General discussion

The primary aim of this thesis was to investigate two methodological aspects of measuring physical behavior from the perspective of stroke rehabilitation. The methodological aspects were: i) the effect of applying different operationalizations of the construct to be measured, and ii) the validity of a measurement device. These aspects were investigated with respect to three components of physical behavior: sedentary behavior, body postures & movements, and arm use. Another aim was to apply physical behavior monitoring to describe daily-life arm use in people after stroke.

More specifically, the effect of different operationalizations of sedentary behavior was assessed on sedentary behavior outcomes in healthy people (***Chapter 2***) and in people after stroke (***Chapter 3***). The validity of two different monitors was assessed: an activity monitor to measure body postures & movements in daily life (***Chapter 4***) and a custom-made activity monitor to measure arm use in daily life (***Chapter 5***). Finally, the latter activity monitor was used to measure the recovery of arm use during the first six months after a stroke, and this was related to the recovery of arm function during the same period (***Chapter 6***). This chapter discusses the main findings in the context of the existing literature, as well as clinical implications, and it offers some recommendations for future research.

MAIN FINDINGS

The main findings of this thesis are summarized in Figure 7.1. It was found that different operationalizations of sedentary behavior had a clear effect on the outcomes related to the total amount of sedentary time and the way sedentary time accumulates in bouts, in healthy people and in people after stroke. In both groups, the differences were not only significant but also large enough to acknowledge differences between the different operationalizations. Next, we found that the Activ8 Physical Activity Monitor [1] (the Activ8) was sufficiently valid to detect body postures & movements in people after stroke. The Activ8 arm use monitor (the Activ8-AUM) was developed and proved to be sufficiently valid to measure arm use during lying/sitting and standing in people after stroke. Therefore, both these activity monitors can be used to measure components of physical behavior in stroke rehabilitation. The results of using the Activ8-AUM in people after stroke showed that, 3 weeks after the stroke, the arm use ratio was low, i.e. the arms were used in a non-symmetrical way and with low use of the affected arm. During the first 26 weeks after the stroke, although the arm use ratio increased it remained significantly lower than the ratio in healthy people, as reported by others[2]. Moreover, both the arm use ratio and its increase showed considerable variability between participants. The arm use ratio seemed to be non-linearly related with arm function, because the positive relation between arm use and arm function was more clearly observed at higher levels of arm function.

This general discussion is approached from two perspectives as described in Figure 7.1, i.e. from the top of the figure that presents the methodological aspects and the application of measuring physical behavior, and from the bottom of the figure that presents the components of physical behavior.

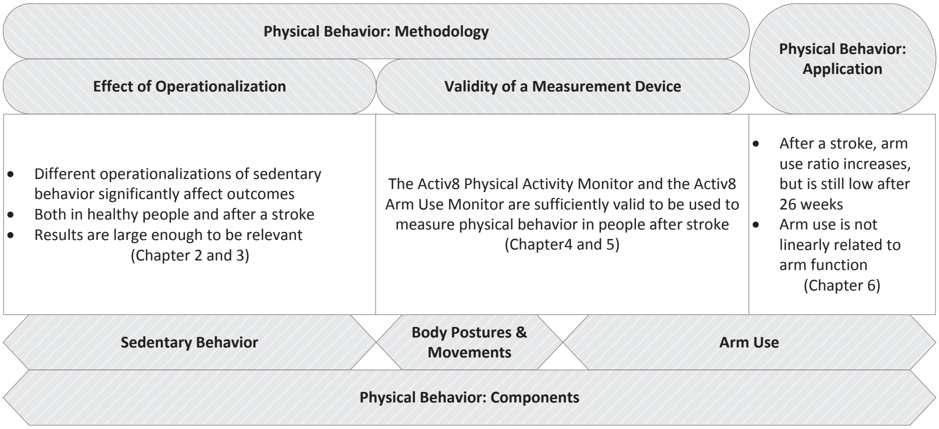

Figure 7.1 Overview of the main findings of this thesis.

