OPTIMIZING STROKE REHABILITATION:

DETERMINING THE THERAPEUTIC DOSE AND INTENSITY TO MAXIMIZE WALKING AND FUNCTIONAL RECOVERY EARLY AFTER STROKE

by

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The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, the dissertation entitled:

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Abstract

Background: Stroke is a serious health concern and a leading cause of disability worldwide. Up to two-thirds of stroke survivors will experience physical and/or cognitive deficits thus requiring ongoing rehabilitation. Determining the appropriate exercise intensity and dose to optimize recovery is one of the top priorities in stroke rehabilitation research.

Purpose: To determine the feasibility and efficacy of higher exercise intensity and dose on walking and functional recovery, cognition, and quality of life in the early phase after stroke.

Methods: Multiple studies were conducted to examine how exercise intensity and dose may influence recovery early after stroke. Two studies were completed to identify and assess the precision of a readily available monitoring device to accurately record step count, a measure of walking dose. The results of these studies contributed to the design and implementation of an ongoing national, multi-site, randomized clinical trial occurring during inpatient stroke rehabilitation, to investigate how higher exercise intensity and dose impact walking and functional recovery, cognition, and quality of life.

Results: From the two studies examining measurement of walking dose, The Fitbit One was identified as a monitoring device that could accurately assess step count (< 10% error), when positioned at the ankle, with individuals post-stroke that had a walking speed greater than 0.4m/s. Preliminary data from the ongoing multi-site randomized clinical trial revealed that individuals who received a higher exercise intensity and dose within their inpatient stroke rehabilitation were able to walk a clinically meaningful longer distance on the six-minute walk test and had a higher perception of their health status compared to those individuals that received usual care physical therapy.

Conclusions: Higher exercise intensity and dose can be accurately measured and safely delivered during inpatient stroke rehabilitation. Furthermore, although preliminary results suggest that higher exercise intensity and dose may be effective at improving walking recovery and quality of life in the early phase after stroke, further analysis will need to be conducted when the complete study population is recruited to verify these findings.

Lay Summary

There are an estimated 60,000 strokes in Canada each year. Up to two-thirds of stroke survivors will experience difficulties with their physical function, such as walking, thinking, and talking, and require rehabilitation. Currently, it is not known what exercise intensity and dose should be prescribed to stroke survivors to optimize recovery. The research comprising this thesis explores how exercise intensity and dose impact recovery after stroke. First, through two different studies, a wearable monitoring device is identified that can accurately measure walking dose, across a variety of speeds, in individuals after stroke. Second, a national, multi-site randomized clinical trial is undertaken to examine the effects of exercise intensity and dose in the early period after stroke when there is the most potential for brain recovery. This study has the potential to improve the function, thinking, and overall well-being of individuals after stroke.

Preface

The research study described in Chapter 2 was conducted at the GF Strong Rehabilitation Research Lab in Vancouver, British Columbia, Canada. Dr. Janice J. Eng and I designed the study jointly. Ethics approval was obtained from the University of British Columbia Clinical Research Ethics Board (H05-70576). I was responsible for the preparation and revision of ethics documents, participant recruitment, data collection and analysis, chapter/manuscript writing and dissemination of findings. I have no conflict of interest with the Fitbit One (Fitbit Inc., San Francisco, CA).

A version of Chapter 2 has been published: Klassen TD, Simpson LA, Lim SB, Louie DR, Parappilly B, Sakakibara BM, Zbogar D, Eng JJ. "Stepping Up" Activity Post-Stroke: Ankle Positioned Accelerometer Can Accurately Record Steps During Slow Walking." Phys Ther 2016 March;96(3):355-360.

Chapters 3-5 contains data and a study protocol related to an ongoing multi-site, national, randomized clinical trial (RCT) called the "Determining Optimal post-Stroke Exercise" (DOSE) study. The trial is registered with Clinicaltrials.gov (NCT01915368) and comprises a collaboration of four academic institutions (University of British Columbia, University of Calgary, University of Toronto, University of Manitoba) and seven inpatient rehabilitation centres across Canada: GF Strong Rehabilitation Centre, Holy Family Hospital, Laurel Place, Carewest Dr. Vernon Fanning Centre, Foothills Medical Center, Riverview Health Centre and Toronto Rehabilitation Institute. The principal investigator for the study is Dr. Janice Eng (University of British Columbia) and the co-investigators are: Tara Klassen (University of British Columbia), Drs. Sean Dukelow and Michael Hill (University of Calgary), Dr. Mark

Bayley (University of Toronto), Drs. Oscar Benavente, Andrei Krassioukov, Jennifer Yao (University of British Columbia) and Dr. Sepideh Pooyania (University of Manitoba).

I was responsible for facilitating the ethics approval processes which was obtained from all universities and health authorities: University of British Columbia Clinical Research Ethics Board and Providence Health Care/Vancouver Coastal Health (H13-01933) and Fraser Health (2015-127); University of Calgary and Foothills/Fanning (REB13-0518); University of Manitoba Health Research Board (H2017:053) and Riverview Health Centre (RA-17-002); University of Toronto and Toronto Rehabilitation Institute (13-7229).

For Chapters 3-5, I was responsible for the start-up and overall management of the randomized controlled trial. My contributions included, but were not limited to: initial preparation/revisions of ethics documents for all sites, development of the intervention and assessment protocols and documentation, assessment and intervention therapist recruitment and training, participant recruitment, problem-solving day-to-day trial issues, data collection, data analysis, chapter/manuscript writing and dissemination of findings. I have no conflict of interest with the StepWatch^{TM} activity monitor (SAM) (modus health, Washington, DC)

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Chapter 4: Klassen TD, Dukelow SP, Bayley MT, Benavente O, Hill MD, Krassioukov A, Liu-Ambrose T, Pooyania S, Poulin MJ, Yao J, Eng JJ. Determining Optimal post-Stroke Exercise

(DOSE): Study Protocol for a Randomized Controlled Trial Investigating Therapeutic Intensity and Dose on Functional Recovery During Stroke Inpatient Rehabilitation.

Chapter 5 is a preliminary analysis of data collected from 53 participants enrolled in the DOSE study between March, 2014 and July, 2017. As the DOSE study is still ongoing, with a goal of recruiting 75 participants in total, the preliminary findings from the chapter will not be disseminated until the DOSE study is completed and the primary study outcome results published.

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List of Abbreviations

5mWT: 5-Meter Walk Test

6MWT: Six Minute Walk Test

ANCOVA: Analysis of Co-Variance

BBS: Berg Balance Scale

BWV: Baseline Walking Velocity

DSST: Digit Symbol Substitution Test

EQ-5D-5L: 5-level EQ-5D version

FAC: Functional Ambulation Classification

CI: Confidence Interval

CIHR: Canadian Institutes of Health Research

CPSR: Heart and Stroke Foundation Canadian Partnership for Stroke Recovery

CSF: Cerebrospinal Fluid

DOSE: Determining Optimal post-Stroke Exercise

HR: Heart Rate

HRR: Heart Rate Reserve

ICH: Intracerebral Hemorrhage

LE: Lower Extremity

M: Meters

MCID: Minimal Clinical Important Difference

MoCA: Montreal Cognitive Assessment

PHQ: Patient Health Questionnaire

RCT: Randomized Control Trial

ROG: Rate of Generation

SAH: Subarachnoid Hemorrhage

SAM: StepWatch™ Activity Monitor

SD: Standard Deviation

SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials

TIA: Transient Ischemic Attack

Acknowledgements

If you want to go fast, go alone.
If you want to go far, go together.
African Proverb

It is almost guaranteed that you are destined to make a change when you ask Dr. Janice Eng, "What am I doing with my life?" After those seven words emerged from my mouth in 2013, my PhD adventure began and my life changed direction. Over the past five years, so many individuals, from all facets of my life, have supported me. I could have never done this without everyone's assistance.

To my primary supervisor, Dr. Janice Eng, thank you for providing me with the most amazing PhD project to work on. I am forever grateful for this opportunity and for your ongoing support and wisdom. You are a remarkable mentor. Thank you.

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I have been fortunate to receive financial funding for my PhD through the Canadian Institutes of Health Research (CIHR) and the University of British Columbia (UBC). Furthermore, the DOSE study was funded by CIHR and the Heart and Stroke Foundation Canadian Partnership for Stroke Recovery (CPSR). This generous financial support enabled my doctoral work and the DOSE study to occur.

A large amount of my time over the past five years has been spent in the Rehabilitation Research Lab at GF Strong. The comradery and support from all staff and students working with Drs. Eng, Miller, Mortenson and Silverberg has been amazing. Furthermore, I was fortunate to have my desk in the "Annex", where special friendships were created and numerous chocolate bars were consumed. To all of you that worked in the "Annex" over the past five years, thank you for all your advice, knowledge, support, and never-ending chocolate supply.

Beyond the Rehabilitation Research Lab at GF Strong, I have had the opportunity to collaborate with members of the Boyd Lab and other students/trainees within the UBC Rehabilitation Sciences Graduate Program and the CPSR National Trainee Association. The best to all of you as you pursue your endeavours and I hope we cross paths again in the future.

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Last, but certainly not least, my family. There are not enough words to express the immense support I have received from my crew: Carl, Sasha, Marley and Peter. Thank you. Also, to the Derksen, Hansen, Hornbeck, Klassen, Parker, Sherrill, Sohi, and Sutherland families. You are always there for me. I love you all. Time to celebrate!

Dedication

To Carl, Sasha, Marley, and Peter:

Thank you for all your love and support throughout this journey.

You enabled me to take this leap and commit, for which I am forever grateful.

~

…Until one is committed there is hesitancy, the chance to draw back, always ineffectiveness.

Concerning all acts of initiative (and creation), there is one elementary truth, the ignorance of which kills countless ideas and splendid plans:

that the moment one definitely commits oneself, then Providence moves too.

All sorts of things occur to help one that would never otherwise have occurred.

A whole stream of events issues from the decision, raising in one's favour all manner of unforeseen incidents and meetings and material assistance,

which no man could have dreamt would have come his way.

I have learned a deep respect for one of Goethe's couplets:

Whatever you can do, or dream you can, begin it.

Boldness has genius, power, and magic in it.

- W.H. Murray

Chapter 1: Introduction

1.1 Stroke Epidemiology

Stroke is a serious global health care problem (Chin and Vora 2014). After 55 years of age, 1 in 5 women, and 1 in 6 men will suffer a stroke (Seshadri et al. 2006). In most countries, it is one of the top four causes of death and is one of the leading causes of adult disability worldwide (Lackland et al. 2014). Unfortunately, up to two-thirds of stroke survivors will experience physical and/or cognitive deficits, thereby requiring extensive medical care and rehabilitation (National Institute of Neurological Disorders and Stroke 2016). The economic impact of stroke care on health care systems worldwide is immense and growing annually (Mittmann et al. 2012). The estimated direct and indirect costs of stroke on the Canadian economy alone amounts to more than 3.6 billion a year (Public Health Agency of Canada 2009).

Over the past century, innovations in clinical medicine and efforts in public health education have resulted in a 20-30% decrease in stroke mortality (Lackland et al. 2014). However, this achievement, combined with a growing aging population, is expected to result in an increased prevalence of stroke survivors over the next 20 years (Krueger et al. 2015). It is of paramount importance to determine optimal ways to maximize functional recovery after stroke to decrease the burden of stroke on individuals, families, and healthcare systems worldwide.

1.2 Stroke Pathophysiology and Etiology

Stroke is a sudden disturbance of blood flow to the brain that most commonly results in neurological symptoms and/or deficits. Signs and symptoms of stroke occur within about 10 seconds of decreased blood flow and may include: weakness on one side of the body (hemiparesis); confusion or difficulty processing thoughts; trouble speaking or understanding speech; numbness on one side of the body; vision abnormalities; difficulty walking; loss of

coordination (Frizzell 2005). If the blood flow is restored within a few minutes to the brain, normal function may return, but brain cell death usually occurs if there is a lack of blood flow to an area for more than a few minutes (Prabhakaran et al. 2015). Permanent neurological damage may present as motor, sensory, and/or cognitive deficits.

There are two main types of stroke: ischemic and hemorrhagic. Ischemic strokes account for approximately 87% of strokes and usually occur secondary to an obstruction of an artery leading to the brain or within the brain (Benjamin et al. 2017). This obstruction may be secondary to a thrombus, which occurs when a blood clot develops in an artery supplying blood to the brain. These blood clots usually occur secondary to repeated build-up of fatty deposits, calcium and clotting factors carried in the blood (Victor and Ropper 2001). The build-up on the vessel wall is perceived as injury, setting off a cascade of events that result in a blood clot, or thrombus, being formed within the vessel. The thrombus may stay in place, occluding blood flow to the brain, or can also break off as an embolus and travel to a distal vessel (Frizzell 2005). Embolic strokes, accounting for about 20% of all strokes, most commonly occur from a cardiac source, with the most common cardiac cause being atrial fibrillation (Victor and Ropper 2001). Finally, about 15-40% of all ischemic strokes are from an unknown cause, referred to as cryptogenic strokes (Zhang and Kasner 2016). Risk factors for ischemic stroke include family history, hypertension, tobacco smoking, diabetes mellitus, obesity, prior transient ischemic attack (TIA), and high cholesterol (Go et al. 2013).

Hemorrhagic strokes account for about 13% of all strokes (Benjamin et al. 2017). This type of stroke usually occurs as a result of a vessel in the brain suddenly rupturing, thus causing blood to leak directly into the brain tissue and/or into the cerebrospinal fluid (CSF), filling the central cavities of the brain, called the ventricles (Frizzell 2005). The cause of the blood vessel

rupture may be from: high blood pressure; a weak spot in a blood vessel wall (most commonly from an aneurysm); or blood vessel malformations in the blood, referred to as arteriovenous malformations (AVM) (Victor and Ropper 2001). The resultant damage from a hemorrhage can occur secondary to: 1) blood not reaching the brain cells beyond the point of rupture (similar to what occurs with an ischemic stroke); or 2) leaked blood from the ruptured vessel irritating and harming brain cells in the area as it increases in volume (Frizzell 2005). The two most common types of hemorrhage are intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). Of all strokes, approximately 10% are ICH strokes, and 3% of are SAH strokes (Benjamin et al. 2017). ICH results from a sudden rupture or an artery or blood vessel within the brain. The sudden increase in blood volume in the brain results in an increase in pressure, which damages the brain cells surrounding the area of rupture. The most common cause for this type of hemorrhage is hypertension (Victor and Ropper 2001). While an intracerebral hemorrhage occurs within the brain, a subarachnoid hemorrhage occurs from damage to a vessel in the subarachnoid space, an area between the brain and the skull (Victor and Ropper 2001). The accumulation of blood volume in this area results in pressure and damage to the brain cells on the surface of the brain. While hemorrhagic strokes have an increased risk of mortality in the first few weeks over ischemic strokes, it is thought that long term functional prognosis is better in stroke survivors with hemorrhagic stroke versus ischemic stroke (Paolucci et al. 2003; Andersen et al. 2009). Risk factors for hemorrhagic stroke include hypertension, trauma, older age, heavy alcohol consumption, non-controlled drugs (amphetamine and cocaine abuse) and Asian or African descent (Frizzell 2005).

1.3 Mechanisms of Recovery After Stroke

There are three primary processes observed local to the area of cell injury/death after stroke that are thought to assist in the early recovery. Firstly, within the initial 8 weeks after stroke, the edema within the brain resolves, which may result in temporary, but not permanent neurological deficits (Inoue et al. 1980). The resolution of edema and improvement of neurological deficits is most often seen with hemorrhagic strokes (Paolucci et al. 2003; Andersen et al. 2009). Secondly, within hours to weeks of an ischemic stroke, there is resolution of the area around the ischemic injury. This area is referred to as the ischemic penumbra, and although it is at risk for infarction secondary to decreased blood flow, it is still an area amenable to recovery (Murphy and Corbett 2009). The reperfusion of blood flow to the ischemic penumbra causes the affected and previously non-firing neurons to resume function, often resulting in clinical and functional neurological improvements. Thirdly, resolution of areas remote to the area of injury may also be restored. This is referred to as diaschesis and may occur within days to months after the stroke. It is thought that areas remote to the stroke site of damage, yet interconnected via brain pathways, can be depressed following the injury and resolution of this may improve clinical symptoms (Nudo, Plautz, and Frost 2001). Along with these processes occurring in the early stage of recovery, there are also events contributing to the long-term recovery and reorganization of the central nervous system. These changes may include: alterations to neurotransmitters (occurring week to years after stroke), unmasking of alternative neural pathways (occurring immediately after injury to a few months post-stroke), and creation of new neural synapses, known as synaptogenesis, which is thought to occur within the first few weeks to months after stroke (Nudo 2003). The capability of the brain to recover after stroke and the extent of the clinical neurological deficits is multifactorial, depending on the extent and

location of area of injury, the connection of the damaged areas to other areas in the brain, and the extent of the above recovery processes occurring.

1.4 Stroke Rehabilitation

Enabling individuals to regain their functional independence, to ultimately maximize their quality of life, is the primary goal of stroke rehabilitation. Over the past twenty years, significant research has been conducted to expand our knowledge on the essential components of therapy to optimize stroke recovery; however, there is still much work to be done. Understanding the type of therapy, timing of therapy, therapy prescription parameters, and methods to objectively monitor the prescribed therapy are imperative components to maximizing functional recovery after stroke (Ward 2017).

1.4.1 Walking Recovery After Stroke

The ability to regain walking independence is one of the most commonly stated rehabilitation goals for individuals post-stroke (Bohannon et al. 1988; Harris and Eng 2004) and the primary reason for referral to inpatient stroke rehabilitation in the United States (Dobkin 2005). Furthermore, the ability to obtain independent ambulation is a dictating factor in determining an individual's discharge destination from the hospital after stroke (Mees et al. 2016). Overall, walking is an extremely important therapeutic goal and a primary focus throughout the stroke rehabilitation continuum.

1.4.2 Task-Specific Therapy Training Approach

Since the late 1990's, there has been a surge of evidence supporting the notion that completing functional based therapy can improve functional outcomes in individuals post-stroke. This therapy approach is referred to as task-specific training. Prior to this time, therapy

primarily focused on inhibiting the impairments that presented in the affected upper and lower extremity (Hesse et al. 2003).

