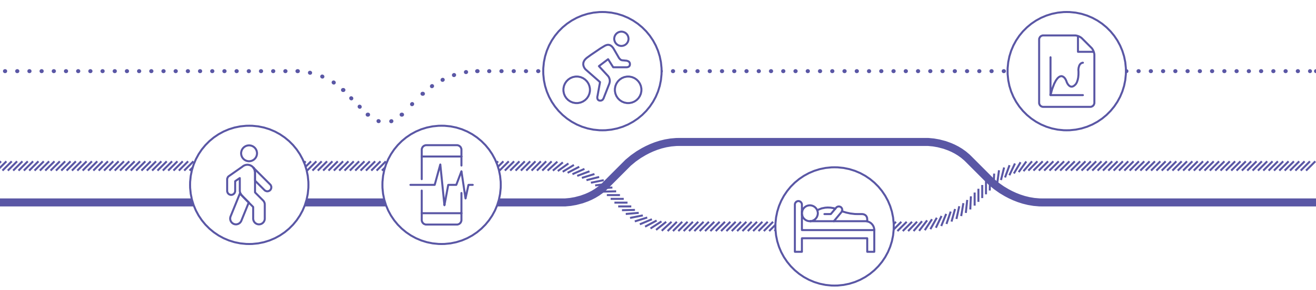
SUMMARY



Patients with chronic conditions often have a less favorable physical behavior pattern compared to the healthy population. Especially for these patients, promoting healthy physical behavior is essential; it stimulates motor recovery and lowers the risk of, for example, cardiovascular disease and diabetes. To improve deteriorated physical behavior levels, physical behavior must be measured objectively and reliably. Wearable sensors, also known as activity monitors, offer the opportunity to provide a comprehensive insight into patients' physical behavior for several consecutive days. Data from these monitors can be used for treatment, for example to monitor progress, support diagnosis, and set appropriate treatment goals. In addition, wearable activity monitors offer the opportunity to automatically generate objective feedback on physical behavior and stimulate self-management without the effort of a professional. Thus, activity monitors have great potential for application in rehabilitation. However, there are still unsolved fundamental issues concerning objective measurement of physical behavior in rehabilitation. This thesis focuses on three themes: the relationship between physical behavior and other domains of functioning, physical behavior outcome measures, and clinical application.

The background of the three main themes is described in the introduction in **Chapter 1**. This chapter also explains the concepts of physical behavior, physical activity, and sedentary behavior as used in this thesis. Chapter 1 ends with a brief overview of the content and the objective of this thesis: to better understand the objective measurement of physical activity behavior in rehabilitation, with the ultimate goal of meaningful application of wearable technology in the future.

Chapter 2 describes the results of a systematic literature review and meta-analysis on the effect of providing objective feedback on physical activity with activity monitors. Included studies compared the physical activity levels of (former) patients of health care institutions who received objective feedback with patients who did not receive feedback. Fourteen randomized controlled trials demonstrated that objective feedback moderately improved physical activity in various patient groups, such as patients with COPD, cardiovascular disease, or stroke patients. The diversity of the interventions in the studies was large, and the effectiveness seems to depend on several factors. One of the factors is whether additional behavioral change techniques are provided, such as goal setting and education about the benefits of physical activity.

The study described in **Chapter 3** aimed to gain insight into the extent to which physical behavior varies within a patient group with comparable symptoms. In this study, 212 patients diagnosed with Multiple Sclerosis (MS) and experiencing severe fatigue wore the Actigraph activity monitor for one week. It was hypothesized that physical behavior cannot be described by one outcome measure, but that multiple outcome measures are needed to provide a representative reflection of physical behavior. A principal components analysis was applied to establish a set of various outcome measures; 15 MS-specific outcome measures were reduced to five outcome measures. Subsequently, these five outcome measures were used in a cluster analysis to identify different types of exercise behavior. Three significantly different types of exercise behavior could be distinguished; sedentary, moderately sedentary, and active. The significant differences between physical behavior types show that it is essential to develop personalized physical behavior interventions that fit the level of the patient.

In **chapter 4**, physical behavior was also quantified by multiple outcome measures, representing four dimensions; the intensity, frequency, distribution, and duration of physical activity. Sixty-nine patients who had a minor stroke or unilateral supratentorial transient ischemic attack (TIA) wore the Activ8 activity monitor for one week during their daily life. They additionally performed three physical capacity tests; the 10-Meter-Walking-Test (10MWT) to determine walking speed, the Timed-Up & GO (TUG) for mobility, and the Mini Balance Evaluation System Test (Mini-BESTest) for static and dynamic balance. The relationship between these three capacity tests and the four physical activity outcome measures was determined. Intensity was significantly related to scores on the 10MWT, the other physical activity outcome measures (frequency, distribution, and duration) were not related to the capacity tests. The possible specific role of physical activity intensity in improving physical capacity requires attention in future research.