PHYSICAL BEHAVIOR: METHODOLOGY

Effect of operationalization

Different operationalizations of sedentary behavior lead to important differences in outcomes, as shown in ***Chapter 2*** and ***3***. During the process of operationalization, the construct to be measured is translated into a measurable variable. However, several options are available regarding how to operationalize a construct. For example, sedentary behavior has been operationalized as 'the amount of time someone sits' [3, 4] or as 'the amount of time with low energy expenditure' [5, 6], whereas the consensus definition combines both of these [7]. Since the effect of applying different operationalizations has not previously been investigated, our use of different operationalizations showed relevant differences in sedentary time and the way in which this time was accumulated.

In this thesis, we studied the effect of operationalization in sedentary behavior; however, this effect is not solely an issue of this specific component of physical behavior. The translation from a theoretical construct to a measurable variable also plays a role in other components. Physical activity is a broad concept of complex behavior that can be operationalized using different dimensions: frequency, intensity, time and type (FITT) [8, 9]. Arm use is a theoretical construct as well that can be operationalized in different ways. For example, it can be operationalized as the number of specific functional activities like drinking and hair brushing [10], or the quality of specific movements like reaching and grasping [11, 12]. In this thesis, we operationalized arm use as '*active movement of parts of the arm, holding objects or leaning during sitting and standing'*.

Besides operationalization, other decisions in measuring physical behavior may also influence the outcome, e.g. the way of calculating the outcome measure. In ***Chapter 6*** we calculated the ratio of arm use as *'the movement counts of the affected arm divided by the movement counts of the unaffected arm'*. We chose this particular formula in order to be in line with other studies on this topic [13, 14]. However, we could also have calculated the ratio as '*the movement counts of the affected arm divided by the movement counts of both arms together'*. In that case, the same arm use would have resulted in a different value of the ratio, which hinders comparison of our results with other studies. Another example of a difference in calculation is the relative duration of physical activity (expressed in %) during one day. In this case it is important to establish what '100%' actually represents; for example, does it literally mean during 24 h, or does it refer to the wear-time of the monitor.

Back in 2012, Taraldsen et al.[15] reported the urgent need to develop consensus on activity protocols and outcome measures. The studies in ***Chapter 2*** and ***3*** confirm this need. The use of similar activity protocols and operationalizations, and calculating outcomes measures in the same way, allows to compare and exchange data across studies. Large meta-analyses can then be performed to investigate health effects and working mechanisms of physical behavior, without the possible confounding effects of methodological aspects. However, it will probably be impossible to reach consensus (100% agreement) on all of these issues. For example, measuring physical behavior in patient populations sometimes requires population-specific choices of those aspects. Therefore, it is important that authors explicitly describe such choices (e.g. in the Methods section of their study). For future research we recommend to measure physical behavior in accordance with other research groups whenever possible, with at least consensus on the definitions of the terms used. Comparison of data should be done with care and only when studies are sufficiently similar in operationalization, way of calculation, and other aspects that influence outcomes.

Validity of a measurement device

In this thesis two devices were validated: in ***Chapter 4*** a commercially available activity monitor to measure body postures & movements (Activ8 Physical Activity Monitor [1]: the Activ8), and in ***Chapter 5*** a custom-made arm use monitor based on Activ8 sensors (Activ8 arm use monitor: the Activ8-AUM). Both devices were considered sufficiently accurate and suitable (small dimensions, user-friendly, and with low costs) to be used in stroke rehabilitation. Despite technological developments and the increasing number of devices, not all commercially available activity monitors can be used in clinical practice. Many of these devices (e.g. the Fitbit, Apple Watch, Garmin watches, etc.) were primarily developed for general use in large groups of healthy people, and less often for a patient population. Firstly, most activity monitors were developed to measure the intensity of physical activity, which is only one of the components of physical behavior. Very often, body postures & movements and arm use, which are important components in stroke rehabilitation, cannot be measured. Secondly, the reported output of the activity monitors is generally limited to certain basic outcome measures (e.g., total time sitting), whereas caregivers in stroke rehabilitation are also interested in other measures (e.g. number of sit-to-stand transfers interrupting sitting behavior). Finally, most commercially available activity monitors have not been validated (or only to a limited extent) for use in patient populations; moreover, the results cannot be generalized because of deviations in movement patterns.