When task-specific training approach was initially applied, it focused on individuals in the chronic phase post-stroke (greater than 6 months after injury) and improving walking recovery. Salbach et al. (2004) demonstrated that exercises to enhance lower extremity recovery and walking resulted in improvements in walking outcome measures (Six Minute Walk Test (6MWT), walking velocity (5-meter walk) and Timed Up and Go) in chronic stroke patients. Similar results were also observed in a task-specific community based exercise programs focusing on lower extremity strength and mobility (Pang et al. 2005). As task-specific interventions proved efficacious in the chronic stroke population, translation of this evidence to the sub-acute stroke population occurred in order to assess its feasibility and efficacy during a time period when neurological and functional recovery post-stroke could potentially be optimized (Jorgensen et al. 1995a; Nudo 2003). Similar improvements in the sub-acute stroke population were also observed in initial studies conducted by Blennerhassett et al. (2004) and English et al. (2007) in which circuit exercise programs, addressing lower extremity strength, balance and walking, resulted in improvements in walking outcome measures. The influx of research examining the task-specific approach resulted in a systematic review investigating the benefit of repetitive task gait oriented training program. Analysis of 21 studies in this research demonstrated a significant treatment effect for task specific programs with respect to gait speed and walking distance (van de Port et al. 2007). A follow-up Cochrane review of 14 trials conducted by French et al. (2010) found similar results; repetitive task training aimed at improving mobility was associated with increased walking distance, walking speed, and sit to stand performance.

Cardiovascular improvements from task specific programs have also become a focus in the past few years. Outermans and colleagues (2010) focused on task-specific training in individuals who were within the first 2-8 weeks post-stroke. This study compared usual care physical therapy versus a high-intensity, task oriented training program to improve balance and gait related activities, as well as cardio-respiratory fitness. Patients in the experimental group achieved significantly greater gains on walking speed (10-meter walk) and walking endurance (6-minute walk test (6MWT)) compared to usual care. Furthermore, results from a treadmill based study focusing on walking recovery initiated in the sub-acute phase post-stroke demonstrated greater improvements in walking endurance and cardiovascular fitness compared to usual physical therapy care (MacKay-Lyons et al. 2013). Overall, there is strong evidence for physical therapy interventions favoring task-specific training in all phases post-stroke, however the specific training parameters (intensity, dose) in the early phase post-stroke are still not well understood and need to be investigated (Veerbeek et al. 2014).

1.4.3 **Aerobic Exercise and Rehabilitation**

There is strong body of evidence supporting the benefits of aerobic exercise on stroke recovery throughout the rehabilitation continuum (Pang et al. 2006; Stoller et al. 2012). These benefits include improvements in cardiorespiratory fitness and walking recovery, and more recently, emerging evidence on its effects on improving cognition (El-Tamawy et al. 2014). Furthermore, evidence from the stroke animal model suggests that aerobic exercise promotes neuroplasticity, and contributes to neural recovery in the early stage after stroke (Ploughman et al. 2015). Although there is limited evidence of this occurring in humans (Mackay et al. 2017), understanding how therapeutic interventions, including aerobic exercise, influences neuroplasticity is an area of high priority in stroke rehabilitation research, particularly in the

early stage after stroke when maximal neuroplasticity is thought to occur (Ploughman et al. 2015; Ward 2017).

Although stroke rehabilitation guidelines recommend that aerobic exercise be prescribed at an intensity of 40-70% heart rate reserve (HRR), for a duration of 20-60 min/session (or multiple 10 minute sessions), at least 3-5 days/week (Billinger et al. 2014), the translation of these recommendations into clinical therapeutic practice appears to be limited. Seminal research demonstrates that aerobic exercise in stroke rehabilitation is low, with less than 3 minutes of a therapy session being spent within a cardiovascular training zone (greater than 40% heart rate reserve (HRR)) (MacKay-Lyons and Makrides 2002). While therapists express that safety concerns, patient characteristics, and institutional barriers are contributing to the limited prescription of aerobic exercise post-stroke (Doyle and MacKay-Lyons 2013; Boyne et al. 2017), innovative approaches to overcoming these clinical barriers need to be investigated so all individuals post-stroke can benefit from the positive effects of aerobic exercise on their recovery.

1.4.4 **Intensity of Rehabilitation**

Defining "intensity" as it relates to optimizing functional recovery in post-stroke rehabilitation is a topic of much debate secondary to the term being used loosely throughout the literature. In some research, intensity refers to the demand on the cardiovascular system, usually objectively measured by an individual's heart rate (MacKay-Lyons et al. 2013). In other studies, intensity refers to the number of repetitions completed by the paretic upper extremity or lower extremity, assessed by counting the number of repetitions completed in a therapy session (Lang et al. 2007). In some research, intensity accounts for the total time duration spent in a physical therapy intervention; more time in therapy equates to a more intensive therapy (English et al. 2015). Recently, the American Congress of Rehabilitation Medicine Stroke Movement

Interventions Subcommittee defined intensity as the "amount of physical or mental work put forth by the client during a particular movement or series of movements, exercise, or activity during a defined period of time." (Page et al. 2012).

Within the clinical practice setting, the recommendations for stroke rehabilitation therapeutic intensity remain nebulous. The Canadian Stroke Best Practice Recommendations state, "Patients should receive rehabilitation therapies of appropriate intensity and duration, individually designed to meet their needs for optimal recovery and tolerance levels (Evidence Level A) (Hebert et al. 2016). The Guidelines for Adult Stroke Rehabilitation and Recovery in the United States declare a similar recommendation, "It is recommended that stroke survivors receive rehabilitation at an intensity commensurate with anticipated benefit and tolerance. (Evidence Level B) (Winstein et al. 2016a). Overall, defining, applying, and measuring intensity in post-stroke rehabilitation is a key component to optimizing functional recovery in individuals post-stroke.

With respect to the cardiovascular system and repetitions conducted by the paretic upper and lower extremity, intensity is low in physical therapy. As mentioned earlier, MacKay-Lyons and colleagues (2002) found that heart rate was within a training zone (40-85% of heart rate reserve) for 2.8 minutes of a 55-minute physical therapy session. Similarly, low intensity has also been observed with respect to upper extremity and lower extremity repetitions within a therapy treatment session (Lang et al. 2007). However, when cardiovascular intensity (MacKay-Lyons et al. 2013) and upper extremity repetitions (Wolf et al. 2006) were increased within physical therapy treatment sessions and applied over a duration of time, significant improvements were achieved in the functional recovery of individuals post-stroke. Objectively measuring the cardiovascular and repetition intensity has also been inconsistent in the literature

to date secondary to limitations in the technology. Lang and colleagues (2007) employed individuals to observe each therapy session and count limb repetitions. This is extremely laborious and not practical in the clinical setting. However, recent technological advances in monitoring equipment over the past five years may enable improved ways to measure therapy intensity for research and clinical purposes (Dorsch et al. 2015; Mansfield et al. 2015).

Another component of intensity applied in post-stroke rehabilitation is the amount of time spent in therapy. Is more physical therapy better to optimize post-stroke recovery? Over the last twenty years, a large number of trials have examined how the amount of therapy may influence functional recovery. However, due to the heterogeneity of trials, it is extremely difficult to ascertain how much therapy results in improvement. For the upper extremity, in the early phase post-stroke, it has been found that an additional 10 hours of motor therapy can alter motor outcomes (Dromerick et al. 2015). Others have found that a minimum of an additional 16 hours needs to be provided in the first 6 months after stroke to obtain significant differences in activities of daily living (Kwakkel et al. 2004). Recently, Lohse and colleagues (2014) applied a regression model to predict improvement during therapy as a function of total time scheduled for therapy and years after stroke. The authors found that large doses of therapy lead to clinically meaningful functional improvements. However, a limitation noted by the authors was that the trials included reported time scheduled for therapy as a measure of dose. To objectively quantify the time and repetitions in therapy, preferred measures would be active time in therapy (minutes) or repetitions of an exercise during therapy. Therefore, the authors called on future research studies to report this data.

In a recent randomized controlled trial investigating the effect of increased physical therapy on improving stroke functional outcomes, more minutes of therapy was not found to be

better when compared to usual care (English et al. 2015). Physiotherapy time was increased by having longer sessions over a 5-day period provided in a group circuit class environment or by increasing the standard physical therapy from 5 days/week to 7 days/week. However, one of the limitations with this study was that the authors did not control for the exercise interventions or rest time during the therapy sessions. The group that received the extended circuit class exercises over the 5 days/week did receive 20 more hours of exercise/week, however, participants actually spent the extra time resting and not doing more exercise when compared to standard care. This finding strongly supports the necessity for future stroke rehabilitation research investigating dose response in therapy and incorporating devices to objectively assess intensity during therapy.

Objectively measuring walking intensity during clinical therapeutic sessions, with respect to step count, remains a significant challenge in stroke rehabilitation. Two major factors contribute to this challenge: 1. Traditional step count devices (i.e. pedometers) that provide instantaneous feedback to patients/clinicians of step count do not accurately measure walking steps at slow walking speeds, which are vastly apparent in individuals post-stroke (Carroll et al. 2012); 2. Devices that do accurately measure walking steps across the variety of walking speeds observed in individuals post-stroke unfortunately do not provide instantaneous feedback (they are primarily used in the research setting), therefore impacting their applicability in a clinical setting. With the emergence of a multitude of new economical, commercially-available, activity monitors that provide instantaneous step count feedback, there is a need to assess whether one of these new devices may be suitable to accurately measure step count across the variety of walking speeds observed in individuals post-stroke. This would be a unique and novel application for these activity monitors as the accuracy of these devices has not been systematically tested across

the variety of walking speeds (from very slow to fast) that can be observed in individuals post-stroke. Furthermore, identifying such a device would make a significant contribution to addressing the current void in stroke rehabilitation with regards to accurately measure walking step count, which is necessary in order to objectively quantify walking intensity in this population.

Overall, moving forward, it is imperative that future stroke rehabilitation research defines how intensity is being assessed in respective studies and both systematically and objectively measures the independent intensity factors (dose, cardiovascular intensity, and repetitions) to optimize post-stroke rehabilitation treatment.

1.4.5 **Timing of Rehabilitation**

Is there a critical time period after stroke to optimize recovery? Results from the Copenhagen Stroke Study demonstrated that in their human sample population of almost 1200 individuals post-stroke, 80% of all participants reached their maximum neurological recovery and functional recovery within 4 weeks and 6 weeks respectively post-stroke (Jorgensen et al. 1995b). Therefore, does therapy initiated within this time frame maximize recovery? Research conducted in the mouse model with an induced stroke demonstrated that early and intensive training within the first two weeks post-stroke was actually deleterious to functional recovery and resulted in an enlarged volume of the lesion (Kozlowski et al. 1996). Recently, a similar question was examined in a human population inquiring how early, intensive therapy impacted functional recovery post-stroke (AVERT Trial Collaboration Group 2015). This large, global, multi-site, randomized clinical trial demonstrated that early, more intensive therapy initiated within the first 24 hours, and applied three times as much in the first 7 days post-stroke, was associated with a poorer outcome, as measured by the Modified Rankin Scale, at 3 months post-

stroke when compared to usual stroke care. Therefore, intensive rehabilitation applied too early post-stroke was not beneficial and may actually be detrimental to recovery. Therefore, is there a better time to optimize functional recovery post-stroke? Biernaskie and colleagues (2004) addressed this question in the stroke induced mouse model by examining the motor outcomes when training was initiated at 5, 14, or 30 days post lesion. The authors found that the best response to training was observed when it was initiated at 5 days post-stroke. An intermediate response was observed when training was initiated at 14 days post-stroke and when training was initiated at 30 days post-stroke, motor outcome results were the same as the controls who were not trained at all. These results suggest that critical periods in stroke recovery do exist in adult mammals (Murphy and Corbett 2009), and perhaps it is within 5-30 days post-stroke (Krakauer et al. 2012). However, given the short one to two-year lifespan of a mouse, it is not known how this timing of recovery observed in the animal model translates to the human population. Implementing randomized controlled trials with humans at this potentially critically stage, the first 7-30 days post-stroke, is imperative to investigate if rehabilitation timing optimizes post-stroke functional outcomes (Dromerick et al. 2015).

1.4.6 **Exercise and Recovery of Cognition After Stroke**

Cognitive deficits are common after stroke, with up to 83% of individuals demonstrating impairments on at least one cognitive domain at 3 months post-stroke (Jokinen-Salmela et al. 2015). Physical activity is promoted to improve cognition after stroke, yet the specific exercise mode, prescription, and timing to maximize the benefits have not been clearly defined. Consistent with the results observed in the healthy aging population, a combined aerobic exercise and strength program appears to be the most beneficial to improve cognition post-stroke (Oberlin et al. 2017), yet the specific exercise parameters (intensity, frequency, duration) and when to

initiate post-stroke remains unclear. Investigating the effect of aerobic exercise +/- other interventions on cognition in the early stage of recovery after stroke (less than 3 months) is an important priority for future stroke rehabilitation research (Hasan et al. 2016; Oberlin et al. 2017).

1.5 Summary

Overall, optimizing functional recovery is of paramount importance to the growing population of stroke survivors that live with residual neurological deficits and the family/caregiver teams and health care system that supports them. From the animal stroke-induced models, it is thought that intensive rehabilitation applied in the early post-stroke period (within 5 days - 4 weeks) benefits functional recovery, but this has not been established in humans. There is also limited knowledge on how intensive exercise can be safely prescribed, tolerated, and implemented during this early post-stroke period, which most often occurs during the inpatient rehabilitation setting. Furthermore, methods to objectively assess, monitor, and progress walking intensity in post-stroke physical therapy sessions have also not been established, therefore making it clinically challenging to appropriately prescribe walking-related exercise parameters to optimize stroke recovery.

1.6 Research Objectives

This thesis will address the above gaps in the post-stroke rehabilitation literature and specifically focus on answering the following research questions:

1. Is there an affordable, commercially available, instantaneous feedback monitoring device that can accurately measure walking steps, accounting for the variable walking speeds that can be seen in individuals post-stroke?

Identifying an accurate monitoring device that can objectively measure walking steps in the clinical setting with individuals post-stroke will have a significant impact on assessing intensity outcome during therapy.

2. Is a high intensity, task-specific, progressive, walking related exercise protocol applied either once or twice a day in the early phase post-stroke (during post-stroke inpatient rehabilitation) more effective than standard care at improving walking recovery and overall function, cognition, and quality of life in individuals post-stroke?

Systematically assessing how therapy intensity and dose applied at a critical time of neurological and functional recovery post-stroke will make a significant contribution to expanding our knowledge on how to maximize recovery for stroke survivors.

Bridging Statement I

To accurately measure walking intensity during stroke rehabilitation, devices are required that can correctly assess the walking steps across the large variety of walking speeds and patterns that can present post-stroke. Furthermore, these devices need to be economical and provide instantaneous feedback to the both the patient and therapist to be used in a clinical setting. Chapter 2 describes the initial investigation to assess the accuracy of a readily available, economical, walking device to measure step count in individuals post-stroke.

A version of Chapter 2 has been published:

Klassen TD, Simpson LA, Lim SB, Louie DR, Parappilly B, Sakakibara BM, Zbogar D, Eng JJ. "Stepping Up" Activity Post-Stroke: Ankle Positioned Accelerometer Can Accurately Record Steps During Slow Walking." Phys Ther 2016 March;96(3):355-360.

Chapter 2: Accurately Measuring Steps During Slow Walking Post-Stroke

2.1 Introduction

Physical activity is extremely low in individuals post-stroke compared to both healthy older adults and those with other chronic diseases (Ashe et al. 2009). Devices, such as pedometers, that measure walking activity can be effective in motivating this population to exercise (Sullivan et al. 2014), and may assist health care professionals to monitor and progress mobility during rehabilitation. However, to our knowledge, no pedometers accurately record steps in this population at slow walking speeds (Carroll et al. 2012; Martin et al. 2012).

With recent technological advances, activity monitors that incorporate accelerometers may provide an alternative to pedometers for accurately measuring walking steps. The Fitbit One is an example of an activity monitor that includes an accelerometer, and is readily available to consumers, providing instantaneous visual feedback of walking steps. Despite the accuracy of the Fitbit One in measuring walking steps in healthy adults at relatively normal walking speeds (0.9-1.78m/s) (Takacs et al. 2014), it provides inaccurate step counts at slow walking speeds post-stroke, particularly less than 0.6 m/s (Fulk et al. 2014). This imprecision observed at slow walking speeds is consistent with another accelerometer, the Acti-Cal Accelerometer, which provides inaccurate step counts in healthy, older adults, at walking speeds between 0.46-0.85m/s (Martin et al. 2012). However, it is perhaps the accelerometer position on the body that may influence the step count accuracy at slow walking speeds. Although both the Fitbit One and Acti-Cal Accelerometer are recommended by the manufacturer to be worn at the waist, one study in older acute surgical patients suggested that step count sensitivity with an accelerometer can be improved for slower walking speeds when positioned at the ankle (Cook et al. 2013). Furthermore, other accelerometers developed for research (not consumer) applications, that do

not provide instantaneous visual feedback, have been found to be valid and reliable for mean walking speeds between 0.55-0.82 m/s when positioned at the ankle in individuals post-stroke (Haeuber et al. 2004; Dobkin et al. 2011).

Overall, measuring walking steps is one way to objectively assess an individual's walking activity and has been used in this regard in settings across the rehabilitation continuum (acute/sub-acute/community) (Dobkin et al. 2011; Cook et al. 2013; Sullivan et al. 2014). However, a readily available device has not yet been identified that can accurately measure walking steps at a range of walking speeds (very slow to normal) in individuals post-stroke with a variety of walking deficits. For this reason, it is necessary to establish how specific walking speeds and positioning on the body may influence the accuracy of activity monitors that provide instantaneous visual feedback for measuring walking steps in individuals post-stroke. Knowledge of this information may assist both individuals post-stroke, and the health care professionals working with them, to obtain accurate, objective data to assess and monitor walking during rehabilitation. Therefore, the objectives of this study were two-fold: (1) examine the effect of walking speed on the accuracy of an accelerometer-based activity monitor in ambulatory individuals post-stroke; and (2) compare the effect of position (waist versus ankle) on the accuracy of an accelerometer-based activity monitor. We hypothesized that: (1) step count accuracy would decline as walking speed decreased; and (2) step count measurements at the ankle would be more accurate than those at the waist for all walking speeds.

2.2 Methods

2.2.1 Participants

Volunteers were recruited from the community through a stroke research registry, flyers posted at recreational facilities, education sessions at stroke support groups and word of mouth.

Individuals satisfying the following inclusion criteria were recruited for the study: at least 3 months post-stroke, able to follow 3-step commands, and able to walk independently for at least 30 meters (orthotic/assistive devices permitted). Exclusion criteria for the study included a major medical condition (i.e.: Multiple Sclerosis, Parkinson's disease, angina) affecting the individual's ability to walk and major surgery in the past 12 months (i.e.: hip replacement, heart surgery). Ethics approval was obtained from the institutional review board and informed consent was obtained from all participants.

2.2.2 **Device**

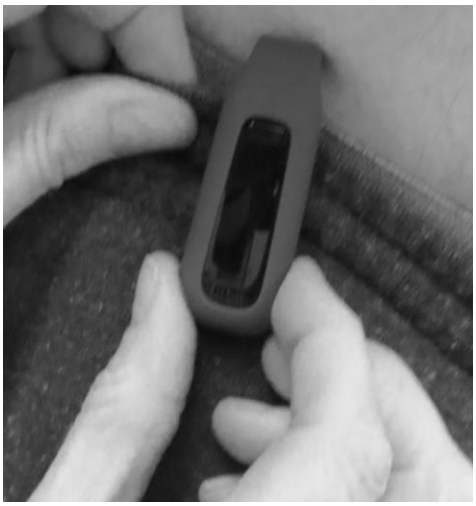
The Fitbit One (Fitbit) (Fitbit Inc., San Francisco, CA) was used for the study. It is a small (4.8cm x 1.9 cm x 1.0cm), commercially available device, containing a triaxial accelerometer that converts acceleration to step counts based on proprietary algorithms. The manufacturer suggests that the Fitbit One be worn on a waist belt or bra (attached by the clip on the back of the device) or put in a pant pocket.