Chapter 5 contains a longitudinal study, in which physical activity was quantified with the same physical activity outcome measures as used in Chapter 4. Thirty-nine severely affected stroke patients wore the Activ8 activity monitor for 7 days at three time points; 3, 12, and 26 weeks after stroke. Motor function of the lower extremity was additionally measured at these time points using the Fugl Meyer Lower Extremity Assessment (FMA-LE) test. The intensity and duration of physical activity increased after stroke, particularly in the first 12 weeks. The frequency and distribution did not show significant changes. The results also showed that physical activity was not or weakly related to the recovery of motor function. Remarkable was the considerable variability in physical activity between patients after stroke.

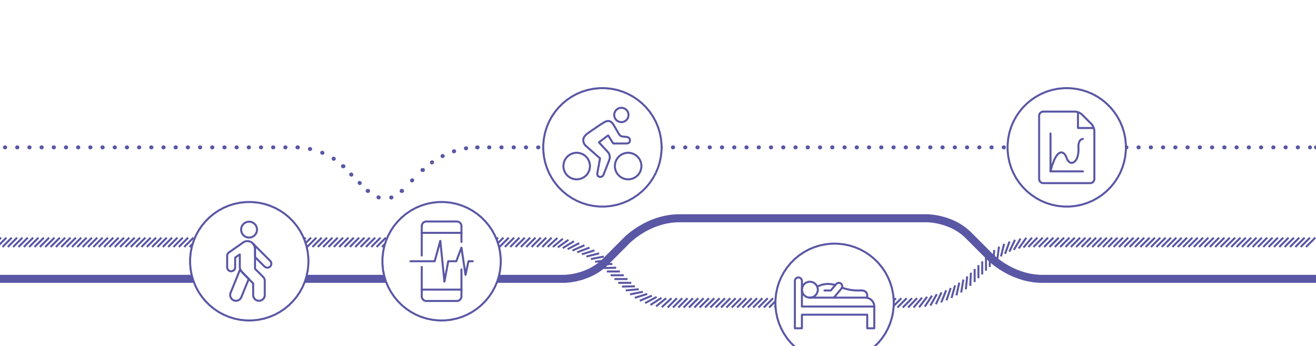
In summary, **Chapters 3, 4, and 5** demonstrate that the results of studies in which physical behavior is objectively measured with an activity monitor are highly sensitive to which outcome measures were used. This sensitivity supports the multi-dimensionality of physical behavior and the importance of expressing physical behavior in more than one outcome measure.

Chapter 6 focuses on the current use of activity monitors in clinical practice. Over 100 physiotherapists involved in the treatment of stroke patients completed an online questionnaire. Besides the current use, questions were asked about the usefulness, appropriate treatment purposes, and barriers to using activity monitors in clinical practice. Twenty-seven percent of therapists already use activity monitors or have used them in the past. Ninety-seven percent of the non-users are open to using it in

the future. Eighty-six percent of the treatment purposes for which activity monitors can be used, such as creating awareness of physical behavior, encouraging self-management, and evaluating treatment, were considered valuable by more than half of the therapists. Barriers were mainly related to patients' lack of skills and knowledge and lack of knowledge among therapists regarding selecting the appropriate activity monitor. Today, the use of activity monitors seems to be mainly determined by skills, beliefs, and attitudes of individual therapists.

The main findings of the studies in this thesis are discussed in **Chapter 7**, along with interpretation in the context of the literature and clinical practice. Despite the potential benefits for therapists and their patients, standard application of activity monitors in rehabilitation care is not yet within reach. Different disciplines will need to work together effectively to realize valuable use in the future, for example, technological and clinical research, the health care system, professional education, and companies developing the wearable technology.

SAMENVATTING



Mensen met een chronische aandoening hebben vaak een minder gunstig beweegpatroon dan mensen zonder een chronische aandoening. Daarom is het juist voor hen essentieel om gezond beweeggedrag te bevorderen; gezond beweeggedrag stimuleert het motorisch herstel en verlaagt het risico op bijvoorbeeld hart- en vaatziekten en diabetes. Om hierop te kunnen inspelen is het van belang dat het beweeggedrag betrouwbaar en objectief gemeten wordt. Draagbare bewegingssensoren, ook wel activiteitenmonitors of activity trackers genoemd, bieden de mogelijkheid om gedurende achtereenvolgende dagen het beweeggedrag objectief te meten. De data uit deze monitors kan bijvoorbeeld gebruikt worden voor het monitoren van voor- en achteruitgang, ter ondersteuning van het stellen van diagnoses en het opstellen van passende beweegdoelen in de revalidatiebehandeling. Daarnaast bieden deze systemen de mogelijkheid om automatisch objectieve feedback op het beweeggedrag te genereren, zodat zelfmanagement van patiënten wordt gestimuleerd, zonder eventuele tussenkomst van een zorgprofessional. Activiteitenmonitors hebben dus veel potentie voor toepassing in de revalidatie. Echter, voor onderbouwde en efficiënte toepassing in de praktijk moeten er nog een aantal belangrijke vragen worden beantwoord. Dit proefschrift richt zich op drie thema's waarbinnen kennishiaten bestaan: 1) de relatie tussen beweeggedrag en andere domeinen van functioneren, 2) de uitkomstmaten van beweeggedrag, en 3) de toepassing van activiteitenmonitors in de klinische praktijk.