The validity of an activity monitor is an important issue when the device is to be used in stroke rehabilitation. To draw correct conclusions about the level of physical behavior, the devices should measure accurately and precisely. However, to be used in stroke rehabilitation, other features need to be considered as well, such as the ease of use for the caregiver, the level of wearing comfort, and the costs. However, although all these requirements are important, the validity and reliability of a device is the most crucial item because of the consequences of conclusions and decisions based on the acquired data.

Although the validity of a device is an important issue, concerns have been raised about validation studies of activity monitors [16]. These concerns are related to the standardization of research (discussed above). In addition, and specifically for validation studies, the lack of harmonization of validation protocols is an important issue. Often, the activity protocols of validation studies are not standardized and are restricted to a limited number of activities performed in a laboratory or in a semi-natural setting. In contrast, activity protocols that include i) a standardized part and ii) a semi-structured part in the home setting, increase both comparability with other studies and ecological validity [16]. Based on experience with our validation study, we also recommend to take into account the *applicability* of the activity protocol in different settings. For example, the protocol to be applied in a home setting needs to be performed in many different types of accommodations. When using similar protocols, the effect of the protocol on the validation outcomes will be minimized, since including easily detectable activities improves the validation results, whereas daily-life activities are more difficult to detect correctly. Standardization needs to be done within certain populations, to make it easier to compare the results of different studies and to start a discussion on the interpretation of validation results: e.g. what is 'good', and when should a device be considered valid. Whenever possible, standardization between certain populations is also good, although most of the time validation studies need to be population-specific which may involve different choices about the activity protocol.

PHYSICAL BEHAVIOR: APPLICATION

In ***Chapter 6***, a custom-made arm use monitor was applied to investigate the recovery of arm use in the first months after a stroke. This was a pilot study within the PROFITS study to assess whether adding measurements of arm use are useful in stroke rehabilitation. The PROFITS study aims to develop a clinical infrastructure to obtain an individualized prognosis of functional recovery after a stroke [17]. In this cohort study, functional outcomes are uniformly evaluated within the full care chain of stroke rehabilitation. The results of the study in ***Chapter 6*** show that arm use and arm function are related, although not one-to-one, indicating that arm use in daily life is a unique construct of physical behavior. Therefore, measurements of arm use are potentially valuable in stroke rehabilitation and may be used to improve the individualized prognosis of functional recovery after a stroke.

Activity monitoring is increasingly applied in medical research. Studies using activity monitors generally aim to assess the health effects of physical behavior; this contributes to the important aim of understanding, preventing and treating diseases. In most of these studies, physical activity has been investigated in large cohort studies in the general population, for example the Rotterdam study [18] and the NHANES cohort [19]. However, it is important to apply ambulatory measurements of other components of physical behavior as well. These components provide insight into other aspects of physical behavior, which might have a different relationship with health and disease. The PROFITS study is an example of applying ambulatory measurements to extend our knowledge on the functional recovery of arm use after a stroke. In this thesis, to facilitate measuring body postures & movements and arm use in people after stroke, two activity monitors were validated. These two monitors proved to be sufficiently valid to be used in stroke research and, therefore, should be applied to extend our knowledge on body postures & movements and arm use in people after stroke.

In addition to application in scientific research, the two activity monitors can also be used in the clinical practice of stroke rehabilitation. Currently, it is becoming increasingly important to measure several outcome measures in order to optimize rehabilitation care. The large differences found between participants, described in ***Chapter 6***, highlight the importance of personalized care. However, measuring physical behavior is not yet a routine assessment in stroke rehabilitation. Recently, the American Heart Association concluded that, although physical activity is increasingly stimulated, it is not yet routinely assessed in clinical practice, in contrast to other cardiovascular risk factors [20]. Therefore, they published a statement [20] including concrete recommendations to stimulate routine assessment of physical activity in healthcare settings. In stroke rehabilitation, routine assessment of other components is also important. The monitoring of body postures & movements and arm use can help to personalize rehabilitation care based on actual functional status and individual progress, like the PROFITS study aims to.