2.2.3 **Procedure**

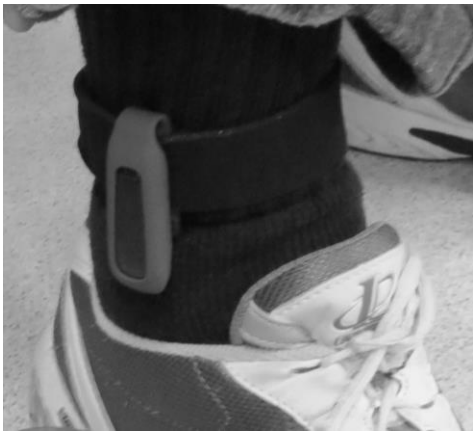
The accelerometer was positioned on each participant's non-paretic side on a waistband (lateral point (Accel-Waist)) and ankle strap (above the lateral malleolus (Accel-Ankle)) (Figure 2.1). Participants walked a distance of 15 meters for 8 walking trials: one trial at a self-selected walking speed and 7 trials from 0.3m/s to 0.9m/s in 0.1 m/s increments. Visual gait analysis of the participant's self-selected walking trial was conducted by a physical therapist or occupational therapist and observed walking characteristics (listed in Table 2.2) were selected from a checklist created by the study team of the most commonly observed gait deviations post-stroke.

Figure 2.1 Photograph of the Fitbit One Positioned on a Participant's (a) Waist and (b) Ankle

a) Fitbit One positioned at the waist



b) Fitbit One positioned at the ankle



At the start of each walking trial, a "pace-setter" (trained assistant) instructed the participant to "walk directly beside him/her." The "pace-setter" used visual (markings on the floor) and auditory (metronome beats via earbuds) feedback to maintain the selected speed. The step count on each accelerometer, obtained by pressing a button on the display, was recorded at the beginning and end of each walking trial. Participants self-determined the amount of sitting or standing rest needed between each walking trial. The order of the 7 trials was randomized for each participant and each trial was video recorded. Two independent viewers counted the actual number of steps from the video recordings of each trial (i.e., considered gold standard). If there was greater than 1 step difference between the two viewers, then a third viewer watched the video and consensus was reached. All data from one viewer was randomly selected and used for the analysis.

2.2.4 **Data Analysis**

Descriptive statistics (means, SD) were used to describe sample characteristics. Accuracy of the Fitbit device at each speed and location was assessed by examining the error between the Fitbit and observed steps. A linear mixed model was created with the restricted maximum-likelihood method to determine the effect of speed and location on the accuracy of the Fitbit (i.e., error between the observed steps and the Fitbit steps). Error was calculated using the following calculation: (Fitbit steps– Observed steps)/Observed steps. Speed (continuous variable centered at its slowest speed (i.e. 0.3m/s)) and location (categorized into ankle/waist) were input as fixed variables. The interaction between speed and location was also explored. A participant variable was input as the random variable to account for the correlation between repeated measurements (i.e., different speeds and locations). A varying intercept model was applied to allow the intercept for each participant to vary. A likelihood ratio test was also used to determine if the

interaction between speed and location statistically improved the model fit and therefore should be retained in the final model. Post-hoc paired t-tests were performed to examine differences in error between the ankle and waist locations at each speed when the likelihood ratio test was statistically significant. Bonferroni-adjusted p-values for multiple comparisons are reported. Finally, diagnostic plots of the final model were examined to investigate violations of regression assumptions. Statistical analyses were performed using R version 3.1.1.

2.3 Results

A total of 43 individuals participated in the study (Table 2.1).

Table 2.1 Participant Characteristics (N=43)

Variable	Mean (SD) or Number [% of participants]
Age (years)	65 (10.66)
Time Since Stroke (Month)	102.8 (70.3); Range = 6 - 307
Sex (Males)	30 [70]
Type of Stroke Ischemic Hemorrhagic	 30 [70] 13 [30]
Most affected side Left Right Both No weakness	 22 [51] 18 [42] 2 [5] 1[2]
Comfortable Gait Speed (m/s)	0.72 (0.30)
Ankle Foot Orthosis No Yes	 32 [74] 11 [26]
Assistive Device None Cane Wheeled-Walker Other Quad Cane	 16 [37] 13 [30] 9 [21] 3 [7] 2 [5]

The majority of participants used an assistive device to ambulate and had an altered walking pattern (Table 2.2). The mean (SD) comfortable walking speed was 0.72m/s (0.3). Data was recorded for each walking trial only if it was within 10% of the assigned speed; therefore, some participants could not complete the faster speeds (Table 2.3). The pace-setter protocol resulted in participants being within 98% of the assigned speeds.

Table 2.2 Walking Impairments Observed During Self-Selected Walking Speed Trial

Walking Impairment	Number of Participants (/43) Demonstrating Impairment*
Minimal paretic hip flexion and knee flexion in swing	20
Paretic pelvic hike and/or circumduction in swing	19
Paretic arm spasticity/flexion	17
Paretic knee hyperextension in stance	14
Paretic foot clearance difficulties during swing (e.g., not wearing AFO)	10
Paretic knee flexion in stance	5
Normal gait patterns, but slow	2
Ataxic gait	1
Shuffling gait	1

*****Participants may exhibit several impairments

Table 2.3 Accuracy of the Accelerometer at Varying Walking Speeds

Assigned Speed (m/s)	Actual Speed Mean (SD) [CI]	Number of Participants Evaluated	Accel-Ankle Zero Counts*	Accel-Waist Zero Counts*	Actual Steps Mean (SD) [CI]	Accel-Ankle Mean (SD) [CI]	Accel-Waist Mean (SD) [CI]	Accel-Ankle Mean % Error[†](SD) [CI]	Accel-Waist Mean % Error[†](SD) [CI]	P-Value**
0.3	0.30 (0.01) [0.30-0.30]	43	1	33	54 (11) [51-57]	49 (15) [45-53]	10 (20) [4-16]	15.8 (22.3) [9.1-22.7]	84.6 (30.5) [75.5-93.7]	p<0.001
0.4	0.40 (0.01) [0.40-0.40]	43	0	20	46 (8) [44-48]	45 (9) [42-48]	20 (21) [14-26]	5.5 (10.3) [2.4-8.6]	59.1 (40.1) [47.1-71.1]	p<0.001
0.5	0.50 (0.02) [0.49–0.51]	40	0	7	40 (8) [38-42]	40 (7) [38-42]	26 (15) [21-31]	4.5 (6.7) [2.4-6.6]	38.3 (33.2) [28.0-48.6]	p<0.001
0.6	0.60 (0.02) [0.59-0.61]	36	0	0	36 (6) [34-38]	36 (6) [34-38]	31 (8) [28-34]	4.0 (4.9) [2.4-5.6]	16.6 (17.8) [10.8-22.4]	p=0.002
0.7	0.69 (0.03) [0.68-0.70]	34	0	0	33 (5) [31-35]	32 (5) [30-34]	29 (7) [27-31]	4.9 (8.2) [2.1-7.7]	11.8 (17.0) [6.1-17.5]	p=0.21
0.8	0.78 (0.04) [0.77-0.79]	32	0	0	31 (5) [29-33]	31 (7) [29-33]	28 (4) [27-29]	6.9 (11.7) [2.8-11.0]	10.1 (13.6) [5.4-14.8]	p=0.84
0.9	0.88 (0.03) [0.87-0.89]	27	0	0	29 (4) [27-31]	28 (4) [26-30]	27 (3) [26-28]	4.9 (8.3) [1.8-8.0]	7.7 (8.9) [4.3-11.1]	p=0.58

(SD) = Standard Deviation
[CI] = Confidence Interval
* Number of participants that the accelerometer counted zero steps for the walking trial
[†] Absolute((Accelerometer steps – actual steps)/actual steps)x100). Note: Calculation performed on individual data so may not equate if calculation completed on group data presented above.
**Paired t-test between Accel-Ankle and Accel-Waist; Bonferroni corrected p-values reported

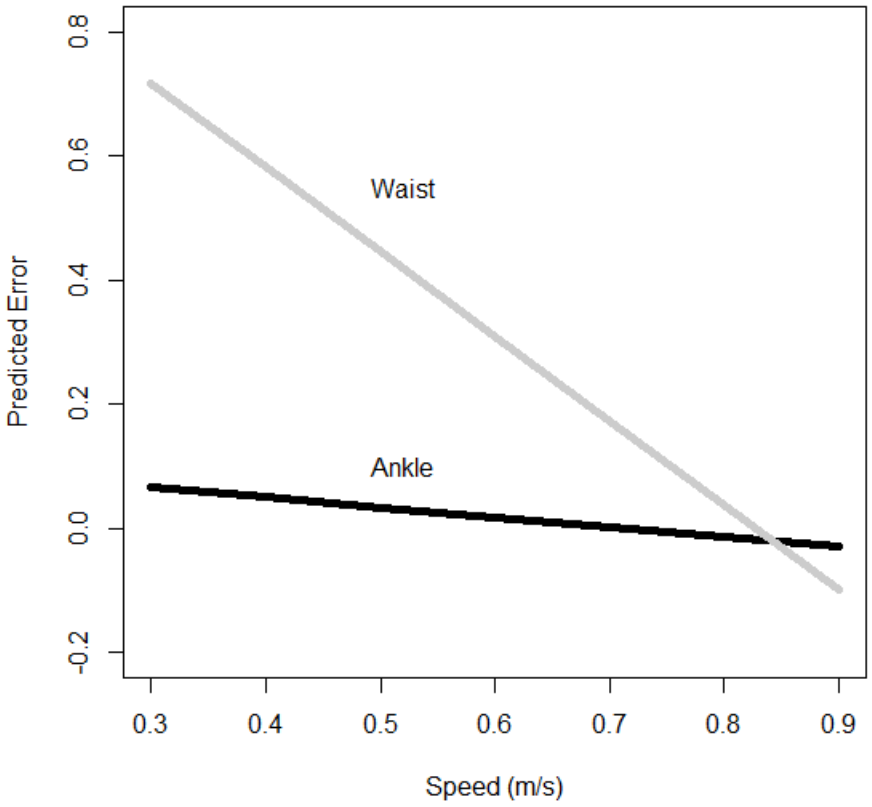
The final linear mixed model resulted in significant effects of speed and location on Fitbit error (Table 2.4). The interaction between speed and location significantly increased the model fit and was therefore retained in the final model. Review of the diagnostic plots did not reveal any violations of the regression assumptions.

Table 2.4 Final Linear Mixed Model Predicting Fitbit Error

	Coefficient	95% Confidence Interval	p value
Intercept	0.11	0.03 to 0.20	0.01
Speed	-0.16	-0.29 to -0.03	0.02
Location: Waist	1.01	0.90 to 1.13	<0.001
Speed/Location interaction	-1.20	-1.39 to -1.02	<0.001

Figure 2.2 displays the relationship between speed and error at the ankle and waist placements. An increase in speed was associated with a decrease in error when the attachment location was held constant. Post-hoc paired t-tests revealed statistically lower mean error at the ankle compared to the waist at speeds ranging from 0.3-0.6 m/s (Table 2.3). No statistically significant differences in mean error were observed between the ankle and waist locations at the three highest speeds (i.e. 0.7-0.9m/s) (Table 2.3). At the slower walking speeds (0.3-0.5m/s), the Accel-Waist recorded a value of "0" for a total of 33, 20 and 7 participants respectively. The Accel-Ankle only recorded a value of "0" for one participant at the slowest walking speed of 0.3m/s (Table 2.3).

Figure 2.2 Estimated Relationship Between Speed and Error for each Accelerometer Location (waist, ankle) Based on the Linear Mixed Model



2.4 Discussion

This study examined the effect of walking speed on the accuracy of an accelerometer-based monitor in ambulatory individuals post-stroke and compared the effect of the position (waist versus ankle) on the accuracy of the monitor. Our findings suggest that the accelerometer is more accurate as walking speed increases from 0.3-0.9m/s. In addition, the accelerometer is more accurate when placed at the ankle, versus the waist, at the slower speeds (0.3-0.6m/s).

The walking speeds selected for this study (0.3-0.9m/s) are representative of the typical gait speeds observed in individuals post-stroke (Perry et al. 1995). By designing a novel "pace-setter" paradigm, it allowed us to systematically test the accuracy of the accelerometer at a wide range of walking speeds without constraining step length or cadence, and while simulating a natural task of walking with a companion. Previous literature with individuals post-stroke has only captured a single comfortable speed and reported accuracy of step count devices at walking speeds greater than 0.6 m/s (Elsworth et al. 2009; Carroll et al. 2012; Fulk et al. 2014). Our study population presented with a variety of walking impairments and although all participants were able to complete the slower walking velocities (0.3-0.4m/s), the study population decreased as the walking speed increased. This is consistent with the heterogeneity observed in the post-stroke population and signifies the importance of identifying a monitor that is accurate at recording step counts at a wide range of walking speeds.

The device step count accuracy was also dependent upon where it was positioned on the body. Although manufacturers commonly recommend that monitoring devices be positioned at the waist, the results supported our hypothesis that the accelerometer positioned at the ankle (versus the waist) was more accurate for speeds between 0.3-0.6m/s. Most importantly, with a modified placement at the ankle, the accelerometer was able to accurately capture steps at speeds

as slow as 0.3m/s. At the slowest walking speeds (0.3-0.5m/s), the waist positioned accelerometer recorded "0" steps for 60/126 walking trials (48%) whereas the ankle positioned accelerometer only recorded "0" steps for 1/126 trials (0.01%). The improved sensitivity and accuracy is likely due to the higher accelerations at the ankle compared to the hip. In individuals post-stroke, propulsion of the non-paretic limb, particularly at the toe-off phase of the gait cycle, has shown to be exaggerated in the attempt to limit single-leg stance time on the paretic, or weak, limb (Chen et al. 2005). At very slow walking speeds, the ankle positioned accelerometer is able to consistently detect the limb acceleration whereas the waist positioned device cannot accurately respond to the limb accelerations until much faster walking speeds (0.8-0.9m/s). Therefore, to accurately monitor walking activity across a range of walking speeds, our results suggest that positioning the accelerometer at the ankle versus the waist yields more accurate results.

2.4.1 **Limitations**

Not all participants could complete the faster walking speeds due to their stroke impairments; however, all could complete the slowest speeds, which was the primary focus of the study. In addition, the speed of each walking trial may not have been representative of the participant's self-selected walking velocity. We assessed a wide range of walking speeds for each participant to capture what typically may be experienced within the course of a day, including slow, comfortable, and fast walking velocities. With respect to device application, we did not require the participants to put on/ take off the device or view the data independently. Although these processes can be successfully completed in a sitting position, using only one upper extremity, some individuals post-stroke with significant visual, perceptual, and/or sensory/motor deficits may have challenges independently donning the device and observing the

data. This may be rectified by having assistance from another person, and/or the device data can also be viewed wirelessly through a compatible mobile device (i.e.: phone/tablet).

2.5 Conclusion

Overall, our results fill a longstanding need for identifying a readily available monitoring device that can provide accurate, instantaneous, visual feedback for the altered and slow walking patterns that occur with stroke. Accurate devices to audit walking activity are imperative to progress rehabilitation research and clinical practice to assess dose-response relationships (Lohse et al. 2014) and provide objective outcome measures (Dorsch et al. 2015) with individuals post-stroke. By accurately assessing a wide range of walking speeds (from very slow to normal), this device would enable health professionals to evaluate patients' progress from the acute to community settings and provide an objective measure to monitor and progress activity.

Bridging Statement II

The success of optimizing recovery for stroke survivors depends upon the translation of research evidence into clinical practice. In Chapter 2, I described a study we conducted to assess the accuracy of a monitoring device to measure step count in individuals post-stroke within a research laboratory environment only during assigned walking steps. The natural next step for this research is to assess the accuracy of the device within a busy clinical environment and when a variety of different mobility activities, as well as rest intervals, are undertaken. Chapter 3 addresses this challenge.

A version of Chapter 3 has been published:

Klassen TD, Semrau JA, Dukelow SP, Bayley MT, Hill MD, Eng JJ. Consumer-Based Physical Activity Monitor as a Practical Way to Measure Walking Intensity During Inpatient Stroke Rehabilitation. Stroke. 2017 Sep;48(9):2614-2617.

Chapter 3: A Consumer-Based Physical Activity Monitor as a Practical Way to Measure Walking Intensity During Inpatient Stroke Rehabilitation

3.1 Introduction

Determining the appropriate exercise intensity and dose to maximize functional recovery in individuals post-stroke has been identified as a top priority in stroke rehabilitation research (Veerbeek et al. 2014). Although it is hypothesized that an increased dose of physical therapy may be essential to optimizing functional outcome post-stroke (Lohse et al. 2014), a recent study demonstrated that increasing total time in physical therapy during inpatient rehabilitation, the early phase post-stroke when the majority of neurological change is thought to occur, did not translate to improved functional recovery (English et al. 2015). Therefore, assessing and accurately measuring other aspects of therapeutic dose (e.g., step count, cardiovascular intensity) may be the key to understanding the critical components of therapy to optimize recovery in individuals post-stroke.

The most commonly stated rehabilitation goal for individuals post-stroke is related to walking recovery (Bohannon et al. 1988). However, measuring walking dose (e.g., step count) in these individuals is challenging. Traditional hip-based pedometers are inexpensive, easy to use, and provide instantaneous feedback, but are not accurate with the variety of walking patterns and slower speeds that present in the post-stroke population (Carroll et al. 2012). On the other hand, research devices, such as the StepWatch™ activity monitor (SAM) (modus health, Washington, DC), are accurate in measuring step count during post-stroke walking activities (Mudge et al. 2007), but are expensive, time-consuming to access the data, and do not provide instantaneous feedback. With recent technological advances, consumer-based physical activity

monitors may be an ideal solution to accurately assess walking activity in stroke rehabilitation. In the previous chapter, we demonstrated that the Fitbit One, a consumer-based physical activity monitor, had 10% or less error in measuring walking steps in individuals with chronic stroke at walking speeds between 0.4-0.9 m/s when positioned at the ankle (Klassen et al. 2015). However, as the 43 participants completed the walking trials over a straight 15-meter distance, a necessary next step is to evaluate the step count accuracy of these devices in the "real world" clinical setting where patients practice a wide variety of therapeutic mobility activities under different postures and with a range of equipment (e.g., plinth, treadmill).