De achtergrond van deze drie thema's wordt beschreven in de inleiding in **hoofdstuk 1.** Ook worden hier de begrippen beweeggedrag, fysieke activiteit en sedentair gedrag toegelicht, zoals gehanteerd in dit proefschrift. Het hoofdstuk sluit af met een beschrijving van de inhoud en doelstelling van dit proefschrift: het beter begrijpen van het objectief meten van beweeggedrag in de revalidatie, met als ultieme doel de technologie waardevol te kunnen toepassen in de toekomst.

Hoofstuk 2 beschrijft de resultaten van een systematisch literatuuronderzoek en meta-analyse naar het effect van het geven van objectieve feedback met behulp van activiteitenmonitors op de fysieke activiteit. In de geïncludeerde studies werd de fysieke activiteit van (voormalige) patiënten van gezondheidszorginstellingen die objectieve feedback kregen vergeleken met patiënten die geen feedback kregen en de standaardzorg ontvingen. Uit 14 gerandomiseerde studies bleek dat objectieve feedback leidde tot een verbetering van de fysieke activiteit van diverse patiëntgroepen, zoals patiënten met COPD, hart- en vaatziekten of een Cerebro Vasculair Accident (CVA). De diversiteit van de interventies in de studies was echter groot, en de effectiviteit lijkt afhankelijk te zijn van verschillende factoren. Een van de factoren is of en welke gedragsveranderingstechnieken er naast de objectieve feedback worden gebruikt, zoals het stellen van doelen en educatie over de voordelen van fysieke activiteit.

Het onderzoek beschreven in **hoofdstuk 3** had als doel inzicht te krijgen in hoeverre het beweeggedrag verschilt binnen een patiëntgroep met dezelfde vermoeidheidssymptomen. Voor dit onderzoek hebben 212 patiënten die gediagnosticeerd zijn met Multiple Sclerose (MS) en ernstige vermoeidheid ervaren een week lang de Actigraph activiteitenmonitor gedragen. De hypothese was dat het beweeggedrag niet te beschrijven is met één uitkomstmaat, maar dat er meerdere multidimensionale uitkomstmaten nodig zijn om een representatief beeld te geven van het beweeggedrag. Om tot een set van diverse uitkomstmaten te komen is een principale componenten analyse toegepast, waarbij 15 uitkomstmaten die voortkomen uit MS-specifieke literatuur gereduceerd werden naar vijf uitkomstmaten. Deze vijf uitkomstmaten zijn vervolgens gebruikt in een clusteranalyse om verschillende typen beweeggedrag te identificeren. Drie significant verschillende typen beweeggedrag konden worden onderscheiden: sedentair, matig sedentair en actief. De grote verschillen in het beweeggedrag binnen de groep vermoeide MS-patiënten laten zien dat het van belang is gepersonaliseerde beweeggedraginterventies te ontwikkelen die aansluiten bij het niveau van de patiënt.

Ook in **hoofdstuk 4** is beweeggedrag gekwantificeerd door meerdere uitkomstmaten die vier dimensies vertegenwoordigden: de intensiteit, frequentie, verdeling en duur van fysiek activiteit. Negenenzestig patiënten die een unilaterale supratentoriale transient ischemic attack (TIA) hebben gehad droegen een week lang de Activ8 activiteitenmonitor tijdens hun dagelijks leven. Tevens voerden zij drie fysieke capaciteitstesten uit; de 10-Meter-Loop-Test (10MLT) om de loopsnelheid te bepalen, de Timed-Up & GO (TUG) voor de mobiliteit en de Mini Balance Evaluation System Test (Mini-BESTest) voor de statische en dynamische balans. Vervolgens is de relatie tussen deze drie capaciteitstesten en de vier uitkomstmaten van fysieke activiteit bepaald. Uit de analyses bleek dat de intensiteit van fysieke activiteit significant gerelateerd was aan de scores op de 10MLT. De andere fysieke activiteit uitkomstmaten (frequentie, verdeling en duur) waren niet gerelateerd aan de capaciteitstesten. De mogelijk specifieke rol die intensiteit van bewegen speelt in het verbeteren van de fysieke capaciteit van deze patiënten zal in de toekomst verder moeten worden onderzocht.