To apply physical behavior monitoring in clinical practice, more work is required. As mentioned, there needs to be a consensus on definitions and methodological aspects (operationalization, outcome measures, etc.). Another previously mentioned condition is the use of valid measurement devices. This validity becomes more important when data are used for medical decision-making that has direct consequences for patients, and even more so when this is on an individual level rather than group level. Moreover, there are practical issues to be considered, including the training of caregivers and an infrastructure to safely store data within medical records. Despite this work, there is no reason to postpone implementing routine assessment of physical behavior in clinical practice. Although new insights into the health impact of physical behavior will continue to update and optimize measuring physical behavior in clinical practice, there is enough evidence and knowledge available to start implementing routine assessment of physical behavior in clinical practice right now.

PHYSICAL BEHAVIOR: COMPONENTS

Sedentary behavior

The results of the studies in ***Chapter 2*** and ***3*** show that sitting/reclining/lying and having a low energy expenditure are two different things. It is possible to sit and spend relatively high amounts of energy, for example during sitting on an active sitting product or when playing a game [21, 22]. On the other hand, it is possible to have a low energy expenditure while standing [22, 23]. Recently, the Sedentary Behavior Research Network finished its Terminology Consensus Project and defined sedentary behavior as: *'any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents (METs) while in a sitting, reclining, or lying posture'* [7]. According to this consensus definition, sedentary behavior requires both components at the same time: a certain body posture *and* a low energy expenditure. The rationale behind the combination of these two components is that low energy expenditure has negative health effects [24] as does muscle inactivity of the large muscle groups [25, 26]. The 'lying posture' part of this definition was recently added and shows that even the definition of sedentary behavior is still developing and changing.

The health effects of sedentary behavior have been studied over many years although, in the beginning, sedentary behavior itself was not measured. In older studies, sedentary behavior was operationalized as the absence or a low amount of moderate-vigorous physical activity [27]. Sedentary behavior was associated with all-cause mortality [28], perceived poor health [29], and obesity [30]. Strictly speaking, these associations are not correct. Sedentary behavior originates from the Latin word *sedere* which means 'to sit', which is not the same as the absence of moderate-vigorous physical activity. During one day, a person can perform sufficient moderate-vigorous physical activity according to the physical activity guidelines and sit the rest of the day. A second person can fail to meet the recommended levels of physical activity, while he/she barely sits; this is nicely illustrated by the accelerometer data of two random people analyzed by Pate et al. [27].

Nowadays, it is possible to measure both components of sedentary behavior using accelerometry. This enables researchers to separate sedentary behavior from light physical activity and to assess the health effects of both separately. The results of such studies show that sedentary behavior seems to have harmful effects on health, irrespective of the level of physical activity [31, 32]. Therefore, sedentary behavior has become a new target for interventions, as its harmful health effects cannot be canceled out by simply meeting the recommended levels of physical activity [33]. Although sedentary behavior is measured instead of physical inactivity, most studies operationalize sedentary behavior as the amount of time sitting [3, 4] or the amount of time with low energy expenditure [5, 6], thus only one component is assessed. However, a more complete understanding of the physiological working mechanism of both components *and* their possible interaction is needed [34]. Therefore, for future research we recommend using activity monitors that assess both components of sedentary behavior. Based on the results of such studies, the two-component definition can be assessed on its validity and be adjusted if necessary. Ideally, a longitudinal cohort study is designed in which both components of sedentary behavior are measured at several time points. Then, the separated *and* combined effect of postures and different levels of energy expenditure can be related to health outcomes, e.g. biomarkers for cardiovascular disease and lipid profiles, as well as mortality rate.

Body postures & movements

In ***Chapter 4***, the Activ8 [1] was validated to measure body postures & movements in people after stroke. Although often used interchangeably, 'physical activity' and 'body postures & movements' are different components of physical behavior. Physical activity has been defined as '*any bodily movement produced by skeletal muscles that results in energy expenditure*' [35], whereas body postures & movements stand apart from energy expenditure and concern the orientation of the body relative to gravity. The aim of measuring physical behavior determines whether physical activity or body postures &

movements needs to be quantified. In health-related issues, energy expenditure is more relevant: a healthy lifestyle includes sufficient moderate-to-vigorous physical activity [36, 37]. On the other hand, body postures & movements are mostly measured to assess motor recovery and muscle function, or to monitor falls. Therefore, it is also important to have valid devices to measure body postures & movements, besides devices that measure energy expenditure.