We evaluated the accuracy of a consumer-based physical activity monitor (Fitbit One) in measuring walking steps in typical inpatient rehabilitation physical therapy sessions early after stroke using the SAM as the "gold standard". Based on our previous research, we hypothesized that a consumer-based physical activity monitor would demonstrate 10% or less error in measuring walking steps during these physical therapy sessions when a wide variety of walking and therapeutic activities were completed (Klassen et al. 2015).

3.2 Methods

3.2.1 Participants

Individuals admitted to one of four participating inpatient rehabilitation units with a diagnosis of stroke that met the following inclusion criteria were screened for this study: within 6 weeks post-stroke with hemiparesis and ability to ambulate at least 5 meters with up to 1 person maximum assist. Exclusion criteria included: any pre-stroke or current health condition (other than stroke) which rendered the individual with a walking disability and/or unstable medical status; inability to understand/follow directions; less than 19 years old. Participants were the first 21 individuals randomized to one of the experimental groups in the Determining

Optimal post-Stroke Exercise (DOSE) randomized clinical trial. As participants in these experimental groups all received a minimum of 30 minutes of walking retraining during their physical therapy session, we could ensure that walking activities would be completed, and thus measured. Ethics approval was obtained from the local Institutional Review Board and informed consent was obtained from all participants.

3.2.2 **Equipment**

The Fitbit One (Fitbit) (Fitbit Inc., San Francisco, California) is an example of an affordable, readily available, consumer-based physical activity monitor that provides instantaneous visual feedback of walking steps (Figure 3.1). It contains a tri-axial accelerometer that converts acceleration to step counts based on proprietary algorithms (cost ~ $90 USD). The StepWatch™ activity monitor (SAM) has been validated to measure step count during walking and clinical therapeutic activities across a variety of patient populations, including stroke, but does not provide instantaneous feedback (Mudge et al. 2007; Busse et al. 2009). It has been identified as the most commonly used research device to measure physical activity post-stroke (Fini et al. 2017). A docking station, computer, and software are required to download the data (total cost ~ $2000 USD, including monitor).

Figure 3.1 Fitbit and SAM Positioned Above Lateral Malleolus On Non-Paretic Limb

3.2.3 **Procedures**

As part of the DOSE study intervention, all participants received at least a once daily, sixty-minute physical therapy session, five days/week, over a four-week period, in which a minimum of thirty minutes was focused on walking re-training (e.g., over-ground, treadmill, stairs). The remaining time in the therapy session (30 minutes or less) typically included non-gait related activities (e.g., upper extremity activities, mat and plinth activities, patient education). Cycling was not included in any session. At the beginning of every session, the SAM and Fitbit were positioned on the participant's non-paretic ankle, above the lateral malleolus (Figure 3.1). The therapist documented the steps recorded by the Fitbit for each session while the SAM data were downloaded for the matching time period.

3.2.4 **Data Analysis**

A linear mixed model was created to compare the number of steps captured by the Fitbit (dependent variable) as a function of the SAM (independent variable). The model treated the variables of the Fitbit and the SAM as fixed effects, while participant and session variables were random effects. The model utilized a varying intercept to account for individual participant performance over several therapy sessions. A second model was used that added the effect of baseline walking velocity (BWV) to the first model to determine if BWV influenced step count. The accuracy of the Fitbit for each therapy session was measured by calculating the error, using this formula: [Absolute value (Fitbit steps – SAM steps)/SAM steps*100]. An overall Fitbit mean error for each participant was then calculated. The participants were then categorized into established stroke functional walking categories based on their baseline walking velocity (measured by the 6-minute walk) to assess the accuracy of the device at a variety of walking speeds: <0.4m/s - household ambulation; 0.4-0.8m/s - limited community ambulation; and

>0.8m/s - full community ambulation (Perry et al. 1995). An overall Fitbit mean error was then calculated for the participants in each walking category. A Bland-Altman plot was also completed to examine the mean differences between the SAM and Fitbit step counts for all 471 therapy sessions, including the limits of agreement.

3.3 Results

A total of 471 sessions were monitored over 21 participants who progressed from a baseline Fitbit mean step count of 1564 (987) to 3353 (1288) over 4 weeks of recording during inpatient therapy (change of 214%) (Table 3.1). On average, participants were 25 days post-stroke at their first session and had a slow walking velocity (0.41 m/s).

Table 3.1 Participant and Physical Therapy (PT) Session Characteristics

Participants (n)	21
Age (mean, (SD))	55 (10)
Type of Stroke (number of Ischemic/Hemorrhagic)	19/2
Total number of PT sessions analyzed (n) (mean PT sessions per participant/SD/range)	471 (22/10/5-40)
Time from stroke to initial monitored PT session (days) mean/SD/range	25/11/12-58
Comfortable walking speed (m/s) mean/SD/range	0.41/0.27/0.10-1.18
Fitbit step count at initial therapy session* mean (SD)	1564 (987)
Fitbit step count at final therapy session* *(approx. 4 weeks later)* mean (SD)	3353 (1288)

*Each therapy session was 60 minutes in duration and included both gait and non-gait related activities.

There was a strong linear relationship (intercept = -139.3, slope = 0.99, 95% CI [0.97,1.01]) between the number of steps captured by the Fitbit compared to the SAM (Figure 3.2). When baseline walking velocity was accounted for, a small improvement was found from the original model (intercept = -129.6, slope = 1.01, 95% CI [0.99,1.03]). The Fitbit mean error was low for faster velocities and higher for slower velocities (10.9% for speeds less than 0.4 m/s) (Table 3.2). Data were scattered about the mean difference in the Bland-Altman plot (Figure 3.3); 5% of points were outside of the limits of agreement (as expected with a normal distribution) and were primarily those with slower baseline walking velocities. With respect to the SAM, the Fitbit slightly underestimated step count in 412/471 therapy sessions.

Figure 3.2 Slope Line of Fitbit Steps versus SAM Steps

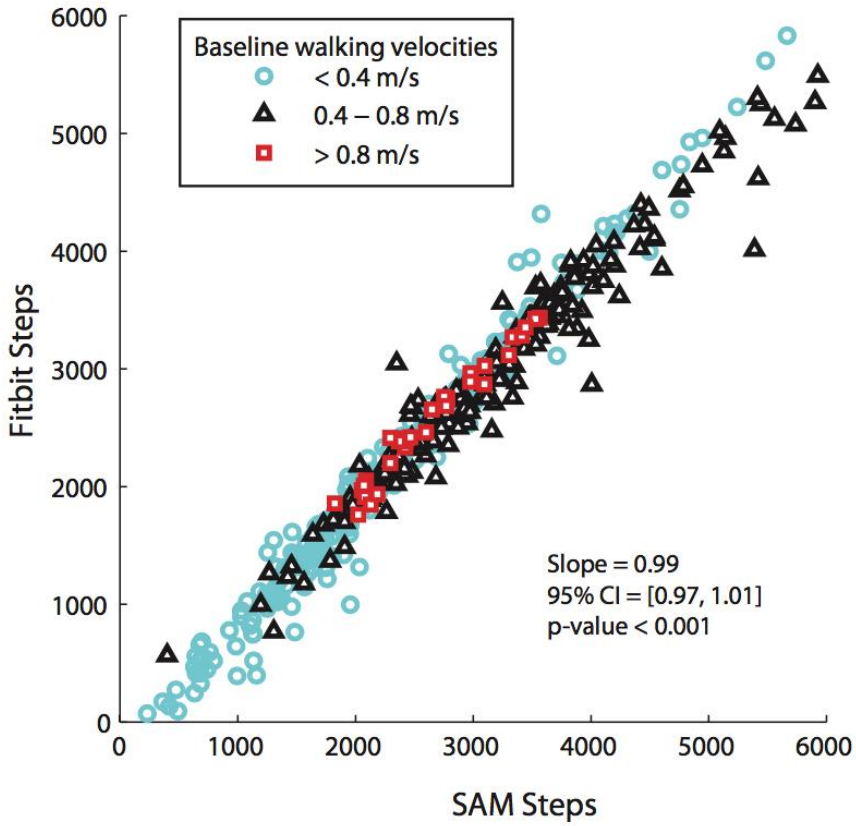
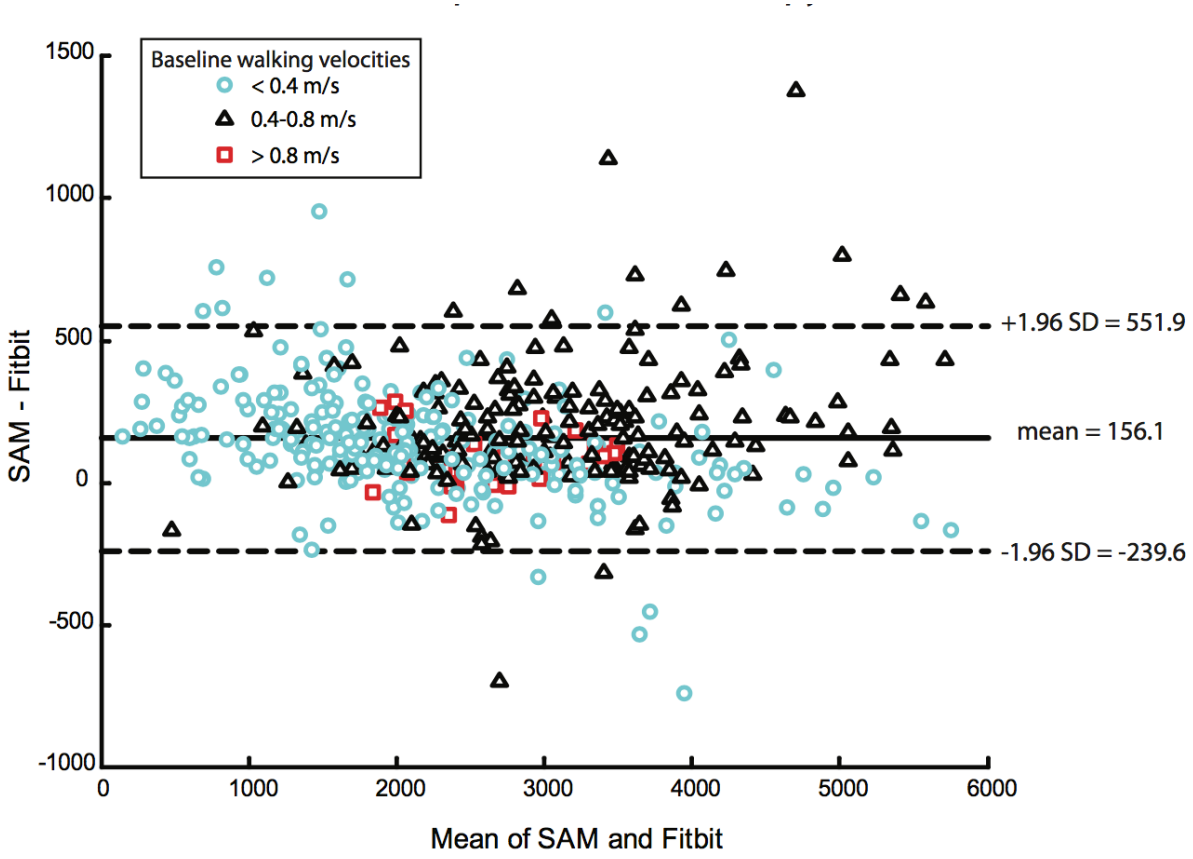


Figure 3.3 Bland Altman Plot of all 471 Intervention Sessions



Solid line: Mean differences between SAM and Fitbit step counts.
Dashed lines: Limits of agreement.

Table 3.2 Accuracy of the Fitbit One Using Perry Gait Categories (Perry et al. 1995)

Baseline walking speed (m/s)	Participants (n)	Total PT sessions monitored (n)	6-minute walk velocity (m/s) Mean (SD)	Fitbit Mean Step Count (SD)	95% CI	SAM Mean Step Count (SD)	95% CI	Fitbit Error (%) Mean (SD)	95% CI
< 0.4 m/s	12	259	0.2 (0.1)	2112 (1091)	1855, 2369	2247 (1013)	1974, 2521	10.9 (5.3)	7.9, 13.9
0.4-0.8 m/s	7	181	0.6 (0.1)	2992 (933)	2557, 3428	3191 (986)	2726, 3655	6.8 (3.0)	4.6, 9.0
> 0.8 m/s	2	31	1.0 (0.2)	2556 (512)	1656, 3455	2639 (512)	1710, 3567	4.4 (2.8)	0.6, 8.2

3.4 Discussion

With a Fitbit error less than 11% for the slowest speeds, this device is appropriate for monitoring walking activities within the inpatient stroke rehabilitation setting where therapy sessions include both walking and non-walking exercises. As the majority of the monitored sessions were from participants who had a mean baseline walking speed less than 0.4m/s, and who progressed to a mean walking speed of 0.8 m/s, it also demonstrates that the device is valid for monitoring the recovery of those with severe walking impairments and thereby addresses a major void in the literature with respect to accurately monitoring step count for this population. The minimal clinical important difference (MCID) for step count during stroke inpatient rehabilitation has not been defined. Participants in our study demonstrated a mean step count change of 214% over the 4 week intervention period (Table 3.1) while another study reported a mean change of 525% in step counts over 3 weeks of stroke inpatient physical therapy sessions with a mean baseline walking velocity (0.44 m/s) similar to that in our study (0.41 m/s) (Table 3.1) (Rand and Eng 2012). Therefore, we expect that weekly goals to increase step counts would very likely exceed the 10% error rate of this device.

Contrary to what the manufacturer recommends, but similar to other research findings, positioning the Fitbit at the ankle optimized the likelihood that it was primarily recording steps from accelerations of the non-paretic lower limb/ankle during weight-bearing, gait related activity (Klassen et al. 2015). The greater Fitbit error observed with slow walking is likely secondary to decreased sensitivity of the device to respond to slow limb accelerations. While a truer gold standard would be video analysis of the steps, the SAM has recorded 96.1% accuracy when a variety of activities of daily living (e.g., kitchen activities, rising from a chair,

taking shoes on/off), including walking, are performed (Busse et al. 2009). Furthermore, as the two devices were compared over a 60-minute session, the device accuracy may differ for a session of shorter or longer duration.

3.5 Conclusion

Objectively measuring therapy dose is essential to understanding and advancing stroke rehabilitation. This study provides preliminary evidence that the Fitbit One may fill the gap of a clinically practical, commercially available, inexpensive device to accurately measure walking steps in individuals post-stroke during inpatient rehabilitation.

Bridging Statement III

As discussed throughout this thesis, the advancement of stroke rehabilitation depends upon identifying the optimal therapeutic parameters (timing, intensity, dose) to maximize recovery. Chapter 4 describes the protocol for the first stroke rehabilitation randomized clinical trial designed to systematically investigate the efficacy of higher exercise intensity and dose on walking recovery, function, cognition and quality of life early after stroke. The protocol uses the technology validated in Chapter 2 and 3, an ankle-positioned accelerometer, to enable the clinician to progress the walking intensity within the therapeutic intervention session.

A version of Chapter 4 has been accepted for publication in the International Journal of Stroke:

Klassen TD, Dukelow SP, Bayley MT, Benavente O, Hill MD, Krassioukov A, Liu-Ambrose T, Pooyania S, Poulin MJ, Yao J, Eng JJ. Determining Optimal post-Stroke Exercise (DOSE): Study Protocol for a Randomized Controlled Trial Investigating Therapeutic Intensity and Dose on Functional Recovery During Stroke Inpatient Rehabilitation.

Chapter 4: Determining Optimal post-Stroke Exercise (DOSE): Study Protocol for a Randomized Controlled Trial Investigating Therapeutic Intensity and Dose on Functional Recovery During Stroke Inpatient Rehabilitation

4.1 Introduction

A top research priority is determining the optimal timing, intensity, and dose of rehabilitation interventions in order to enhance stroke recovery (Veerbeek et al. 2014). Contrary to expectations (Lohse et al. 2014), recent clinical trials have shown that increasing the therapy dose in both the acute and chronic stages post-stroke, had either adverse effects, or no effects, on the functional outcome (AVERT Trial Collaboration Group 2015; Lang et al. 2016). It is possible that the timing of therapy in these studies influenced the results; data from stroke-induced animal models demonstrate that an optimal therapeutic window for intensive task-specific rehabilitation may exist between the acute and chronic stage post-stroke (Biernaskie et al. 2004).

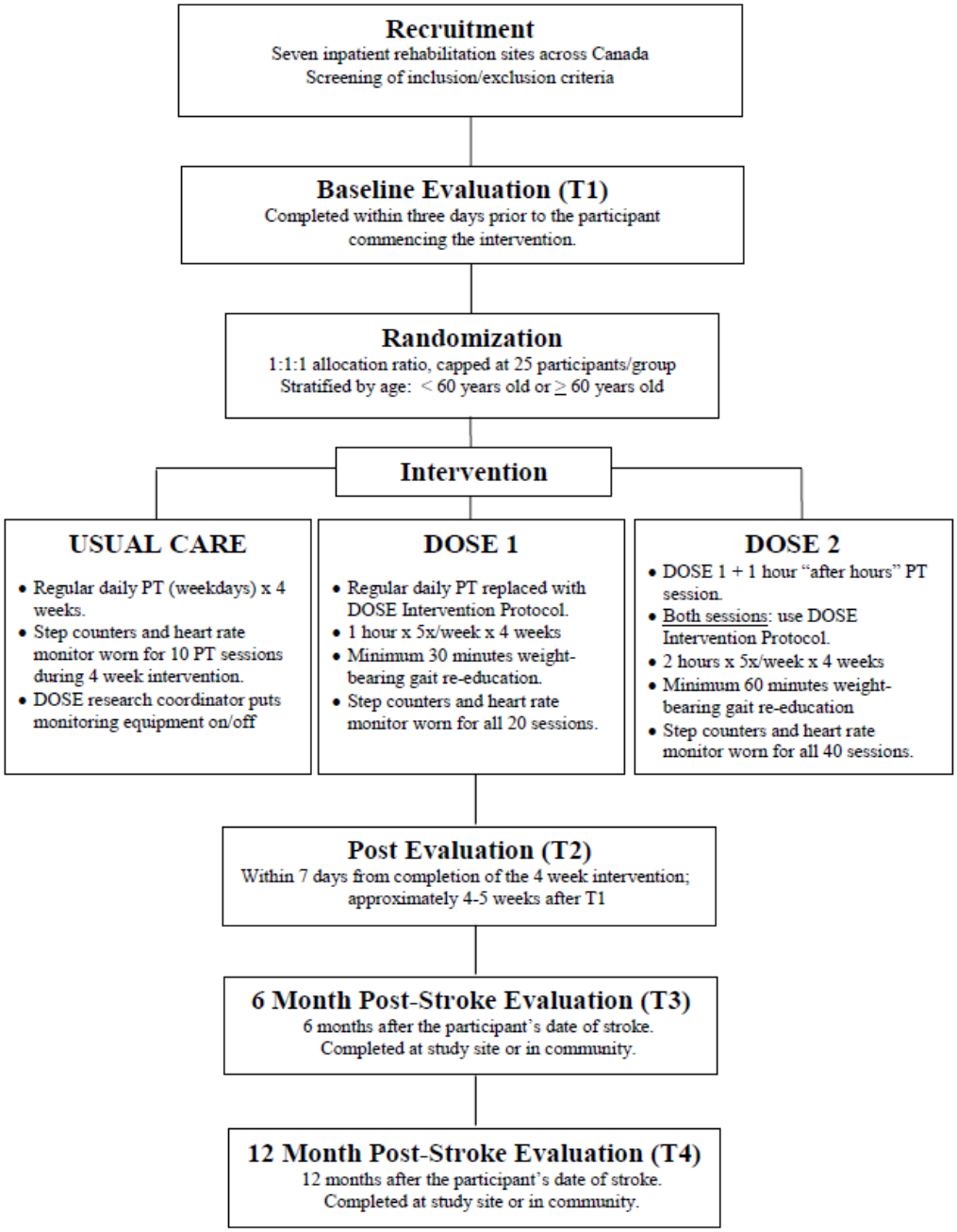
Here, we present a study designed to systematically investigate whether varying doses of a higher intensity, task-specific walking related intervention, measured and manipulated by wearable sensor instrumentation, and delivered in the early stage post-stroke (after acute care), can improve walking recovery, and secondarily, impact physical function, cognition, and overall well-being.