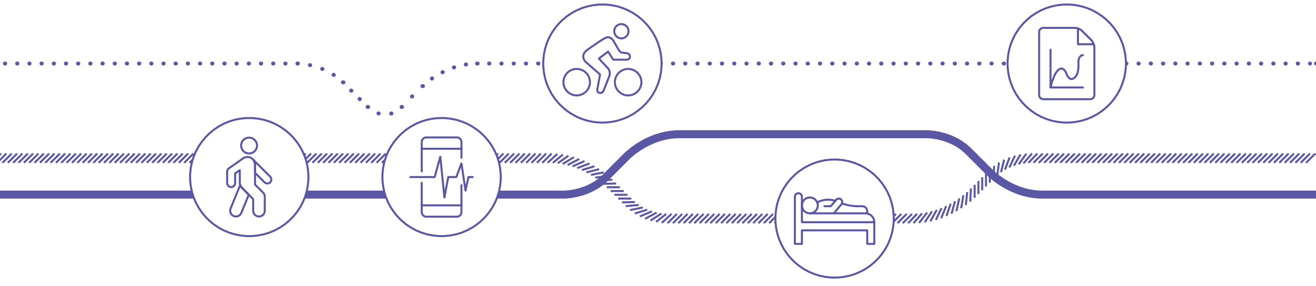
In **hoofdstuk 5** zijn dezelfde uitkomstmaten van fysieke activiteit gebruikt in een longitudinale studie bij CVA-patiënten. In dit onderzoek droegen 39 ernstig aangedane patiënten die een CVA hebben gehad de Activ8 activiteitenmonitor gedurende een week; 3, 12, en 26 weken na de dag van hun CVA. Tevens werd op deze momenten de motorische functie van de onderste extremiteit gemeten met behulp van de Fugl Meyer Lower Extremity Assessment (FMA-LE) test. De intensiteit en duur van de fysieke activiteit verbeterde, met name in de eerste 12 weken na de CVA. De frequentie en de verdeling van fysieke activiteit lieten geen duidelijke veranderingen zien. Daarnaast was de fysieke activiteit niet of nauwelijks gerelateerd aan het herstel van motorische functie. Opvallend in deze studie was de grote variatie in fysieke activiteit binnen de patiëntgroep.

Zowel **hoofdstuk 3**, **hoofdstuk 4** als **hoofdstuk 5** laten zien dat de resultaten van studies waarin het beweeggedrag objectief wordt gemeten met activiteitenmonitors gevoelig zijn voor welke uitkomstmaten er zijn gebruikt. Deze gevoeligheid bekrachtigt de multi-dimensionaliteit van beweeggedrag en het belang van het uitdrukken van het beweeggedrag in meer dan één uitkomstmaat.

Hoofdstuk 6 gaat in op het huidige gebruik van activiteitenmonitors in de klinische praktijk. Ruim 100 fysiotherapeuten die betrokken zijn in de behandeling van CVA-patiënten hebben een online vragenlijst ingevuld. Naast het huidige gebruik werd onder andere gevraagd naar de bruikbaarheid, geschikte behandeldoeleinden en barrières ten aanzien van het gebruik van activiteitenmonitors in de klinische praktijk. Zevenentwintig procent van de therapeuten maakt al gebruik van activiteitenmonitors of heeft daar in het verleden gebruik van gemaakt. Negenenzeventig procent van de therapeuten die nog geen gebruikt maakt staat er wel open voor in de toekomst. Achtenzestig procent van de behandeldoeleinden waarvoor activiteitenmonitors kunnen worden ingezet, zoals het creëren van bewustzijn van het beweeggedrag, het stimuleren van zelfmanagement en het evalueren van de behandeling werd als waardevol beschouwd door meer dan de helft van de therapeuten. Barrières die therapeuten ervoeren hadden vooral te maken met het gebrek aan kennis bij patiënten en gebrek aan kennis bij henzelf ten aanzien het kiezen van de geschikte activiteitenmonitor. Vandaag de dag lijkt het gebruik van activiteitenmonitors vooral bepaald te worden door de vaardigheid, de overtuiging en de attitude van een individuele therapeut.

De belangrijkste bevindingen van de studies in dit proefschrift worden bediscussieerd in **hoofdstuk 7**, samen met de interpretatie in de context van de literatuur en de klinische praktijk. Het standaard toepassen van activiteitenmonitors in de revalidatiezorg ligt nog niet binnen handbereik, ondanks de potentiële voordelen voor de patiënten en hun therapeuten. Verschillende disciplines zullen effectief moeten samenwerken om waardevol gebruik in de toekomst te realiseren, denk hierbij aan bijvoorbeeld technologisch en klinisch onderzoek, het gezondheidszorgsysteem, het beroepsonderwijs en bedrijven die de technologie ontwikkelen.

DANKWOORD



Het “boekje” is af! Blij en trots dat het zover is gekomen. Ik heb (bijna altijd) met veel plezier gewerkt aan het onderzoek in dit proefschrift. Soms best een puzzel om dit te combineren met het onderwijs, maar voor mij was juist deze afwisseling zeer welkom. In beide werelden heb ik veel mensen mogen leren kennen, en veel van deze mensen mogen leren. Zonder hen was het mij natuurlijk nooit gelukt om dit te bereiken! Ik wil hen dan ook graag bedanken.