In the general population and in rehabilitation populations there are reasons to measure body postures & movements, instead of energy expenditure, when assessing physical behavior. For healthy aging, use of the musculoskeletal system to maintain muscle function is a highly relevant aspect [38]. To assess that use, body postures & movements need to be measured, instead of energy expenditure or physical activity. In stroke rehabilitation, motor recovery is an important goal that strives to mobilize people to change from mainly lying and sitting, to standing and walking [39]. From the perspective of energy expenditure, sitting and standing still are relatively similar [22, 23], whereas these activities differ physiologically [24]. Upright activities, including standing, activate large muscle groups and will prevent deconditioning of the locomotion system [24]. Thus, especially in people after stroke, measuring body postures & movements in addition to energy expenditure is relevant to assess functional status and motor recovery.

Data on body postures & movements can also be used to improve other measurements, e.g. to optimize estimates of energy expenditure [40]. Moreover, these data can improve measurements of arm use. Arm movements due to walking are often described as a confounder of measuring arm use [14, 41-43]. Information on body postures & movements can be used to separate arm movements caused by walking and whole-body movements, from arm movements related to actual arm use. Also, when measuring sedentary behavior, it is important to be able to validly measure body postures & movements, as body posture is one of the requirements of sedentary behavior.

Arm use

Arm use is a relevant component of physical behavior in people after stroke, because they might have disturbed motor function of the arm. Therefore, in ***Chapter 6*** we performed a pilot study to assess the recovery of arm use and its relation with arm function. In this thesis, arm use was defined as '*active movement of parts of the arm, holding objects or leaning during sitting and standing*'. Thus, arm use implies conscious and intended movements of a person. The advantage of including all those movements is that a more complete measure is obtained of actual arm use in daily life, as compared to only using specific activities (e.g. hair brushing, eating) or movements (e.g. reaching). To measure arm use, we developed and validated the accelerometer-based Activ8 arm use monitor (the Activ8-AUM), described in ***Chapter 5***. Although the use of accelerometry to measure arm use has limitations, it is currently the preferred technique due to the lack of other widely applicable and accepted techniques [44]. The main limitation of accelerometry is that it measures accelerations, i.e. movement, which makes it impossible to measure static arm use, such as holding an object. Moreover, arm movements are neither essential nor sufficient for functional arm use. To minimize this latter problem, we defined arm use as *' … during sitting and standing'*, which excludes arm movements due to walking and other whole-body movements. In addition, we applied a threshold to the movement counts above which they are classified as arm use. Applying a threshold to accelerometry data proved successful in other studies [13, 45, 46]. The study in ***Chapter 5*** shows that, overall, the Activ8-AUM correctly detected 75% of arm use, although arm use without movement and non-use with movement were not so well classified. Unfortunately, the effect of including body postures & movements in the analysis of arm use has only been investigated to a limited extent. Until now, only one study has shown that the correlation of activity counts with the Box and Block test improved significantly when walking bouts were excluded [47].

The results of the study in ***Chapter 6*** show that data on arm use can be useful to assess functional recovery after a stroke. However, since that was a pilot study, future research needs to examine the recovery of arm use in larger groups, including important determinants of arm use recovery, e.g. neglect, apraxia, and received therapy. Another important determinant to be considered is arm dominance. Studies on patients with Complex Regional Pain Syndrome have shown that, whether or not the dominant arm or non-dominant arm was affected, had an impact on the amount of arm use [48, 49]. After stroke, when the restitution of arm use fails, recovery can result from compensational strategies [50]. The success of these strategies might be influenced by the fact that the dominant or non-dominant arm can be affected.

In order to use measurements of arm use to unravel the working mechanism of arm use recovery and to improve and personalize stroke rehabilitation, measurements may be improved by adding sensors that are based on technologies other than accelerometry. For example, Leuenberger et al. [47] used an inertial measurement unit to quantify functionally relevant arm use. This device combines an accelerometer, a gyroscope and a magnetometer and showed promising results; however, the high correlation with the Box and Block test was not better than the correlation with only accelerometry data when walking bouts were excluded. Another possible improvement could be the use of an individual and self-learning algorithm to detect the optimal threshold to distinguish between arm use and no arm use, based on movement counts measured by accelerometry.