4.2 Methods

4.2.1 Trial Design

This multi-site, national clinical trial will use a randomized, controlled, open-label, parallel, single-blind (evaluators), 3-arm design. Figure 1 provides an overview of the study procedures.

Figure 4.1 Overview of study procedures



4.2.2 **Patient Population**

Consecutive patient admissions to one of seven inpatient rehabilitation study sites, with a diagnosis of stroke, will be screened for study eligibility. Inclusion criteria are: within 10 weeks post-stroke with lower extremity hemiparesis; pre-stroke disability <2 on the Modified Rankin Scale; ability to ambulate ≧5 meters with up to one person maximum assist and assistive/orthotic device as required; over-ground walking speed <1.0m/s; able to understand and follow directions; greater than 18 years of age; and successful completion of a graded exercise stress test. Individuals will be excluded from the study if they: have a pre-stroke health condition that includes a gait disorder, neurological condition (e.g. Multiple Sclerosis), serious medical or painful condition (e.g. active cancer or chronic pain); or participation in an experimental drug or exercise rehabilitation study.

4.2.3 **Randomization**

Participants will be randomized on a 1:1:1 ratio, stratified by age (<60 or ≧60), and capped at a maximum of 25 patients/group using an internet-based dynamic allocation randomization. Allocation will be fully concealed using the web-based platform as it will be generated in real-time.

4.2.4 **Intervention**

It is expected that all participants will complete the intervention portion of the study (4-week duration), along with the baseline and post-evaluations, while admitted on the inpatient rehabilitation unit. If a participant is discharged from the inpatient unit prior to completing all intervention sessions, then all attempts will be made to bring the participant back to the facility daily, as an outpatient, so the remaining intervention session(s) and the post-evaluation can be completed. If it is not possible for the participant to return daily as an outpatient, then the post-

evaluation will be completed at time of discharge from the inpatient rehabilitation unit. The total number of completed intervention sessions for each participant will be recorded.

Control Intervention (Usual Care)

Participants randomized to the control intervention will receive usual care, inpatient physical therapy for four weeks, which typically progresses upper and lower limb functional exercises as tolerated. The physical therapist(s) treating control participants will have no information on the study protocol. During ten of the physical therapy sessions, the study coordinator will place monitoring equipment on the participant, but will not disclose any of the monitoring information to the participant or treating therapist. The study coordinator will advise the treating physical therapist to provide the participant's usual physical therapy care, using the available equipment in a standard stroke rehabilitation setting (e.g., parallel bars, overhead harness, treadmill+/- support harness), when the participant is wearing the monitoring devices. The equipment will measure exertion (Alpha Mio heart rate monitor wrist watch, MioGlobal, Vancouver, BC) and stepping repetitions (Fitbit One, Fitbit Inc, San Francisco, CA; StepWatch^{TM} Activity Monitor (SAM), modushealth, Washington, DC).

Experimental Interventions (DOSE1 or DOSE2)

Some physical therapists on the inpatient rehabilitation team will be trained to deliver the DOSE1 intervention and the first session of the DOSE2 intervention. These same physical therapists will also be approached to deliver the second DOSE2 intervention, which occurs outside of the regularly scheduled inpatient rehabilitation therapies, most commonly from 4-5pm daily. As the second DOSE2 intervention takes place after standard work hours, therapists from the health authority or community will also be approached, and trained, to deliver the second DOSE2 intervention. DOSE therapists will not treat control participants.

Therapists participating in the DOSE study will all complete an intervention training program prior to treating their first participant. The training program will be approximately 4 hours in duration and will consist of both written materials and "hands-on" practical training. The written manual will provide the therapist with the specific details of the intervention protocol, including methods of progression, recording of data, and instructions on how to use the monitoring devices. Therapists will receive ongoing support during the intervention from their site coordinator, and the site coordinator will check-in with the therapist on a minimum weekly basis to assess how the therapist is adhering to the intervention protocol guidelines.

DOSE1

Participants randomized to the DOSE1 intervention will have their standard inpatient physical therapy session replaced by the experimental intervention program for a total of 20 sessions (1 hour/day, 5 days/week, for 4 weeks). The intervention protocol will focus on the completion of a minimum of 30 minutes of weight-bearing, walking-related activities that will progressively increase in intensity (heart rate and step count) over the four-week intervention period using the available equipment in a standard stroke rehabilitation setting (e.g., parallel bars, overhead harness, treadmill+/- support harness). The remaining time in the 60-minute therapy session will be allocated to other physical therapy activities specific to the participant's recovery (e.g. upper extremity exercises, home exercise program). Participants will wear the same monitoring equipment as the control group, but they will be worn in all 20 intervention sessions. The physical therapist will use the data collected from the Fitbit One and heart rate monitor to provide feedback to the participant and to progress the intervention over the 4-week period (Figure 4.2).

DOSE2

Participants randomized to the DOSE2 intervention group will have their standard inpatient physical therapy session replaced by the exact same procedures that the DOSE1 group receives. In addition, the DOSE2 group will also receive an extra, one hour exercise session, 5 days/week, for 4 weeks, that will occur outside of the standard rehabilitation day (i.e., from 4-5pm daily). The content of the second daily exercise session will be similar to the DOSE1 protocol, in that it will contain a minimum of 30 minutes of weight-bearing walking related activities and the remaining time will be dedicated to weight-bearing lower extremity exercises (e.g., strengthening, balance exercises).

Figure 4.2 Progression of DOSE1 and DOSE2 Interventions

<table>
<tr><th>Exercise Domain</th><th>Baseline Training Parameters</th><th>Methods to Modify Intensity</th><th>Re-assessment</th><th>Measures to Monitor Intensity</th></tr>
<tr><td rowspan="3">Weight Bearing Gait Related Activities

<u>Monitoring Equipment:</u>
 
Alpha Mio
 
Fitbit One
 
SAM</td><td>Start with <u>≥</u>40% HRR (RPE <u>≥</u>4) and progress to >60% HRR (RPE <u>≥</u> 6) by the end of the 4th week</td><td>Increase walking distance
Increase walking time
Increase walking speed
Decrease rests
Decrease therapist/external assistance (harness/bungee/ walking aid)</td><td>Weekly</td><td>Continuous HR monitor
RPE (Borg 1-10 Scale)
Amount of therapist assistance
Amount of BWS (if approp.)
Speed of treadmill
Number of rest breaks
Number of repetitions/sets
Number of steps
Minutes in HR training zone</td></tr>
<tr><td colspan="4"><u>GOAL:</u> The initial therapy session starts with a goal of achieving 2000 steps over the 60 minute therapy session, with a minimum of 30 minutes of gait-related activity. The HR monitor will provide feedback on the time spent <u>≥</u>40% HRR within the gait-related activity time. From the heart rate monitor and Fitbit step data, the therapist will gradually progress the intervention over the 4 weeks, manipulating both the HR and step intensity. The <u>ultimate</u> goal is that by the end of the 4 week intervention, the participant is doing a minimum of 30 minutes of continuous weight bearing gait related activities at <u>≥</u>60%HRR with >2000 steps/therapy session. This goal can be achieved in numerous ways, including the manipulation of exercise and rest time during walking intervals. An example of HR intensity progression is shown below.
<table>
<tr><th>Week</th><th>%HRR</th><th>Total Minutes</th><th>Minutes of Exercise</th><th>Minutes of Rest</th><th>Reps</th></tr>
<tr><td>1</td><td>40</td><td>30</td><td>5</td><td>2</td><td>~4</td></tr>
<tr><td>2</td><td>45</td><td>30</td><td>5</td><td>2</td><td>~4</td></tr>
<tr><td>3</td><td>50</td><td>30</td><td>6</td><td>2</td><td>~4</td></tr>
<tr><td>4</td><td>60</td><td>30</td><td>6</td><td>2</td><td>~5</td></tr>
<tr><td>Progression</td><td>Increase or maintain</td><td>Increase or maintain</td><td>Increase or maintain</td><td>Decrease or maintain</td><td>Decrease or maintain</td></tr>
</table>
**Try to manipulate one variable at a time. With that manipulation, other variables may change.*</td></tr>
<tr><td rowspan="2">Strengthening / Activation Activities</td><td>Start with 8-10 RM, complete 2-3 sets.</td><td>Increase resistance
Increase repetitions from 8 to 10
Increase sets from 2-3
Increase/decrease therapist assistance
Modify environment</td><td>Weekly</td><td>Amount of resistance
Number of repetitions
Number of sets
RPE (Borg 1-10 Scale)
Amount of therapist assistance
Change in environment</td></tr>
<tr><td colspan="4"><u>GOAL:</u> Participant will progressively increase in strength training exercise intensity over the 4 week training duration through modifications of resistance and/or repetitions and/or therapist assistance.</td></tr>
<tr><td rowspan="2">Functional Training / Balance Activities</td><td>Start with 8-10 RM, complete 2-3 sets.
Start with 40-60% of HRR (RPE of 4-6)
Start with the minimum amount of therapist assistance to promote optimal movement pattern with activity</td><td>Increase resistance
Increase sets from 2-3
Increase intensity: aiming for >60% of HRR or RPE <u>≥</u> 6
Decrease therapist /external assistance with activity
Increase interval/decrease rest time
Modify environment</td><td>Weekly</td><td>Continuous HR monitors
RPE (Borg 1-10 scale)
Amount of therapist assistance
Number of repetitions
Number of rest breaks
Change in environment</td></tr>
<tr><td colspan="4"><u>GOAL:</u> Participant will progressively increase in intensity in the functional training exercises over the 4 week training duration through modifications of resistance and/or repetitions and/or therapist assistance, and/or aerobic intensity</td></tr>
</table>

4.2.5 **Outcome Measures**

Baseline descriptive measures will include: age, sex, date and type of stroke, and stroke severity. Trained and blinded study evaluators will conduct the outcome measures at four time points. Table 4.1 provides an overview of the assessment measures for each evaluation.

Table 4.1 Overview of Study Outcome Measures

Measure	Domain	Baseline Evaluation (T1)	Post-Evaluation (T2)	6 Month Evaluation (T3)	12 Month Evaluation (T4)
Primary Outcome Measure					
6 minute walk[1]	Function	✓	✓	✓	✓
Secondary Outcome Measures					
Isometric Knee Extension[2]	Impairment	✓	✓	✓	✓
5 meter walk[3]	Function	✓	✓	✓	✓
Functional Ambulation Classification[4]		✓	✓	✓	✓
Berg Balance Scale[5]		✓	✓	✓	✓
StepWatch™ Activity Monitor[6]				✓	✓
Mean step count and heart rate		Collected from 10 intervention sessions (Sessions 6-15)			
EQ-5D-5L[7]	Quality of Life	✓	✓	✓	✓
Patient Health Questionnaire-9[8]		✓	✓	✓	✓
Montreal Cognitive Assessment[9]	Cognition	✓	✓	✓	✓
Trails A+B[10]		✓	✓	✓	✓
Digit Symbol Substitution Test[11]		✓	✓	✓	✓

[1]Fulk et al. 2008; [2]Bohannon et al. 2012; [3]Salbach et al. 2001; [4]Mehrholz et al. 2007; [5]Blum and Korner-Bitensky 2008; [6]Mudge et al. 2007; [7]Golicki et al. 2015; [8]Williams et al. 2005; [9]Toglia et al. 2011; [10]Tamez et al. 2011; [11]Zinn et al. 2007

Primary Outcome Measure

The primary outcome measure is the 6-minute walk test measured at the post-evaluation. The 6-minute walk test is an established valid and reliable measure for assessing walking recovery early after stroke (Fulk et al. 2008).

Secondary Outcome Measures

The secondary outcome measures will assess stroke impairment, functional independence, quality of life, and cognition.

4.2.6 **Sample Size Estimates**

Based on the assumption that participants in the experimental groups (DOSE1 and DOSE2) will cover at least 50m more in the 6-minute walk (175m total), compared to the control group (125m) at the post-evaluation (Perera et al. 2006; Barak et al. 2014), we calculated that a total sample of 75 participants is required (25/group) to detect a clinically relevant effect size of 40%, with 85% power, at 0.05 alpha, and adjusted for an attrition rate of 15%.

4.2.7 **Statistical Analyses**

An intention-to-treat analysis will be used for all participants randomized to an intervention group. Missing data will be assessed and analyzed as appropriate.

Primary and Secondary Outcomes (all continuous variables)

An analysis of co-variance (ANCOVA) will be conducted to detect group differences (Usual Care, DOSE1 and DOSE2) in the primary outcome measure (6-minute walk test) using the baseline 6-minute walk test as the co-variate. The secondary measures will also utilize ANCOVA analyses. The significance level will be set at 0.05 and all statistical tests will be two-tailed.

4.2.8 **Safety and Adverse Event Monitoring**

Participant safety, during the duration of the study, will be of the utmost concern. Therefore, all sites will report minor and serious adverse events that occur from the baseline evaluation through to the 12-month follow-up evaluation. A Data Safety Monitoring Board will receive reports outlining adverse events and study enrollment three times a year.

4.3 Discussion and Summary

As this study design systemically manipulates exercise intensity and dose, at a critical time period of neurological recovery post-stroke, important knowledge will be acquired with

respect to the active therapy ingredients that influence the recovery of walking. Secondly, the novel use of monitoring equipment during the intervention portion of the study will enable the therapists to monitor and systematically progress each participant's walking intensity, and also provide an overall quantification of walking dose during inpatient rehabilitation. Finally, embedding the research study into clinical stroke rehabilitation units will support the seamless translation of the research findings into clinical practice at the study completion.

Bridging Statement IV

Recruitment for the DOSE study began in March, 2014. Over the course of the next three years, I started seven clinical study sites across the country to recruit the target sample population of 75 participants. As of July 31, 2017, fifty-three participants were recruited for the DOSE study. Taking into account both the lengthy study recruitment period and completion of three manuscripts contributing to my thesis, my supervisory committee supported a preliminary analysis of the DOSE study data collected up to July 31, 2017 to comprise Chapter 5. The data in Chapter 5 will remain confidential until the entire study sample population is recruited and the complete data set is re-analyzed.

Chapter 5: Preliminary Analysis of the Determining Optimal post-Stroke Exercise (DOSE) Randomized Clinical Trial

5.1 Introduction

As thoroughly described in the previous chapters, it is essential to determine the appropriate timing and critical therapeutic components of stroke rehabilitation to maximize recovery for millions of stroke survivors worldwide.

The culmination of years of research from both the stroke animal and human models suggests that a critical time period may exist, between about two weeks to 3-months post-stroke, when neural recovery is at its peak (Jorgensen et al. 1995b; Biernaskie et al. 2004; Teasell et al. 2015). Understanding how therapeutic intensity and dose interacts with this period of maximal neural recovery is paramount to optimizing recovery in individuals post-stroke. The Determining Optimal post-Stroke Exercise (DOSE) study is a randomized clinical trial specifically designed to address this important knowledge gap.

The DOSE study enrolled its first participant in March, 2014 and is still ongoing, with a target goal of 75 participants. This chapter describes the preliminary findings from an interim data analysis conducted on fifty-three participants recruited between March, 2014 – July, 2017. The analysis is comprised of data collected from both the participants' interventions and outcome evaluations. Although the DOSE study now includes seven sites across Canada, only data from six sites is included in this analysis as the seventh site did not start recruitment until September, 2017.

5.2 Methods

5.2.1 Trial Design and Oversight

The study protocol and design for this ongoing phase II, national, multi-site, randomized controlled trial has been outlined in Chapter 4. The study protocol was reported using the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines (Chan et al. 2013). In brief, this study uses an open-label, parallel, single-blind (evaluators), 3-arm design. Ethics approval was obtained from the academic and health authority institutional review boards for each study site, and every enrolled study participant provided written informed consent.

With respect to monitoring participant safety and study enrollment, a Data Safety and Monitoring Board was created at the onset of the study and reports were sent to them three times/year outlining adverse events and participant recruitment.

5.2.2 Participants, Screening and Randomization

Consecutive patient admissions into each of the six study inpatient rehabilitation units (British Columbia: G.F. Strong Rehabilitation Centre, Holy Family Hospital, Laurel Place; Alberta: Carewest Dr. Vernon Fanning Centre, Foothills Medical Centre; Ontario: Toronto Rehabilitation Institute) with a diagnosis of stroke, between March 1, 2014 - July 1, 2017, were screened for study eligibility. Inclusion criteria included: within 10-weeks post-stroke with lower extremity hemiparesis; pre-stroke disability <2 on the Modified Rankin Scale; ability to ambulate ≥5 meters with up to one person maximum assist and assistive/orthotic device as required; over-ground walking speed <1.0m/s; able to understand and follow directions; greater than 18 years of age; and successful completion of a graded exercise stress test. Individuals were

excluded from the study if they: had a pre-stroke health condition that included a gait disorder, neurological condition (e.g. Multiple Sclerosis), serious medical or painful condition (e.g. active cancer or chronic pain); were already enrolled in an experimental drug or exercise rehabilitation study.

Individuals that met the inclusion criteria and consented to participate then proceeded to the baseline evaluation. After the baseline evaluation, participants were randomized to an intervention group on a 1:1:1 ratio and stratified by age (<60 or ≥60), using a fully concealed internet-based dynamic allocation randomization that was generated in real-time.

5.2.3 **Outcome Measures**

The outcome evaluations, assessing the primary and secondary outcome measures, were conducted by trained and blinded study evaluators at four time points: baseline, post-evaluation (approximately 5 weeks after the baseline evaluation), 6-months post-stroke, and 12-months post-stroke. Descriptive participant characteristics, including age, sex, date and type of stroke, and stroke severity were also collected at the baseline evaluation. Each evaluation took approximately 60-90 minutes to complete. All outcome measure assessment forms are in Appendix C. As the outcome measures were only listed in the DOSE study protocol paper (Chapter 4), they are more fully described here.