Allereerst alle deelnemers aan de verschillende studies die zijn beschreven in dit proefschrift. Ik wil jullie graag bedanken dat jullie, ondanks het werken aan het herstel, de tijd en moeite wilden nemen voor deelname aan wetenschappelijk onderzoek.

Daarna mijn begeleidingsteam. Prof. dr. Gerard Ribbers, bedankt voor de mogelijkheid om als een vreemde eend in de bijt vanuit de Haagse hogeschool onder jouw supervisie te mogen promoveren. Ik ben je heel dankbaar voor jouw begeleiding, ook al was het soms een zoektocht naar hoe we onze samenwerking en mijn proefschrift vorm gingen geven. Jouw kritische vragen en klinische blik brachten me steeds verder, zelfs wanneer de documenten behoorlijk rood terugkwamen. In de loop der jaren voelde ik me steeds meer onderdeel worden van de afdeling revalidatiegeneeskunde met, op een gegeven moment, jou als afdelingshoofd. Ik denk dat menig ander afdelingshoofd een voorbeeld kan nemen aan hoe jij ons als junioren betrokken hebt bij de veranderingen binnen afdeling. Ook ben ik je dankbaar voor de mogelijkheid om verbonden te blijven aan de afdeling. Ik hoop op mooie samenwerkingsprojecten in de toekomst!

Onmisbaar waren ook mijn beide co-promotoren dr. Hans Bussmann en dr. Monique Berger. Hans en Monique, Monique en Hans, ik weet niet zo goed bij wie ik moet beginnen. Ik ontmoette jullie beide bijna 7 jaar geleden, tijdens het sollicitatiegesprek voor de functie docent/onderzoeker “activiteitenmonitoring” bij Bewegingstechnologie en in het FAST@HOME project, waarin ik, vrij brutaal, aangaf dat ik wel wilde, maar vooral wanneer ik kon promoveren op dit onderwerp. Toen ik het eenmaal was geworden kreeg ik wel wat koudwatervrees. Veilig vanuit het oosten, moest ik mij tussen het geweld in het westen gaan begeven. Maar wat ben ik dankbaar dat ik dit onder jullie vleugels heb mogen doen. Ik durf wel te stellen dat ik met jullie beide, of wij met z’n drieën, een bijzondere band heb opgebouwd.

Hans, zo’n 6 jaar lang, bijna elke week een één-op- één overleg, waarin we elkaar steeds beter hebben leren kennen. Toegegeven; af en toe was ik geïrriteerd dat ik met meer vragen weg liep dan ik binnenkwam (toch nog een extra analyse, opnieuw nadenken over …. etc). Maar veelal heb ik genoten van onze samenwerking. Naast dat jij me als expert wegwijs hebt gemaakt in de wereld van activiteitenmonitoring, heb ik onze persoonlijke gesprekken als heel waardevol ervaren. Op lastige momenten kon ik op je begrip rekenen. Heel fijn dat we konden schipperen tussen de inhoud en het persoonlijke, met de nodige dosis humor. Dat voelt vrij uniek in de academische wereld. Daarnaast vind ik het geheel terecht dat je uiteindelijk ook promotor bent als ius promovendi. Ik ben trots dat ik jouw eerste promovendus ben!

Monique, jij had dubbel geluk! Zowel binnen het onderzoek als onderwijs mocht ik genieten van jouw betrokkenheid. In het onderzoek als mijn co-promotor, maar in het onderwijs als mijn naaste collega, waarmee ik om 7:35 op spoor 4 van station Amsterdam-Zuid stond: een oprechte Amsterdammer en ervaren praktijkgericht onderzoeker met een soms wat bescheiden tukker (“óógpotlóód!”) aan het begin van haar carrière. Wat vooraf misschien best ingewikkeld leek, die verschillende petten, ging ons juist goed af. Voor mij een feest om dit samen te doen. Zonder jouw aanstekelijke energie was ik niet gekomen waar ik nu ben! Jij hebt me steeds op verschillende manieren weten te motiveren wanneer ik vast liep. Net als met Hans, bespreken we meer dan alleen de inhoud van het onderzoek en ik ben dan ook heel blij dat we nog niet van elkaar af zijn! Ik kijk er naar uit om in een nieuwe setting, met jou als lector, dus wederom onder jouw vleugels, praktijkgericht onderzoek te mogen doen!

Mijn dank gaat tevens uit naar de andere betrokken auteurs bij de artikelen uit mijn proefschrift: Prof. Dr. Vincent de Groot, Prof. dr. Vivian Weerdesteyn, Prof. dr. Ruud Selles, dr. Ruben Regterschot, dr. Edwin van Weegen, dr. Jetty van Meeteren, dr. Heleen Beckerman, Gerlinde van der Stok en dr. Jolanda Roelofs.