GENERALIZABILITY OF THE RESULTS

In ***Chapter 6***, the arm use of people after stroke was assessed during the first 26 weeks after their stroke. The inclusion criteria were kept intentionally broad in order to increase generalizability, although people with severe mental and severe communication problems were excluded. People with severe communication problems were excluded due to practical reasons, i.e. it is important that participants of a clinical study understand both the aim of the research and their rights as a participant. Since this exclusion was based on a practical reason and not related to the research itself, the results might be generalizable to people with communication problems. However, the results are not generalizable to people with severe mental problems, e.g. with neglect or apraxia. This latter type of conditions influence a person's physical behavior (including arm use), possibly leading to other recovery patterns in both arm function and arm use.

CLINICAL IMPLICATIONS OF THIS THESIS

This thesis investigated important aspects of measuring physical behavior that need to be considered when applying these measurements in clinical practice. The need to measure physical behavior in clinical practice was described in the section 'Physical Behavior: Application'. Routine assessments are not only important in stroke rehabilitation but throughout clinical practice. In general, it can personalize care, just like all other variables which are measured to determine a personal treatment plan. However, when information on physical behavior is used in clinical practice, it needs to be regularly assessed. A change in physical behavior should be a trigger to evaluate the reason for that changed behavior and to (possibly) change the treatment plan. For example, the results presented in ***Chapter 6*** show that, in daily life, arm use does not always recover in a straight line upwards. By regular assessment of arm use, non-use of the arm can be detected and tackled during, e.g., hand therapy. This early approach may prevent learned non-use on the longer term.

FUTURE RESEARCH

The previous sections made some recommendations for future research on specific issues. It is important to continue developing the field of measuring physical behavior because of its relationship with health research and the importance of measuring physical behavior during stroke rehabilitation. The working mechanism of physical behavior and the health effects of changed physical behavior, both positive and negative, need more in-depth study. Hopefully, new insights will allow to further optimize guidelines for a healthy lifestyle and interventions in stroke rehabilitation. Moreover, the development and validation of activity monitors need to be continued, with a focus on devices suitable for application in clinical practice. Therefore, developers need to collaborate with caregivers and patients about the requirements, needs, and wishes for such devices. Additionally, the potential of activity monitors to provide feedback on physical behavior should be investigated and developed. Feedback can be used as an important element of interventions aimed at improving physical behavior in both the general population as well as in rehabilitation populations.