5.2.3.1 Primary Outcome Measure

The six-minute walk test, a valid and reliable measure to assess walking recovery early after stroke was measured at the post-evaluation (Fulk et al. 2008). During the assessment, the evaluation therapist instructed the participant, from a standardized protocol, to cover as much distance as possible walking on a 38m indoor oval track (or at least 30m straight path) with their customary walking/orthotic devices. If necessary, the minimum amount of external physical

assistance was provided to the participant to maintain personal safety (up to 1 person maximum assist). The total distance covered (in meters) during the six-minute walk was used for the primary analysis.

5.2.3.2 Secondary Outcome Measures

The majority of the secondary outcome measures were assessed at all four time points, and included assessments of stroke impairment, function, quality of life, and cognition. The StepWatch™ Activity Monitor was only used at the 6 and 12 month evaluations and assessed the participant's daily walking activity within their home and community. The measures of intensity from the therapeutic intervention sessions (step count and heart rate) were also included as a secondary outcome.

Intervention Therapeutic Intensity

Step Count: A Fitbit One monitor (Fitbit Inc, San Francisco, CA) was attached to a Velcro band and placed around each participant's non-paretic ankle (above the lateral malleolus) and recorded the number of walking steps for the duration of the intervention session. Participants in the study intervention groups (DOSE1 and DOSE2) wore the Fitbit One for all study intervention sessions. Individuals in the Usual Care group wore the Fitbit One for the middle 10 sessions (sessions 6-15). For the statistical analysis, the data from intervention sessions 6-15 was used for all study groups.

Time spent at ≥40% heart rate reserve (HRR): An Alpha Mio heart rate monitor wrist watch (MioGlobal, Vancouver, BC) was used to measure cardiac exertion and collected the amount of time during the intervention session that each participant spent equal to or above their 40% HRR. Each participant's 40% HRR was calculated based on the heart rate values obtained from their study stress test at baseline, and this data was set in the participant's own personalized

intervention heart rate watch. At the beginning of the intervention session, the watch was placed on the participant's wrist and the timer started. The timer was then stopped at the completion of the intervention session and the time spent ≥ 40% HRR was displayed on the watch and recorded on the intervention data sheet. Participants in the study intervention groups (DOSE1 and DOSE2) wore the heart rate monitor watch for all study intervention sessions, while individuals in the Usual Care group wore the watch for the middle 10 sessions (sessions 6-15) only. For the statistical analysis, the data from intervention sessions 6-15 was used for all study groups.

Stroke Impairment

Isometric knee extension: Using a standardized procedure, the participant's bilateral lower extremity strength (maximal isometric quadriceps contraction) was measured using a handheld dynamometer. This assessment has been demonstrated to be a reliable measure to assess lower extremity strength in individuals post-stroke (Bohannon, 1997). A total of 3 repetitions were conducted on each lower extremity, and the average score of the paretic lower extremity (N/kg) was used.

Function

5-meter walk (5mWT): The 5mWT is a recommended measure to assess walking disability in the first five weeks post-stroke (Salbach et al. 2001). The 5mWT was assessed by having the participant walk a distance of 9 meters at a comfortable pace, but only the time it took for the participant to walk the middle 5-meter distance was recorded by the evaluation therapist. The participant used their preferred customary walking/orthotic devices and external physical assistance was provided, if necessary, to maintain personal safety (up to 1 person maximum assist). The participant completed the walking distance two times, and an average time for the 5-

meter distance was calculated. The participant's walking velocity over the 5 meters was calculated using the following equation: (5 meters)/ (average time to walk 5 meters) (in seconds).

Functional Ambulation Classification (FAC): The FAC is a 6-point scale that assesses walking independence (Holden et al, 1984). This measure was used during the 6-minute walk test and 5-meter walk evaluations to score the participant's walking independence.

Berg Balance Scale (BBS): The BBS is a valid and reliable measure of balance in the post-stroke population (Blum and Korner-Bitensky 2008). It includes 14 items, which progressively increase in balance difficulty, and each item is rated on a 4-point scale. During the evaluation, the participant was not permitted to use an assistive device, but wore their customary orthotic device if needed. The evaluation therapist only provided manual assistance to the participant during the assessment to ensure safety. The maximum score that can be obtained on this assessment is 56. A higher score demonstrates less balance impairment.

Quality of Life:

EQ-5D-5L: The EQ-5D-5L is one of the most widely used general health status questionnaires in individuals post-stroke, and has been validated in acute stroke (Golicki et al. 2015). The questionnaire assesses the participant's personal evaluation of their health across 5 domains (mobility, self-care, usual activities, pain, anxiety/depression) and also includes a health value score (/100). For the health value score, the participants evaluate their own health on a visual scale from 0 – 100, with 0 being "the worst health you can imagine" and 100 being "the best health you can imagine". The evaluation therapist explained the questionnaire to the participant and the participant completed it independently. The participant's health value score (/100) was used.

Patient Health Questionnaire (PHQ)-9: The PHQ-9 is a self-report questionnaire that has been used with individuals post-stroke to assess depression (Williams et al. 2005). The questionnaire includes 9 items that are rated on a scale of 0 (no daily effect) to 3 (significant effect daily), and a final tenth item that is reported on a 4-point scale. The evaluation therapist explained the questionnaire to the participant and the participant independently completed it. The participant's total score on the 9 items (/27) was used.

Cognition:

Montreal Cognitive Assessment (MoCA): The MoCA screening instrument (Version 1) was used to evaluate cognitive impairment and has been validated in the inpatient rehabilitation setting with individuals post-stroke (Toglia et al. 2011). It assesses several cognitive domains: attention and concentration, executive function, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. The assessment is scored out of a total of 30 points; 26 points and above is considered normal (Nasreddine et al. 2005).

Trail Making Test (Trails A+B): The Trail Making Test was used to assess executive cognitive function, particularly visual scanning and letter/number recognition. This measure has been used with stroke survivors, including those in the early phase post-stroke (Tamez et al. 2011). A maximum of 8 minutes was provided to complete both tests (Hashimoto et al. 2006). For both the Trails A + B, a rate of generation score (total numeric completed responses/total time to complete responses (in seconds)) was calculated. A higher rate of generation score suggests better cognitive function.

Digit Symbol Substitution Test (DSST): The DSST was used to assess cognitive function, specifically working memory, visuospatial processing, and attention. The DSST has been used in the acute stroke population to assess executive cognitive function (Zinn et al. 2007). All

participants were given one minute to complete as many symbols as possible. A total score was calculated (correct responses – errors).

5.2.4 Study Intervention Protocols

Participants in the study were randomized to one of three intervention groups: Usual Care, DOSE1 or DOSE2. Front-line physical therapists were responsible for treating participants in the study. Within a clinical physical therapy team, only 1-2 therapists were trained to deliver the study intervention (DOSE1 and DOSE2) and participated in a 4-hour workshop to learn the study protocols. The other physical therapists on the team did not learn the study protocol, and were therefore responsible for treating the participants randomized to the Usual Care group. When staff turnover occurred, the ratio of study intervention therapists (DOSE1/DOSE2) to Usual Care therapists was re-assessed, and more study intervention therapists were trained if necessary.

5.2.4.1 Usual Care

Participants randomized to the control intervention received usual care, inpatient physical therapy for four weeks, which typically progressed upper and lower limb functional exercises as tolerated. During ten of the physical therapy sessions (sessions 6-15), the monitoring equipment (Alpha Mio heart rate monitor wrist watch, Fitbit One, and StepWatch^{TM} Activity Monitor (SAM), was placed on the participant at the beginning of the physical therapy session and removed at the end of the physical therapy session. The physical therapist was asked to continue the participant's usual physical therapy care during these ten monitored sessions, using the available equipment within the stroke rehabilitation unit. Data obtained from the monitoring equipment was not disclosed to the participant or treating therapist.

5.2.4.2 DOSE1

Participants randomized to the DOSE1 intervention had their standard inpatient physical therapy session replaced by the experimental intervention program for a total of 20 sessions (1 hour/day, 5 days/week, for 4 weeks). The intervention time was designed to match what was typically delivered during inpatient physical therapy (Usual Care). The intervention protocol focused on the completion of a minimum of 30 minutes of weight-bearing, walking-related activities that progressively increased in intensity (heart rate and step count) over the four-week intervention period using the same therapy equipment that was available to the control group. The remaining time in the 60-minute therapy session was dedicated to other physical therapy activities specific to the participant's recovery (e.g. upper extremity exercises, home exercise program). Participants wore the same monitoring equipment as the control group, but all 20 intervention sessions were monitored. Data collected from the Fitbit One and heart rate monitor was used by the physical therapist to provide feedback to the participant and to progress the intervention over the 4-week period.

5.2.4.3 DOSE2

Participants randomized to the DOSE2 intervention group had their standard inpatient physical therapy session replaced by the exact same protocol that the DOSE1 group received (described above). In addition, the DOSE2 group also received an extra, one hour exercise session, 5 days/week, for 4 weeks, that occurred outside of the standard rehabilitation day (i.e., typically from 4-5pm daily). The content of the second daily exercise session was similar to the DOSE1 protocol, in that it contained a minimum of 30 minutes of weight-bearing walking related activities, but the remaining time within the hour session was dedicated to weight-bearing

lower extremity exercises (e.g., strengthening, balance exercises). The monitoring equipment was worn for all 40 intervention sessions.

5.2.4.4 Progression of DOSE1 and DOSE2 Intervention Protocols

As mentioned in Chapter 4, the intervention protocols for both the DOSE1 and DOSE2 groups were designed to achieve the following goals within a 60-minute intervention session: i) complete a minimum of 30 minutes at an intensity $\geq$ 40% HRR, gradually progressing to >60% HRR by the end of the four weeks; ii) achieve greater than 2000 walking steps. Depending on each participant's initial functional level, client-centered goals incorporating the intervention protocol parameters were created by the therapist and participant at the onset of the intervention, and gradually progressed throughout the four-week duration.

5.2.5 Statistical Analyses

Participants enrolled from March 1, 2014 - July 31, 2017 were included in this preliminary data analyses. We analyzed the baseline and post-evaluation, but not the 6 and 12-months post-stroke evaluations as there was not sufficient data to date. In addition, the intensity (step count and heart rate) of the physical therapy sessions was analyzed.

Based on previous literature, we hypothesized that participants in the experimental groups (DOSE1 and DOSE2) would cover at least 50m more in the 6-minute walk (175m total), compared to the control group (125m) at the post-evaluation (Perera et al. 2006; Barak et al. 2014). It was calculated that a sample size of 75 participants (25/group) was required to detect a clinically relevant effect size of 40%, with 85% power, at 0.05 alpha, and adjusted for an attrition rate of 15%.

Demographics and baseline characteristics were summarized by treatment group using percentage and frequencies, or mean, median, standard deviation and range as appropriate. The distribution of all variables was visually and statistically assessed for normality.

An intention-to-treat analysis was used for all participants randomized to an intervention group. The difference across treatment arms in the primary outcome, distance covered in the 6-minute walk test at post-evaluation, was examined using an ANCOVA model with the baseline 6-minute walk test results as the co-variate. All model assumptions were tested (Vickers 2005; Feng et al. 2014). For the purpose of this analysis, an outlier was defined as a standardized residual greater than +/- 3 standard deviations. If an outlier existed, then a sensitivity analysis was performed with the outlying data removed.

An ANCOVA, using the baseline 6MWT as a co-variate, was used to analyze the following secondary measures collected at the post evaluation: paretic lower extremity strength, 5-meter walk, FAC (5-meter walk), Berg Balance Scale, EQ-5D-5L, PHQ-9, MoCA, Trails A, Trails B, and DSST. The intervention data (heart rate intensity and step count) was analyzed using an ANOVA.

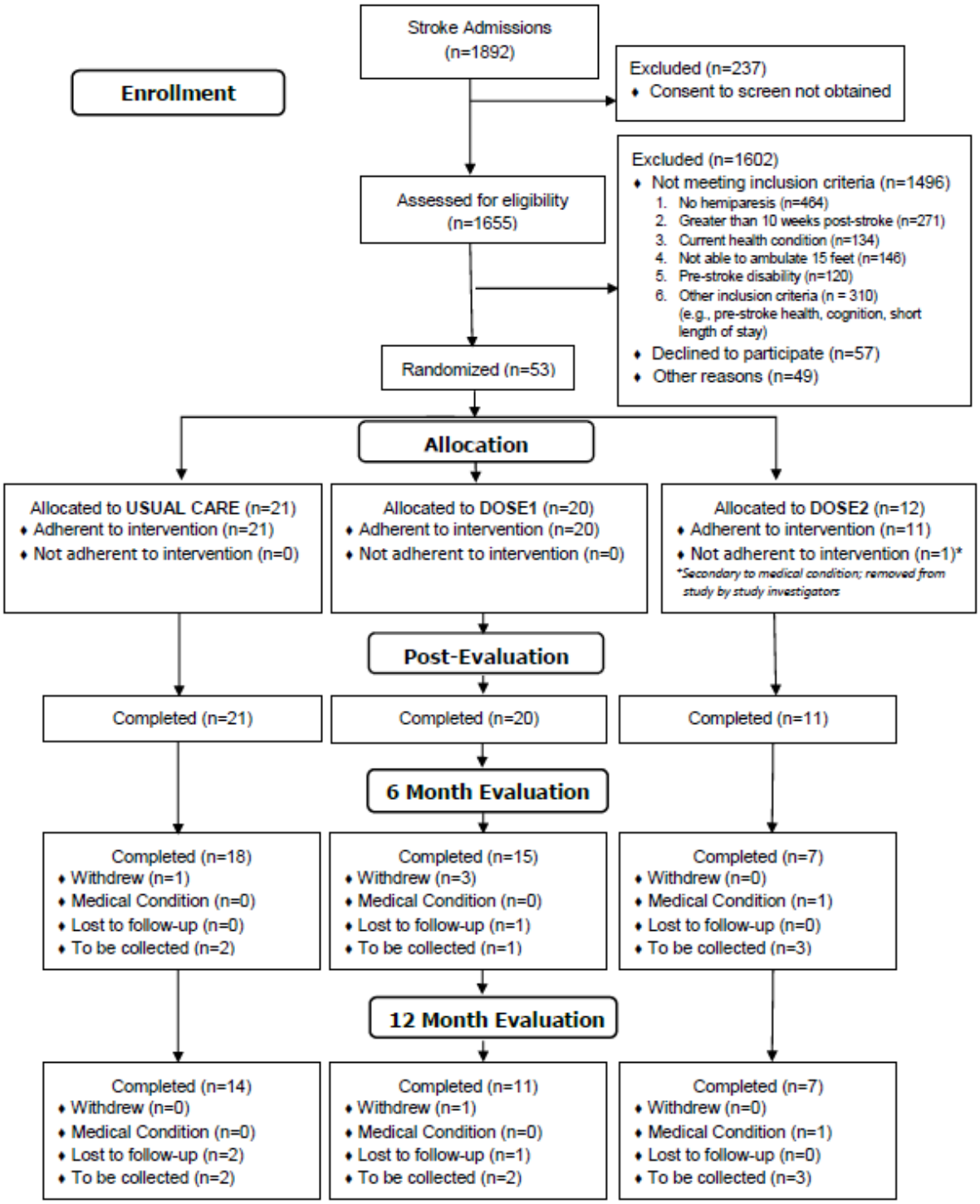
For all analyses, the significance level was set at 0.05 and all statistical tests were two-tailed. If there was a significant main effect across the three treatment arms, then post-hoc analysis using Tukey's test was completed to account for multiple comparisons. SPSS (Version 24) and R was used to conduct the analyses.

5.3 Results

Between March, 2014 - July, 2017, 1892 patients were admitted to one of the participating study sites, of which 1655 of them were assessed for study eligibility. 1496 patients did not meet the study inclusion criteria. The three most frequent reasons for exclusion

upon patient interview/chart screening was that the participant: did not have hemiparesis (n=464); had a stroke that occurred greater than 10 weeks prior to being admitted to inpatient rehabilitation (n=271); was not able to ambulate 15 feet (n=146). Fifty-three participants were recruited to the study and randomized to Usual Care (n=21), DOSE1 (n=20), or DOSE2 (n=12). All enrolled participants completed the post-evaluation, except one participant that had a cardiac episode during the intervention and was removed from the study by the study investigators. This participant received cardiology follow-up over the course of a month and no cardiac concerns were identified. Please see Figure 5.1 on the next page for participant recruitment and flow through the study from March, 2014 – July, 2017.

Figure 5.1 Participant Recruitment and Flow in the DOSE Study from March, 2014 – July, 2017



Descriptive characteristics for the fifty-three participants can be observed in Table 5.1 below. At the baseline evaluation, there were similarities across all groups with respect to mean age, time from stroke to study randomization, and 5-meter walking velocity (de Boer et al. 2015). For all of the fifty-three participants, the mean age was 56(12), 40% were female, and 48 had an ischemic stroke. Furthermore, participants, on average, were randomized to an intervention group within 4-weeks post-stroke, and their baseline 5-meter walking velocity was 0.42m/s. These baseline characteristics are very similar to other walking rehabilitation trials conducted during inpatient stroke rehabilitation (MacKay-Lyons et al. 2013).

Table 5.1 Demographic and Baseline Clinical Characteristics of the Study Participants

	ALL GROUPS (n=53)	**USUAL CARE (n=21)**	**DOSE1 (n=20)**	**DOSE2 (n=12)**
Age (yrs) - Mean ± SD (range)	56±12 (27-76)	56±14 (32-76)	55±12 (27-73)	58±7 (40-68)
Male sex – n (%)	32 (60)	13 (62)	13 (65)	6 (50)
Time from stroke to randomization (days) Mean ± SD (range)	27±11 (6-58)	26±11 (6-43)	28±11 (16-58)	26±10 (11-40)
Side of hemiparesis	L=29; R=24	L=13; R=8	L=8; R=12	L=8; R=4
Dominant side	L=0; R=53	L=0, R=21	L=0; R=20	L=0, R=12
Type of Stroke	Ischemic=48 Hemorrhagic=5	Ischemic=20 Hemorrhagic=1	Ischemic=17 Hemorrhagic=3	Ischemic=11 Hemorrhagic=1
Stroke Location	Cortical=13 Sub-Cortical=35 Unknown=5	Cortical=7 Sub-Cortical=11 Unknown=3	Cortical=2 Sub-Cortical=17 Unknown=1	Cortical=4 Sub-Cortical=7 Unknown=1
Baseline 5m walk (m/s) Mean ± SD (range)	0.42±0.22 (0.07-1.08)	0.39±0.21 (0.07-0.86)	0.45±0.25 (0.15-1.08)	0.43±0.20 (0.17-0.88)
NIH Stroke Scale (/42) Mean ± SD (range)	5±3 (0-11)	5±3 (1-11)	4±3 (0-10)	5±2 (0-8)

*One-way ANOVA or Kruskal-Wallis H test used for continuous data; Chi-square or Fisher's exact test used for categorical data

As stated earlier, the DOSE1 and DOSE2 intervention sessions were designed to be approximately one hour in duration, matching the customary inpatient rehabilitation physical therapy duration. On average, the duration of the intervention sessions was the following: i) Usual Care = 42(11) minutes; ii) DOSE1=52(5) minutes and iii) DOSE2 = 105(11) minutes (50(9) minutes for session 1 and 55(6) minutes for session 2). The secondary outcome intervention intensity data, collected from the step counter and heart rate monitor from the 10 intervention therapy sessions (sessions 6-15 in each intervention group) is displayed in Table 5.2.