Ook gaat mijn dank uit naar de kleine en grote promotiecommissie. Prof. dr. Mirjam Vollenbroek, speciale dank gaat uit naar jou. Bedankt voor de keren dat ik als dorpsgenoot kon aankomen met vragen over mijn loopbaan voordat ik in Den Haag/Rotterdam begon. Ik vind het dan ook “onmeunig” mooi dat je aanwezig bent bij de afsluiting van dit promotietraject.

Een deel van mijn tijd als promovendus bracht ik door op de “16e” in het ErasmusMC in Rotterdam. Fijn om hier lief en leed te delen met andere junior onderzoekers en promovendi tijdens lunch en borrels. Maar ook successen te vieren met taart van Koekela. Bedankt hiervoor! In het bijzonder wil ik hier Marloes, Suzie en Lianne bedanken; ook buiten werktijd wisten we elkaar te vinden, o.a. tijdens de “Friday Offices” met natuurlijk een borrel na afloop. Fijn om met jullie te over onderzoek, professionele ontwikkeling, en privé-kwesties te discussiëren. Ookal werken we niet meer allemaal samen, ik hoop dat er nog vele sessies mogen volgen.
Daarnaast wil ik Herwin bedanken voor de bijdrage aan de dataverwerking in Matlab en Raphaela voor de ondersteuning bij het verzamelen van de data in de PROFITS studie binnen Rijndam.

Het andere deel van de tijd bracht ik door op de Haagse hogeschool, bij de opleiding Mens & Techniek - Bewegingstechnologie en het lectoraat Technologie voor Inclusief Bewegen en Sport (voorheen bij het lectoraat revalidatie). Collega’s van het BT-team: jullie wil ik bedanken voor jullie interesse in mijn onderzoek, maar ook jullie flexibiliteit en geduld. Het is soms best ingewikkeld; ambitieuze teamleden die hun tijd moeten verdelen over onderwijs en onderzoek. Hier ga ik nog wel even mee door, maar ik ben erg blij dat ik nog steeds deel uit mag maken dit team, ik voel me er thuis! Willem, bedankt voor jouw positieve energie tijdens onze gesprekken en het constant meedenken over mijn professionele ontwikkeling. Het was soms best een puzzel, het verdelen van taken en aanstellingen, maar keer op keer kregen we dit voor elkaar! Caroline, wat fijn om mijn hart over (de gang van zaken rondom) mijn proefschrift te kunnen luchten bij iemand met jouw expertise en ervaring, dank daarvoor! Jorine, gaandeweg de jaren ben ik steeds meer met je gaan samenwerken, het afstuderen, blok 4, en wat is dit fijn! We vullen elkaar goed aan. Met name dank voor hoe flexibel je bent, wanneer het voor mij lastig werd door mijn drukke programma. Manon, ook bedankt voor jouw flexibiliteit, nooit te beroerd om even snel te reageren op korte vragen, of dingen over te nemen wanneer ik vast liep. Wat ben ik blij met zulke collega's!

Het zaadje voor mijn promotietraject was geplant tijdens mijn werkzaamheden in het FAST@HOME project, dat naast de Haagse hogeschool, ook bij Basalt (voorheen Sophia Revalidatie) was ondergebracht. Arend & Jorit, bedankt voor jullie interesse in mijn specifieke onderzoek en dat het mogelijk was hiermee door te gaan vanuit FAST@HOME. Berber & Manon, ook fijn om met jullie het leed dat promoveren heet te delen tijdens onze koffiemomentjes en etentjes. Jullie gingen me al voor, maar straks zijn we alle drie PhD!

Ook wil ik de vele studenten bedanken die hun stage of afstuderen hebben gedaan binnen een van de studies van mijn promotietraject. Werken met jullie was vaak heel verfrissend!

Daarnaast zijn er ook tal van mensen die niet direct betrokken, maar minstens zo waardevol waren gedurende mijn promotietraject:

Lieve vriendinnen; de "zaterdag" groep uit Geesteren, oud-Donitaters uit Groningen, oud-VWO-genootjes, bedankt voor jullie interesse, medeleven en vooral het zorgen voor welkome afleiding in de vrije tijd! Ookal bewandelt iedereen hun eigen pad en wonen we niet allemaal bij elkaar om de hoek, fijn dat er nog zo goed contact is en het altijd gezellig is als we samen zijn!

Van deze groep wil ik natuurlijk in het bijzonder Maartje K., onze creatieve geest, bedanken. Ik ben heel blij dat jij de omslag wilde ontwerpen, hij is echt gaaf geworden! Daarnaast wil ik ook mijn paranimfen Ester en Maartje H. bedanken, jullie durven het aan om aan mijn zijde te staan op 6 juli. Ik kijk er naar uit om dit samen met jullie te beleven. Met een gerust hart durf ik jullie dan ook te betrekken in de outfit- en feestvoorbereidingen. Ook jammer dat we niet meer alle drie in Amsterdam wonen, maar zonder jullie was die tijd lang niet zo leuk geweest! Die etentjes na lange werkdagen mis ik echt. Maar gelukkig gaan we niet ver weg en zien we elkaar nog vaak.