REFERENCES

1. Remedy Distribution Ltd. Activ8 Physical Activity Monitor [Internet]. 2015 [cited 2018 Jun 27]. Available from: http://www.activ8all.com/.
2. Bailey RR, Lang CE. Upper-limb activity in adults: referent values using accelerometry. *J Rehabil Res Dev*. **2013**;50:1213-1222.
3. Paul L, Brewster S, Wyke S, Gill JM, Alexander G, et al. Physical activity profiles and sedentary behaviour in people following stroke: a cross-sectional study. *Disabil Rehabil*. **2016**;38:362-367.
4. Tieges Z, Mead G, Allerhand M, Duncan F, van Wijck F, et al. Sedentary behavior in the first year after stroke: a longitudinal cohort study with objective measures. *Arch Phys Med Rehabil*. **2015**;96:15-23.
5. Butler EN, Evenson KR. Prevalence of physical activity and sedentary behavior among stroke survivors in the United States. *Top Stroke Rehabil*. **2014**;21:246-255.
6. Moore SA, Hallsworth K, Plotz T, Ford GA, Rochester L, et al. Physical activity, sedentary behaviour and metabolic control following stroke: a cross-sectional and longitudinal study. *PLoS One*. **2013**;8:e55263.
7. Tremblay MS, Aubert S, Barnes JD, Saunders TJ, Carson V, et al. Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act*. **2017**;14:75.
8. Cavill N, Kahlmeier S, Racioppi S. Physical Activity and Health in Europe: Evidence for Action. *Copenhagen, Denmark: WHO Regional Office for Europe*. **2006**.
9. World Health Organization. International Classification of Functioning, Disability and Health (ICF). *Geneva, Switzerland: WHO*. **2001**.
10. Lemmens RJ, Janssen-Potten YJ, Timmermans AA, Smeets RJ, Seelen HA. Recognizing complex upper extremity activities using body worn sensors. *PLoS One*. **2015**;10:e0118642.
11. van Meulen FB, Reenalda J, Buurke JH, Veltink PH. Assessment of daily-life reaching performance after stroke. *Ann Biomed Eng*. **2015**;43:478-486.
12. van Meulen FB, Klaassen B, Held J, Reenalda J, Buurke JH, et al. Objective Evaluation of the Quality of Movement in Daily Life after Stroke. *Front Bioeng Biotechnol*. **2015**;3:210.
13. Doman CA, Waddell KJ, Bailey RR, Moore JL, Lang CE. Changes in Upper-Extremity Functional Capacity and Daily Performance During Outpatient Occupational Therapy for People With Stroke. *Am J Occup Ther*. **2016**;70:7003290040p1-7003290040p11.
14. Thrane G, Emaus N, Askim T, Anke A. Arm use in patients with subacute stroke monitored by accelerometry: association with motor impairment and influence on self-dependence. *J Rehabil Med*. **2011**;43:299-304.
15. Taraldsen K, Chastin SF, Riphagen, II, Vereijken B, Helbostad JL. Physical activity monitoring by use of accelerometer-based body-worn sensors in older adults: a systematic literature review of current knowledge and applications. *Maturitas*. **2012**;71:13-19.
16. Lindemann U, Zijlstra W, Aminian K, Chastin SF, de Bruin ED, et al. Recommendations for standardizing validation procedures assessing physical activity of older persons by monitoring body postures and movements. *Sensors*. **2014**;14:1267-1277.
17. NeuroControl. PROFITS | NeuroControl [Internet]. [cited 2018 Oct 29]. Available from: http://neurocontrol.nl/profits/.
18. Ikram MA, Brusselle GGO, Murad SD, van Duijn CM, Franco OH, et al. The Rotterdam Study: 2018 update on objectives, design and main results. *Eur J Epidemiol*. **2017**;32:807-850.

19. Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS). NHANES - National Health and Nutrition Examination Survey [Internet]. [cited 2018 Oct 30]. Available from: http://www.cdc.gov/nchs/nhanes.htm.
20. Lobelo F, Rohm Young D, Sallis R, Garber MD, Billinger SA, et al. Routine Assessment and Promotion of Physical Activity in Healthcare Settings: A Scientific Statement From the American Heart Association. *Circulation.* **2018**;137:e495-e522.
21. Dickin DC, Surowiec RK, Wang H. Energy expenditure and muscular activation patterns through active sitting on compliant surfaces. *J Sport Health Sci.* **2017**;6:207-212.
22. Mansoubi M, Pearson N, Clemes SA, Biddle SJ, Bodicoat DH, et al. Energy expenditure during common sitting and standing tasks: examining the 1.5 MET definition of sedentary behaviour. *BMC Public Health.* **2015**;15:516.
23. Judice PB, Hamilton MT, Sardinha LB, Zderic TW, Silva AM. What is the metabolic and energy cost of sitting, standing and sit/stand transitions? *Eur J Appl Physiol.* **2016**;116:263-273.
24. Hamilton MT, Hamilton DG, Zderic TW. Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. *Diabetes.* **2007**;56:2655-2667.
25. Fountaine CJ, Johann J, Skalko C, Liguori GA. Metabolic and Energy Cost of Sitting, Standing, and a Novel Sitting/Stepping Protocol in Recreationally Active College Students. *Int J Exerc Sci.* **2016**;9:223-229.
26. Pesola AJ, Laukkanen A, Tikkanen O, Finni T. Heterogeneity of muscle activity during sedentary behavior. *Appl Physiol Nutr Metab.* **2016**;41:1155-1162.
27. Pate RR, O'Neill JR, Lobelo F. The evolving definition of "sedentary". *Exerc Sport Sci Rev.* **2008**;36:173-178.
28. Crespo CJ, Palmieri MR, Perdomo RP, McGee DL, Smit E, et al. The relationship of physical activity and body weight with all-cause mortality: results from the Puerto Rico Heart Health Program. *Ann Epidemiol.* **2002**;12:543-552.
29. Yancey AK, Wold CM, McCarthy WJ, Weber MD, Lee B, et al. Physical inactivity and overweight among Los Angeles County adults. *Am J Prev Med.* **2004**;27:146-152.
30. Salmon J, Bauman A, Crawford D, Timperio A, Owen N. The association between television viewing and overweight among Australian adults participating in varying levels of leisure-time physical activity. *Int J Obes Relat Metab Disord.* **2000**;24:600-606.
31. Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. *Ann Intern Med.* **2015**;162:123-132.
32. Wilmot EG, Edwardson CL, Achana FA, Davies MJ, Gorely T, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia.* **2012**;55:2895-2905.
33. Morton S, Fitzsimons C, Hall J, Clarke D, Forster A, et al. Sedentary behavior after stroke: A new target for therapeutic intervention. *Int J Stroke.* **2018**;Jul 1.
34. Gonzalez K, Fuentes J, Marquez JL. Physical Inactivity, Sedentary Behavior and Chronic Diseases. *Korean J Fam Med.* **2017**;38:111-115.
35. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* **1985**;100:126-131.
36. Health Council of the Netherlands. Beweegrichtlijnen 2107. *The Hague, the Netherlands: Health Council of the Netherlands.* **2017**.
37. World Health Organization. Global Recommendations on Physical Activity for Health. *Geneva: WHO.* **2010**.