A total of 195 sessions from the Usual Care group, 198 sessions from the DOSE1 group, and 219 sessions from the DOSE2 group were analyzed. Within these physical therapy sessions, the Usual Care group spent approximately 26(23)% of the therapy time within an aerobic training zone (≥40% HRR), while the DOSE1 and DOSE2 groups spent 50(17)% or more time of each physical therapy session within an aerobic training zone. Thus, the Usual Care group spent 11(10) minutes per day, DOSE1 group spent 26(10) minutes per day, while the DOSE2 group spent a total of 57(25) minutes over the two sessions/day in an aerobic training zone. Furthermore, the mean step count for individuals in the Usual Care group within the therapy session was 534(370) steps. More than 4-times the number of steps was completed per therapy session by participants in the DOSE1 or DOSE2 groups (2236(1044) and 4932(1278) respectively). Thus, the DOSE2 group completed more than double the steps of the DOSE1 group per day. No serious adverse events occurred for any participants during the intervention sessions.

Using a one-way ANOVA, analysis of the intervention data between the groups demonstrated a significant difference on the two variables measured: total time spent in an aerobic training zone (≥40% HRR) within the therapy session and total steps taken within the

therapy session ($p<0.005$). On post-hoc testing using Tukey test, all three groups (Usual Care and DOSE1, Usual Care and DOSE2, and DOSE1 and DOSE2) were significantly different from one another ($p<0.005$).

Table 5.2 Summary of the Physical Therapy Intervention Data

Values are means (SD) and [95% confidence intervals (CI)]
Medians [interquartile ranges: 25-75%]
All data obtained from intervention sessions 6-15

	USUAL CARE (n=21)		**DOSE1*** (n=20)		**DOSE2*** (n=11)	
	Mean ± SD [95% CI]	Median [25-75%]	Mean ± SD [95% CI]	Median [25-75%]	Mean ± SD [95% CI]	Median [25-75%]
Total time spent above 40% HRR during PT session (minutes)	11±10 [7-15]	11 [2-18]	26±10 [21-31]	27 [20-34]	57±25 [40-74]	58 [45-74]
Total Fitbit step count during PT session	534±370 [365-702]	507 [296-702]	2236±1044 [1747-2724]	2259 [1476-2993]	4932±1278 [4074-5791]	4783 [4051-6221]

* P-value<0.005 when comparing Usual Care to DOSE1, Usual Care to DOSE2 and DOSE1 to DOSE2 with respect to all tested variables within the PT session (total time spent above 40% HRR, and total step count). Analysis conducted using one-way ANOVA with post-hoc Tukey.

The 6-minute walk test was completed by all 53 participants at baseline and 52 participants at post-evaluation (98% completion rate) (Table 5.3). There was no statistically significant difference for the main factor (group) in average distance walked at post-evaluation in the ANCOVA model (adjusted for baseline 6-minute walk test) (Table 5.3). A single outlier was identified in distance walked in the post evaluation (standardized residual of 3.74), and a sensitivity analysis was performed with the outlier removed (Table 5.4). With the outlier removed, a larger difference in mean distance covered on the 6-minute walk between the usual care and the DOSE2 group was observed (control=259m, DOSE1=313m, DOSE2=333m;

p=0.078). As the main effects across the three treatment arms was not significant, post-hoc analysis was not done, but effect sizes are presented demonstrating that the change in the 6-minute walk distance from baseline to post-evaluation for the DOSE1 and DOSE2 groups are 0.4 and 0.7 standard deviations respectively from the mean change in the Usual Care group. Both the DOSE1 and DOSE2 groups exceeded the minimal clinically important difference of 50m (54m and 74m respectively) on the 6-minute walk over the Usual Care group (Perera et al. 2006).

Table 5.3 Primary Outcome Results: 6-Minute Walk Test (6MWT) at Post-Evaluation (m)

Outcome Measure	**Group**	**Participants (N) at baseline/ post-evaluation**	**Baseline Evaluation** Mean (SE) [95% CI]	**Post-Evaluation** Mean (SE) [95% CI]	**p-value***	**Effect size#** [95% CI]
6-Minute Walk (m)	Usual Care	21/21	123 (16) [90-156]	279 (24) [231-328]	0.393	-
	DOSE1	20/20	135 (23) [86-183]	313 (25) [263-362]		0.24 [-0.4-0.9]
	DOSE2	12/11	142 (19) [100-184]	333 (33) [266-400]		0.49 [-0.3-1.2]

*ANCOVA (with baseline 6MWT as co-variate)
#Hedge's effect size relative to Usual Care

Table 5.4 Primary Outcome Results: 6-Minute Walk Test (6MWT) at Post-Evaluation (m) With Outlier Removed

Outcome Measure	**Group**	**Participants (N) at baseline/ post-evaluation**	**Baseline Evaluation** Mean (SE) [95% CI]	**Post-Evaluation** Mean (SE) [95% CI]	**p-value***	**Effect size#** [95% CI]
6-Minute Walk (m)	Usual Care	20/20	122 (17) [87-157]	259 (21) [217–301]	0.078	-
	DOSE1	20/20	135 (23) [86-183]	313 (21) [270–355]		0.44 [-0.2-1.1]
	DOSE2	12/11	142 (19) [100-184]	333 (28) [276-391]		0.73 [0.0-1.5]

*ANCOVA (with baseline 6MWT as co-variate)
#Hedge's effect size relative to Usual Care

For the secondary outcome measures (Table 4), there was no statistically significant difference for the main factor group on the assessed outcomes in ANCOVA models, with the exception of the health value score (/100) on the visual scale from the EQ-5D-5L. Post-hoc tests for the EQ-5D-5L demonstrated a statistically significant difference between the Usual Care and DOSE2 group (control=64, DOSE1=74, DOSE2=80, p=0.01), but not between other pair-wise comparisons. The effect size for the mean change in the DOSE2 group was 0.6 standard deviations from the mean change in the Usual Care group.

Table 5.5 – Secondary Outcome Measure Results

Domain	Outcome Measure	Intervention Group	Participants (N) at baseline/ post-evaluation	Baseline Evaluation Mean (SE) [95% CI]	Post-Evaluation Mean (SE) [95% CI]	p-value*	Effect size# [95% CI]
Impairment	Paretic LE Strength (N/kg)	Usual Care	21/20	15 (3) [10-20]	19 (3) [14-25]	0.846	-
		DOSE1	18/19	12 (2) [7-17]	17 (3) [12-23]		0.09 [-0.5-0.7]
		DOSE2	12/11	16 (4) [8-24]	19 (4) [12-26]		-0.07 [-0.8-0.7]
Function	5-meter walk (m/s)	Usual Care	21/21	0.39 (0.05) [0.29-0.48]	0.81 (0.06) [0.69-0.93]	0.272	-
		DOSE1	20/20	0.45 (0.06) [0.33-0.57]	0.90 (0.06) [0.77-1.02]		0.12 [-0.5-0.7]
		DOSE2	12/11	0.43 (0.06) [0.30-0.56]	0.97 (0.08) [0.81-1.14]		0.53 [-0.2-1.3]
	FAC: 5-meter walk (/6)	Usual Care	21/21	3 (0.2) [3-3]	5 (0.2) [4-5]	0.999	-
		DOSE1	20/20	3 (0.2) [2-3]	5 (0.2) [4-5]		0.00 [-0.6-0.6]
		DOSE2	12/11	3 (0.4) [2-4]	5 (0.3) [4-5]		0.00 [-0.7-0.7]
	Berg Balance Scale (/56)	Usual Care	21/21	32 (3) [26-39]	47 (2) [44-50]	0.210	-
		DOSE1	20/20	34 (3) [28-40]	48 (2) [44-51]		-0.07 [-0.7-0.5]
		DOSE2	12/11	34 (4) [26-42]	51 (2) [47-56]		0.14 [-0.6-0.9]
Quality of Life	EQ-5D-5L (/100)	Usual Care	21/20	52 (6) [40-64]	65 (3) [58-71]	0.017†	-
		DOSE1	20/20	62 (4) [54-70]	74 (3) [68-80]		-0.04 [-0.7-0.6]
		DOSE2	12/11	52 (5) [41-62]	80 (4) [71-88]		0.61 [-0.1-1.4]
	PHQ-9 (/27)	Usual Care	21/20	7 (1) [5-10]	6 (1) [3-8]	0.620	-
		DOSE1	20/20	5 (1) [3-7]	4 (1) [2-6]		0.0 [-0.6-0.6]
		DOSE2	12/11	7 (1) [6-10]	5 (2) [2-8]		0.24 [-0.5-1.0]

*ANCOVA using 6-minute walk distance at baseline as the co-variate.

†Post-hoc Tukey's test = significant difference (0.01) between Usual Care and DOSE2

Domain	Outcome Measure	Intervention Group	Number of participants (N) at baseline/ post-evaluation	Baseline Evaluation Mean (SE) [95% CI]	Post-Evaluation Mean (SE) [95% CI]	p-value*	Effect size# [95% CI]
Cognition	MoCA (/30)	Usual Care	21/20	24 (1) [21-26]	25 (1) [23-27]	0.713	-
		DOSE1	20/20	23 (2) [20-26]	25 (1) [23-27]		0.14 [-0.5-0.8]
		DOSE2	12/11	24 (1) [22-27]	26 (1) [23-29]		0.24 [-0.5-1.0]
	Trails A‡	Usual Care	21/20	0.32 (0.04) [0.24-0.40]	0.35 (0.05) [0.25-0.44]	0.269	-
		DOSE1	20/20	0.40 (0.04) [0.32-0.48]	0.46 (0.05) [0.36-0.55]		0.16 [-0.5-0.8]
		DOSE2	11/11	0.35 (0.05) [0.25-0.46]	0.42 (0.07) [0.29-0.55]		0.23 [-0.5-1.0]
	Trails B‡	Usual Care	20/20	0.10 (0.01) [0.07-0.13]	0.11 (0.02) [0.08-0.14]	0.945	-
		DOSE1	20/18	0.10 (0.01) [0.07-0.13]	0.12 (0.02) [0.09-0.15]		0.24 [-0.4-0.9]
		DOSE2	11/11	0.10 (0.01) [0.08-0.14]	0.12 (0.02) [0.08-0.16]		0.26 [-0.5-1.0]
	DSST	Usual Care	21/20	18 (2) [13-22]	21 (2) [17-26]	0.440	-
		DOSE1	20/20	21 (2) [17-26]	25 (2) [20-30]		0.11 [-0.5-0.7]
		DOSE2	11/11	22 (3) [16-28]	26 (3) [20-33]		0.10 [-0.6-0.8]

*ANCOVA using 6-minute walk distance at baseline as the co-variate.

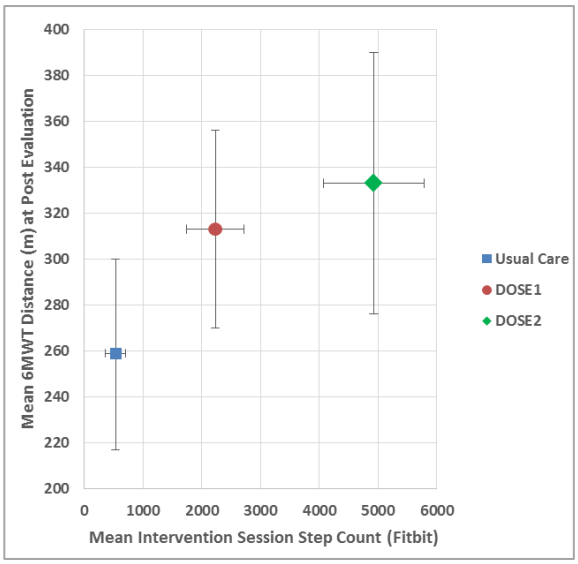
‡Rate of generation (ROG) calculated for Trails A and B. Rate of generation = total numeric completed responses/total time to complete responses (in seconds).

Figure 5.2 below displays the relationship between the mean distance walked in the 6-minute walk test/group at the completion of the 4-week intervention and the mean intervention session intensity (minutes spent ≥ 40%HRR and step count/group).

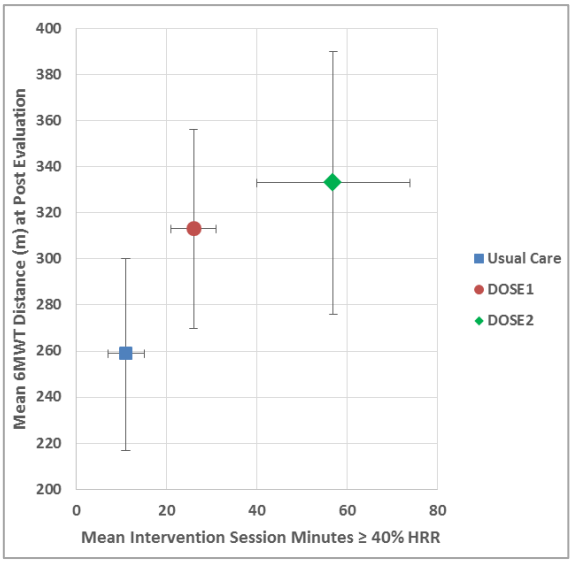
The curvilinear relationship of the mean 6-minute walk distance at post-evaluation to the step count (Figure 5.2a) shows that the most improvement (54m) in the 6-minute walk appears to be related to a mean intervention session count of just over 2000 steps, with a slight improvement (20m) when the step count increases to almost 5000 steps. Similarly, this relationship is also observed with the heart rate intensity data (Figure 5.2b). The most improvement in the 6-minute walk (54m) appears to be in the first 30 minutes of aerobic intensive exercise, with a slight improvement (20m) when the heart rate intensity more than doubles in duration.

Figure 5.2 Relationship of 6MWT at Post-Evaluation to Intervention Session Intensity

(a) Post 6MWT and Step Count*



(b) Post 6MWT and Minutes ≥ 40%HRR*



*Error bars represent 95% confidence intervals (CI)

5.4 Discussion

Although this multi-site, randomized clinical trial is still ongoing, this preliminary analysis of 53 participants provides an interim examination of whether the experimental intervention protocols are being delivered and tolerated as designed, and the potential effects of these interventions on functional recovery, cognition, and quality of life early after stroke.

Firstly, with respect to the participant's clinical characteristics and demographics at baseline, it appears that the study randomization, incorporating stratification by age, has been effective so far in balancing the clinical and personal characteristics between the intervention groups. As the projected sample size in this study is relatively small (75 participants), it was initially determined that only one stratification variable would be applied at randomization based upon the stratification estimation calculations that were conducted (Kernan et al. 1999; Silcocks 2012). Therefore, as age has been shown to have an impact on recovery after stroke (Kugler et al. 2003), and the study sites differed in admitting age demographics, age was selected as the stratification variable. From our current study population, our mean age across groups is on the younger side for individuals post-stroke (56±12; range = 27-76), but this is secondary to the majority of participants being recruited from study sites that have inpatient admission criteria for age being less than, or equal to, 60 years old. Furthermore, as initial motor severity is another important variable that affects stroke recovery (Jorgensen et al. 1995a), it was decided a priori that the baseline 6-minute walk distance would serve as a co-variate when analyzing the primary and secondary outcomes measures.

The therapeutic dose for the study intervention protocol was designed to build upon what is typically provided during stroke inpatient rehabilitation in Canadian hospitals, which is a similar health service model to many European, Australian, Asian, and United Kingdom

rehabilitation models. Currently, patients in Canadian stroke inpatient rehabilitation centres receive approximately 60 minutes of physical therapy daily, and for the purpose of this trial, this represents 'Usual Care'. 'DOSE1' was designed to increase the cardiovascular intensity and walking steps within the physical therapy session, while keeping the total duration of the session to the standard 60 minutes. The 'DOSE 1' session duration of 60 minutes was consciously designed to be approximately the same length of time as a 'Usual Care' physical therapy session to optimize the future translation of the protocol into clinical practice, should it be found to be feasible and effective. For 'DOSE2', the step count and heart rate intensity provided in 'DOSE1' was applied two times/day, therefore providing an additional 20 hours of intervention over 'DOSE1'participants. The additional 20 hours of intervention in 'DOSE2' exceeds the recommended amount (16 hours) of augmented therapy found to be necessary to observe a difference between control and experimental groups early after stroke (Kwakkel et al. 2004).

Assessing the intervention protocol fidelity is essential to determining if the study protocol is being delivered as intended and if it is able to be tolerated by the participants. In stroke rehabilitation exercise intervention trials, the delivery of rigorous, well-defined, intervention protocols can often be challenging secondary to the variability of participants' personal characteristics and clinical presentations post-stroke.

In this trial, the experimental intervention protocols ('DOSE1' and 'DOSE2') were designed to deliver a minimum of 30 minutes of weight-bearing, walking related exercise within the 60-minute therapy session, while keeping the participants' heart rates above their 40% heart rate reserve during this time. In the 'DOSE1' and 'DOSE2' groups, the aerobic intensive time delivered to the participants is very close to the protocol target time of 30 minutes/session (26 and 57 minutes respectively), and is about 2.5 to 5 times longer than the time the 'Usual Care'

group spends above a 40% heart rate reserve. At this time, it appears that the greatest gain in walking (as measured by the 6-minute walk at post-evaluation) occurs with an increase in up to 30 minutes of aerobic activity, with only a minimal improvement in walking distance when the aerobic intensity is increased over this time.

With respect to the step count intensity, the DOSE1 and DOSE2 groups had a goal to complete approximately 2000 walking steps within each 60-minute intervention session. This target was exceeded in both experimental groups, resulting in over 4-times the number of steps being completed by participants within each therapy session in DOSE1 and DOSE2 compared to participants in the Usual Care group. Furthermore, similar to the relationship observed between heart rate intensity and walking distance covered on the 6MWT at post-evaluation, the most gains in the 6-minute walking distance at post-evaluation were observed when participants were completing up to 2500 steps/intervention session, with minor walking improvement when the step count/intervention session is doubled.

Although the therapy sessions for both the DOSE1 and DOSE2 groups are approximately 10 minutes longer over the Usual Care group, it would be extremely unlikely, based on the participants' mean walking velocity from the baseline 6-minute walk (0.43m/s) that the 1700 step count difference could be accounted for if an extra 10 minutes was provided in the therapy session, and walking was only completed during that time (Burioka et al. 2014). Even a very generous estimate of 1 step/second would only produce an additional 600 steps over the 10-minute period.