Wie onze tijd in Amsterdam ook een stuk prettiger maakten zijn mijn schoonouders, Eveline en Rob. Bedankt voor jullie interesse, support, en discussies over de wetenschap. Het was ook erg fijn dat Maurits en ik vaak bij jullie konden aanschuiven na een lange werkdag.

Dan mijn familie. Oma, vaak vroeg jij of ik nu niet een keer was uitgestudeerd. Jij vond het wel een keer mooi geweest. Voor nu is het even klaar hoor. Wat ben ik dankbaar dat jij dit allemaal nog mee mag maken. Ik kijk er naar uit om dit boekje bij je langs te brengen. Mijn broer Bram en zus Liesan, we zijn alle drie in verschillende vakgebieden beland maar kennen soortgelijke eigenschappen en daarmee uitdagingen. Zeker doorzettingsvermogen is jullie beide niet vreemd. Als jongste kon ik altijd bij jullie afkijken, dank voor deze inspiratie, en voor jullie onvoorwaardelijke steun. Ook Marloes en Rutger (en natuurlijk Mijs, Guus en Lou), dank voor jullie interesse, fijn dat jullie deel uit maken van ons gezin. Dan mijn ouders, pap en mam. Doe maar normaal, dan doe je al gek genoeg, was het credo dat we meekregen. Ik ben zo dankbaar hoe jullie ons altijd hebben gestimuleerd het beste uit onszelf te halen, zonder er te veel druk op te leggen. Alles was goed en bespreekbaar, als we ons best deden, doorzetten en vooral ons gelukkig voelden. De beste basis die ik mij kan bedenken voor waar ik nu sta!

Maurits, als ik dit dankwoord een jaar eerder had geschreven kwam je als laatst aan bod. Nu is dat plekje voor iemand anders. Je hebt het hele traject van het begin tot het eind van heel dichtbij meegemaakt. Dankjewel voor je steun, geduld, begrip, het meelezen, het motiveren, de afleiding, de spiegel voorhouden, en alles nog meer. Ik had dit met niemand anders willen delen dan met jou.

Als laatste, Fien. Kleine, lieve, vrolijke, dame. Wat geweldig dat je er bent, zo aan het einde van dit traject. Voor jouw komst stelde ik mijn verdediging graag even uit. Nu al bedankt voor alles wat je ons geeft, en wat nog komen gaat!

ABOUT THE AUTHOR

Curriculum Vitae

Hanneke Braakhuis was born on the 23rd of June, 1990, in Almelo, the Netherlands, and grew up in the town of Geesteren. She attended secondary school (VWO, profile Nature & Health) at St. Canisius in Almelo and graduated in 2008. In the same year, she started to study Human Movement Sciences at the Rijksuniversiteit Groningen. During the second year of her Masters, she chose the track "Rehabilitation & Functional Recovery". Her Master thesis consisted of a study on ambulatory monitoring of physical activity and heart rate and estimating physical fitness at Roessingh Research and Development in Enschede. Here, she first got introduced to research involving ambulant and objective monitoring of physiological variables.

Next to her growing interest in research, she was interested in teaching. Therefore, during her Masters, she attended the teacher program at the Department of Human Movement Sciences at the Vrije Universiteit in Amsterdam and did a teaching internship at the bachelor program of physiotherapy at Saxion University of Applied Sciences, Enschede.

After obtaining her Master's degree in Human Movement Sciences and the teachers' certificate in 2013, she started as a lecturer at the Institute of Sport Studies of the University of Applied Sciences Arnhem and Nijmegen (HAN). Still interested in research, though, after 1,5 years, she took on the position as a researcher in the FAST@HOME project at the Hague University of Applied Sciences (THUAS) and the Department of Rehabilitation Medicine at the Erasmus University Medical Center. She was responsible for the work package on ambulatory monitoring of physical behavior of stroke patients. Subsequently, this project was further expanded into her PhD project on physical behavior measurement in rehabilitation. During the PhD project, she was a lecturer at Human Movement Technology of the THUAS.

Currently, Hanneke still works as a lecturer at Human Movement Technology. In addition, she is a researcher in the research group "Assistive Technology for Mobility and Sports" of the THUAS. She is also still involved at the Department of Rehabilitation Medicine of the ErasmusMC as a "liaison" with the THUAS.

List of publications

This thesis is based on the following international peer-reviewed publications

Braakhuis, H. E. M, Berger, M. A. M, & Bussmann, J. B. J.(2019). Effectiveness of healthcare interventions using objective feedback on physical activity: A systematic review and meta-analysis. *Journal of rehabilitation medicine*, *51*(3), 151-159.