38. McLeod M, Breen L, Hamilton DL, Philp A. Live strong and prosper: the importance of skeletal muscle strength for healthy ageing. *Biogerontology*. **2016**;17:497-510.
39. Cumming TB, Thrift AG, Collier JM, Churilov L, Dewey HM, et al. Very early mobilization after stroke fast-tracks return to walking: further results from the phase II AVERT randomized controlled trial. *Stroke*. **2011**;42:153-158.
40. Bonomi AG, Plasqui G, Goris AH, Westerterp KR. Improving assessment of daily energy expenditure by identifying types of physical activity with a single accelerometer. *J Appl Physiol*. **2009**;107:655-661.
41. Rand D, Eng JJ. Predicting daily use of the affected upper extremity 1 year after stroke. *J Stroke Cerebrovasc Dis*. **2015**;24:274-283.
42. Urbin MA, Waddell KJ, Lang CE. Acceleration metrics are responsive to change in upper extremity function of stroke survivors. *Arch Phys Med Rehabil*. **2015**;96:854-861.
43. Uswatte G, Giuliani C, Winstein C, Zeringue A, Hobbs L, et al. Validity of accelerometry for monitoring real-world arm activity in patients with subacute stroke: evidence from the extremity constraint-induced therapy evaluation trial. *Arch Phys Med Rehabil*. **2006**;87:1340-1345.
44. Lang CE, Waddell KJ, Klaesner JW, Bland MD. A Method for Quantifying Upper Limb Performance in Daily Life Using Accelerometers. *J Vis Exp*. **2017**;Apr 21.
45. Uswatte G, Miltner WH, Foo B, Varma M, Moran S, et al. Objective measurement of functional upper-extremity movement using accelerometer recordings transformed with a threshold filter. *Stroke*. **2000**;31:662-667.
46. Schasfoort FC, Bussmann JB, Stam HJ. Ambulatory measurement of upper limb usage and mobility-related activities during normal daily life with an upper limb-activity monitor: a feasibility study. *Med Biol Eng Comput*. **2002**;40:173-182.
47. Leuenberger K, Gonzenbach R, Wachter S, Luft A, Gassert R. A method to qualitatively assess arm use in stroke survivors in the home environment. *Med Biol Eng Comput*. **2017**;55:141-150.
48. Schasfoort FC, Bussmann JB, Stam HJ. Impairments and activity limitations in subjects with chronic upper-limb complex regional pain syndrome type I. *Arch Phys Med Rehabil*. **2004**;85:557-566.
49. Schasfoort FC, Bussmann JB, Zandbergen AM, Stam HJ. Impact of upper limb complex regional pain syndrome type 1 on everyday life measured with a novel upper limb-activity monitor. *Pain*. **2003**;101:79-88.
50. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet*. **2011**;377:1693-1702.