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Activity and Movement (ICAMPAM), Bethesda, Maryland, The United States, 21-23 June 2017

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Braakhuis, H. E. M., Berger, M. A. M., Van Der Stok, G. A., Van Meeteren, J., De Groot, V., Beckerman, H., & Bussmann, J. B. J. Three distinct physical behavior types in fatigued patients with multiple sclerosis. Oral presentation at 6th International Conference on Ambulatory Monitoring of Physical Activity and Movement (ICAMPAM), Maastricht, The Netherlands, 26-28 June 2019

Braakhuis, H. E. M, Roelofs, J. M., Berger, M. A. M, Ribbers, G. M., Weerdesteyn, V., & Bussmann, J. B. J. Intensity of daily physical activity–a key component for improving physical capacity after minor stroke? Oral presentation at Dutch Congress of Rehabilitation Medicine (DCRM), Utrecht, the Netherlands, 7-8 November 2019

Meesters J., van der Ent, M., **Braakhuis, H.**, van Haastrecht, K., Innovations and strategies to enhance physical activity in your rehabilitation centre. Workshop at Dutch Congress of Rehabilitation Medicine (DCRM), Utrecht, the Netherlands, 7-8 November 2019

Braakhuis, H. E. M, Roelofs, J. M., Berger, M. A.M, Ribbers, G. M., Weerdesteyn, V., & Bussmann, J. B. J. Intensity of daily physical activity–a key component for improving physical capacity after minor stroke? Oral presentation at 11th World Congress for Neurorehabilitation (WCNR), digital conference, 7-11 October 2020

PhD portfolio

Name PhD student: Hanneke Braakhuis Erasmus MC Department: Rehabilitation Medicine Research School: NIHES	PhD period: 2015 - 2021 Promotors: Prof. Dr. G.M. Ribbers, Dr. J.B.J. Bussmann, Dr. M.A.M. Berger

	Year	**Workload (ECTs)**
Language courses		
English as a Medium of Instruction (EMI) skills, The BSN Language Centre, The Hague	2016	2,3
Writing a scientific article, Taalcentrum VU, Amsterdam	2019	3
Courses - Research skills		
Basiscursus Regelgeving en Organisatie voor Klinisch Onderzoekers (eBROK®), Nederlandse Federatie van Universitair Medische Centra (NFU)	2017	1,5
Research integrity, ErasmusMC, Rotterdam	2018	0,3
NIHES: Biostatistical Methods II: Classical Regression Models [EP03] (including exam)	2019	4,3
NIHES: Repeated Measurements [CE08] (attendence)	2020	1,7
Lecturing outside the Hague University of Applied Sciences (THUAS)		
Research skills, clinical technology, TU Delft	2017	0,3
Minor rehabilitation medicine, ErasmusMC	2018	0,6
Minor rehabilitation medicine, ErasmusMC	2019	0,6
Lectures neurorehabilitation master medicine, ErasmusMC	2019	0,5
Supervising students related to the PhD project		
1 masterthesis human movement sciences VU	2017	1,4
4 internships human movement technology THUAS	2017-2020	2,1
4 bachelorthesis human movement technology THUAS	2016-2019	1,8
Presentations		
Poster presentation IBIA, The Hague, The Netherlands	2016	0,3
Poster presentation ICAMPAM 2017, Bethesda, Maryland, USA	2017	0,3

Poster presentation Rehabmove 2019, Groningen, The Netherlands	2019	0,3
Oral presentation ICAMPAM 2019, Maastricht, The Netherlands	2019	0,5
Oral presentation DCRM 2019, Utrecht, The Netherlands	2019	0,5
Workshop DCRM 2019, Utrecht, The Netherlands	2019	0,5
Oral presentation WCNR 2020, Digital Conference	2020	0,3
Multiple oral presentations during research meetings at the department of rehabilitation medicine ErasmusMC	2015-2020	0,6
Attendance at international conferences and symposia		
IBIA 2016, The Hague, The Netherlands	2016	0,9
ICAMPAM 2017, Bethesda, Maryland, USA	2017	1,1
RehabMove 2018, Groningen, The Netherlands	2018	0,9
DCRM 2018, Groningen, The Netherlands	2020	0,6
ICAMPAM 2019, The Netherlands	2019	1,1
DCRM 2019, Utrecht, The Netherlands	2019	0,6
WCNR 2020, Digital conference	2020	0,6
Seminars and workshops		
VvBN PhD day, UT, Enschede	2015	0,3
VvBN day, Utrecht	2018	0,3
VvBN day, Utrecht	2019	0,3
VvBN meeting physical activity guidelines, Utrecht	2017	0,1
VvBN meeting rehabilitation, Utrecht	2019	0,1
VvBN PhD-day ErasmusMC, Rotterdam	2017	0,3
Other activities		
Organizing committee VvBN PhD-day, ErasmusMC	2017	1,5
Deputy of juniors in the academic staff at the department of rehabilitation medicine, ErasmusMC	2019-2020	3
Board member of Physical Activity Community ErasmusMC (PACE)	2018-2020	3
Co-coordination master research medicine, ErasmusMC	2018-2020	0,5
Participation research meetings department of rehabilitation medicine	2015-2020	7
Total		45,9