Overall, the experimental groups are meeting the study intervention protocol targets and being tolerated by the participants with respect to total therapy time, time spent in the aerobic training zone, and number of walking steps completed within a therapy session.

The primary outcome, the 6-minute walk, is being conducted at the post-evaluation, immediately after the 4-week intervention is completed. This time-point was selected for two reasons: 1) it provided an opportunity to assess the immediate effect of the intervention and 2) it occurred within the early time period after the initial stroke onset. The secondary outcomes are being collected at all four time points: baseline, post-evaluation, 6-months post-stroke and 12-months post-stroke. The 6 and 12-month evaluations were included to assess the long-term retention of the intervention programs (as no formal study intervention is being applied after the post-evaluation) and to also gain further insight into longitudinal functional recovery after stroke. The data from the 6 and 12-month evaluations are not included in this interim analysis secondary to the large number of enrolled participants that have not yet completed them.

Although preliminary statistical analyses have been conducted on the primary and secondary measures, it is imperative to remember that the current sample size is not powered sufficiently to appropriately interpret the statistical results. With that said, this interim analysis of the primary outcome, the 6-minute walk at post-evaluation, suggests that there is potential for the experimental groups ('DOSE1' and 'DOSE2') to achieve better outcomes on the 6-minute walk compared to participants in the 'Usual Care' group.

The primary outcome data was first analyzed with all participants (n=53), and then a sensitivity analysis was conducted with one outlier removed, secondary to this data point having a standardized residual greater than 3 in the distance walked in the post-evaluation 6-minute walk. The study participant that was removed was a young, very fit and healthy man, whose mechanism of stroke was secondary to a spontaneous event, a carotid artery dissection. His pre-stroke lifestyle and health was not consistent with the majority of individuals recruited into the study who had significant stroke risk factors (i.e., hypertension, obesity, diabetes, and/or

smoking). Therefore, as this gentleman's walking recovery was statistically different from the rest of the study population, his 6-minute post-evaluation walking data was excluded, and the sample population (n=52) was re-analyzed.

Although there is no statistical difference as measured by the p-value ($p<0.05$) between Usual Care and the experimental groups (DOSE1 and DOSE2) on the 6-minute walk at post-evaluation upon re-analysis, the medium effect sizes for DOSE1 and DOSE2 (0.44 and 0.73 respectively) demonstrate a difference between the means of the intervention groups and usual care. In addition, it is important to note that the increased walking distance in the experimental groups exceeded 50m over the control group, which is considered a meaningful clinical change in this measure, in this early period after stroke (Perera et al, 2006).

With respect to the secondary outcome measures in this preliminary analysis, a significant difference was only observed on the total health score of the EQ-5D-5L, a quality of life measure, for participants in the DOSE2 group. This may be interpreted in that individuals that received the 2x/day, higher intensity aerobic exercise intervention, perceived they had better health at the end of the 4-week intervention, compared to the participants that received the other intervention groups ('DOSE1' and 'Usual Care'). Furthermore, this improvement in health perception was observed without a comparable statistically significant improvement in recovery with respect to walking, overall function, and cognition.

5.5 Conclusion

Overall, this interim analysis of the 53 participants enrolled in the DOSE trial confirms that the three intervention groups are currently balanced with respect to participant demographics and clinical characteristics, and that the intervention protocols are being delivered as designed, and the higher intensity and dose can be tolerated by the participants.

Preliminary results from both the primary and secondary outcomes suggest that individuals that receive a four-week higher intensity aerobic exercise intervention during inpatient physical therapy stroke rehabilitation may have improved walking recovery and an improved perception of their health status immediately after completing the intervention. However, these findings need to be confirmed once recruitment is complete on a total study population of 75 participants, and appropriate conclusions made at that time.

Chapter 6: Overall Discussion and Future Directions

Stroke is a serious global health concern. While advances in acute medical interventions and public health education over the last century have decreased mortality after stroke, this has resulted in more individuals living with disability. Given the aging demographics of most countries, this population will continue to rise over the next 20 years. The goal of effective rehabilitation is to maximize functional recovery, restore independent living, and return people to their activities of daily living as quickly as possible. The advancement and translation of stroke rehabilitation research into clinical practice is critical to ensure that we continue to decrease the burden of stroke on individuals, their family and caregivers, and society.

Currently, one of the major limitations in stroke rehabilitation is understanding the optimal timing, therapeutic dose, and intensity to maximize recovery. As research scientists strive to build this evidence-based knowledge, equal challenges exist in translating this information into clinical practice. In particular, limitations in technologies to accurately measure therapeutic intensity present a significant barrier for clinicians. Improved methodologies are needed for quantitative measurement of rehabilitation dose and intensity to enable clinicians to adjust rehabilitation and provide instantaneous feedback to patients.

The research conducted for this thesis specifically addresses the aforementioned knowledge gaps. Chapters 2 and 3 describe two studies that were conducted to identify a "clinically-friendly" device that could accurately measure walking step count during inpatient stroke rehabilitation with patients that have a wide variability of walking speeds and gait patterns. Chapters 4-5 then describe the design and preliminary results of an ongoing multi-site randomized clinical trial that is assessing the effectiveness of varying doses of higher intensity exercise on walking, functional recovery, cognition, and quality of life. This study is specifically

looking at the effectiveness of exercise intervention strategies during the early phase after stroke, which is a critical time for neural recovery. The findings from these studies will make significant contributions to the advancement of both stroke rehabilitation research and clinical practice.

The study presented in Chapter 2 was designed to identify a monitoring device that was readily available, provided instantaneous feedback, and could accurately measure step count across a wide variability of walking speeds commonly observed in the early phase after stroke. Participants in this study were evaluated at varying walking speeds (0.3-0.9 m/s) and the Fitbit One device was placed on both the hip and ankle to assess step count accuracy. When the Fitbit One was placed at the ankle, accurate readings were obtained when individuals in the chronic phase post-stroke walked a 15-meter distance at a variety of walking speeds; measurements had less than 10% error at 0.4 m/s walking speed, and the accuracy improved as the speed increased up to 0.9m/s. This study, which was performed in a controlled research setting, was the first study to establish the accuracy of the Fitbit One device across a wide range of walking speeds in individuals post-stroke. Since the device was economical, readily available, and provided instantaneous feedback, the confirmed accuracy of measurement motivated our next study (Chapter 3), which assessed the device's accuracy when used in a clinical setting.

In Chapter 3, I described a study to assess the accuracy of the Fitbit One device when used in a busy clinical therapeutic environment with patients in the early phase of recovery after stroke. During a typical inpatient physical therapy session, individuals may participate in a variety of exercises, including walking; these varying types of movements were not evaluated during our initial testing of the device's accuracy. Thus, it was essential to assess whether the accuracy of the device was maintained in a more realistic clinical setting.

Along with the Fitbit One, participants in this study also wore an additional device called the StepWatch™ Activity Monitor (SAM). Although the SAM monitor is generally considered the "gold-standard" for measurement of step count in stroke rehabilitation research settings, it is not commonly used in the clinical setting. In large part, this occurs because it does not provide instantaneous step count, and is too expensive for public health authorities to purchase; the SAM costs approximately $2000 USD for one monitor and the required monitor loading dock and supporting software.

The data from this study was collected from the one-hour, higher aerobic and walking intensity physical therapy session that participants completed within the multi-site randomized clinical trial described in Chapter 4. Comparison of the accuracy of the two devices in measuring step count demonstrated that the two devices were almost identical in measuring step count, and that the accuracy of the Fitbit One in the clinical setting was almost the same as the research setting. Combined, the findings from the studies conducted in Chapter 2 and 3 address a major gap in stroke rehabilitation by validating the use of a readily available, cost-effective, user-friendly device that can accurately measure step count in in stroke patients with a wide variability of walking speeds and patterns.

How do we move forward and translate this new knowledge into clinical practice? Although previous research studies have endorsed step count monitors during inpatient rehabilitation, the devices were not "clinically-friendly" as they did not permit instantaneous feedback to the clinicians (Dorsch et al. 2015; Mansfield et al. 2015). Rather, a research assistant was required to download the data and translate the information back to the clinician and patient at a later time, a procedure that creates a serious barrier to adoption and integration of data within a clinical rehabilitation program. Results from one of the studies found that providing step count

feedback to the patients did not alter their walking amount as compared to patients that were not provided step count feedback (Mansfield et al. 2015). However, these results may have been different if the clinician provided the data to the patient immediately after completing the therapeutic session and target walking goals were made directly at that time. Evidence from the chronic stroke population suggests that step count feedback is a strong motivator for patients to participate in walking (Sullivan et al. 2014).

What if increasing walking activity during inpatient rehabilitation could be addressed by modifying the clinical stroke rehabilitation environment? Imagine an inpatient rehabilitation ward where step count and heart rate monitors are placed on a patient's wrist/ankle immediately upon admission to the unit and this information is transmitted wirelessly to monitors throughout the ward and hospital, providing the patient with verbal and visual feedback in real time throughout the day. Clinicians could access the data at any moment during the day and make therapeutic goals with their patient. Therapeutic intensity would very likely increase. Patients would likely be more engaged. Future research in this area needs to explore the use of accurate wearable technologies that provide instantaneous feedback and ultimately transmit wirelessly to monitors so both patients and clinicians have access at all time to this data. Do these devices increase therapeutic intensity and maximize patient's recovery? Furthermore, patient motivation and perceptions to wearable technologies have not been explored in the stroke inpatient rehabilitation setting. Is this feedback motivating to patients and can it encourage an increased therapeutic intensity in a safe manner? These research questions require further exploration to effectively and safely translate wearable monitors into inpatient stroke rehabilitation.

Chapters 4 and 5 describe the design and preliminary results of an ongoing randomized controlled trial to systematically investigate how varying dose and intensity of exercise influence

walking and functional recovery, along with cognition and quality of life. This study is novel in two ways. First, the intervention protocol varies exercise intensity and dose to test whether higher exercise intensity and dose can be delivered and tolerated during the early phase after stroke. Second, this is the first study to test varying dose and intensity of exercise on walking recovery, overall function, cognition and quality of life during inpatient stroke rehabilitation, which is a critical time for neural recovery. Results from this randomized controlled trial will contribute to the design of optimal therapeutic protocols for the delivery of stroke rehabilitation.

In order to be proficient at a task, you must practice it. In stroke rehabilitation, this common-sense rule is referred to as "task-specific training". Research has demonstrated that in chronic stroke survivors, stationery cycling will improve patients' physical endurance to complete a walking test, but these patients will not, on average, cover as much distance on a walking test compared to someone that specifically trained with walking practice (Sullivan et al. 2007). This knowledge was one component that was incorporated into the novel design of the intervention protocol that was used in the randomized controlled trial described in Chapters 4 and 5. The primary goal of the intervention protocol was to improve individuals' walking recovery while they were admitted in inpatient rehabilitation. To be successful, the intervention protocol needed to meet several criteria: include over-ground walking activities; use the equipment available in a standard inpatient rehabilitation setting; have a selection of exercises so that the intervention could be personalized to each enrolled participant, yet still meet the required minimum of 30 minutes at $\geq$ 40% HRR; be able to be progressed in intensity on a weekly basis; be monitored by devices that provided the clinicians with instantaneous feedback that could be recorded and immediately reported back to the participant; and be delivered within a standard one hour inpatient physical therapy session. Furthermore, the comparison of the experimental

groups (DOSE1 and DOSE2) allowed for the systematic assessment of how dose, in addition to therapeutic intensity, may influence walking and functional recovery.

This intervention protocol sought to address knowledge gaps in stroke rehabilitation pertaining to the role of therapeutic dose and intensity on walking recovery in the early phase after stroke. In recent years, two studies have separately investigated higher therapeutic dose and higher therapeutic intensity delivered during inpatient rehabilitation (MacKay-Lyons et al. 2013; English et al. 2015). This is the first intervention protocol to systematically combine both factors and investigate the effects. An important component of this intervention protocol is that it incorporated clinicians working on the rehabilitation unit to deliver the intervention protocols. As research has shown that the translation of research evidence into clinical practice can be arduous and prolonged (Westfall et al. 2007), intentionally including clinicians from the beginning was a conscious decision by the study investigators to aid with the clinical translation of the research findings at the completion of the trial.

As described in Chapter 5, adherence to the intervention protocol guidelines appears to be successful based on the preliminary analysis. Individuals receiving the experimental intervention groups (DOSE1 and DOSE2) are close to the targeted minimum of 30 minutes of higher intensity aerobic exercise ($\geq$40%HRR) and are completing, at minimum, four-times as many steps within each intervention session. Furthermore, no serious adverse events have occurred and no participants have voluntarily withdrawn during the intervention period.

Future research directions with this novel intervention protocol will need to explore how to successfully integrate the protocol into clinical practice. Success with this endeavour will depend upon both clinician and patient uptake of delivering, and participating, in higher intensity exercise. Although not included in this thesis, a study has been conducted that explores the

DOSE study therapists' perceptions to administering the intervention protocol (Connell et al. 2017). This study found that, in general, the clinicians had positive experiences providing the high intensity intervention. However, the therapists also expressed that they may need to adapt the intervention protocol to accommodate their beliefs about ensuring that the patients had appropriate movement quality during the intervention. Furthermore, it was also suggested that the implementation of a higher intensity intervention protocol during inpatient stroke rehabilitation would require some system changes at the level of the facility/health authority to support the clinicians and patients to endorse the delivery and uptake of higher intensity exercise in the early phase after stroke. Some of this support may include, but is not limited to: purchase of step counter and heart rate monitoring devices; clinician education regarding the delivery of higher intensity exercise; and incorporation of an initial cardiac assessment to ensure higher intensity exercise is safe for each patient.

Finally, it will be important to replicate the study described above in assessing clinicians' perceptions regarding the delivery of higher intensity exercise during stroke inpatient rehabilitation with the DOSE study participants. This will help to identify and understand the potential barriers from the patient's perspective in completing higher intensity exercise early after stroke. By obtaining both the clinicians' and participants' perspectives on delivering and participating in higher intensity exercise, the successful uptake of the intervention protocol into standard inpatient stroke rehabilitation will likely be greatly enhanced.

Aristotle said that "the whole is greater than the sum of its parts" and this is an apt description of the research comprising this thesis. Both the identification and validation of an improved monitoring device, and the study of exercise dose and intensity, are important contributions to stroke rehabilitation research. However, when combined, they have enabled a

multi-site randomized controlled trial that will provide new insights into how higher intensity exercise and dose affects walking and functional recovery, as well as cognition and quality of life.

To our knowledge, the study described in Chapters 4 and 5 is the first randomized controlled trial to systematically investigate the effect of higher intensity exercise on walking and functional recovery, cognition, and quality of life at a time when maximal neurological recovery is occurring.

The first key component of this trial is the timing of the study. The trial is occurring during inpatient rehabilitation, which usually occurs within the first three months post-stroke, where the animal literature has identified that maximal neurological recovery is occurring (Biernaskie et al. 2004). It is not known in humans if recovery after stroke can be optimized with the addition of a higher intensity and higher dose of exercise delivered within this same period. This is vital knowledge to obtain as research has shown that higher dose exercise delivered early after stroke (within the first 7 days) has deleterious effects on recovery (AVERT Trial Collaboration Group 2015). Furthermore, as the majority of stroke rehabilitation research occurs with the chronic stroke population (greater than 6-months post-stroke), results from this study may encourage future research within this critical neural recovery time frame within all aspects of stroke rehabilitation.

It is crucial to remember that the results reported in Chapter 5 are preliminary findings from an incomplete sample population; the final analysis must be conducted when the trial has recruited the complete sample population of 75 participants (25 individuals/intervention group). Only myself, and three of the DOSE principal investigators, have been exposed to these preliminary results; this preliminary data will absolutely not be shared with any of the DOSE

therapists or assessors until the complete sample population of 75 have been recruited and the primary and secondary outcomes are re-analyzed. Furthermore, an embargo will be put on this thesis, thus not making it available to the public and retaining the confidentiality of this preliminary analysis. The embargo will be maintained until the primary and secondary outcomes have been re-analyzed with the complete study population and published.

Although there is no statistical significance between the intervention groups on the primary outcome, walking recovery immediately after the 4-week intervention, there is a trend that the experimental intervention groups (DOSE1 and DOSE2) walk farther on the 6-minute walk test compared to the control group. Most importantly, participants are able to tolerate the high doses of exercise during inpatient stroke rehabilitation. In DOSE 2, participants completed, on average, 57 minutes of exercise above 40% HRR, and 4932 walking steps within the two intervention sessions. Although the relationship between the intervention intensity and walking performance seems to have the greatest benefit with the DOSE1 intervention, there are still meaningful gains with the additional time provided in the DOSE2 intervention.

Another interesting result at this time is the significant finding within the secondary outcomes, with the total health score on the quality of life measure, the EQ-5D-5L. It is interesting to see that individuals that receive a higher intensity, higher dose exercise intervention during inpatient rehabilitation perceive their health as being better, despite there not being a significant difference in their functional recovery compared to individuals that don't do as much exercise. It may be of interest in future neurorehabilitation trials that the primary outcome measure assesses the effect on the participant's quality of life (participation level of the International Classification of Functioning, Disability and Health) instead of at the traditional impairment and activity level. This sentiment was also endorsed in a recent trial investigating

dose-response in post-stroke upper extremity recovery during inpatient rehabilitation (Winstein et al. 2016b). In this study, no significant differences were found on the primary outcome, an activity level measurement (Wolf-Motor Function Test) by delivering a higher dose of upper extremity exercise. However, one of the suggestions from the authors for future neurorehabilitation trials was to consider selecting primary outcomes that are sensitive to patient participation and quality of life.

Finally, not included in Chapter 5, but vital to the overall conclusions from the randomized clinical trial is the long-term retention of the intervention protocol. This data is being collected at the 6 and 12-month post-stroke follow-up evaluations and will be analyzed when the total sample population is recruited. Previous research investigating the long-term outcomes of physical function after an exercise intervention was delivered in the first year post-stroke found that individuals' activity was maintained four years later when tested (Langhammer et al. 2014). It will be interesting to see if any differences observed at the post-evaluation, immediately after the intervention protocol, are sustained at the 6 and 12 month evaluations, or if all the exercise groups equalize. This knowledge will have an important impact on the design of future research trials investigating exercise post-stroke and whether it may be beneficial to implement follow-up exercise intervention periods, after the initial intervention exercise bout, to maintain or potentially improve function, cognition and quality of life.

In addition to the future research directions that have been suggested above, the natural progression from the Phase II clinical trial described in Chapters 4 and 5 will be to conduct a Phase III clinical trial to examine efficacy further. If the preliminary data holds true when the complete participant population is recruited, we will have learned that the higher intensity intervention protocol is feasible, safe, and potentially effective. A future trial may be expanded

into more sites, to achieve a greater sample population, and a stepped wedge cluster randomised controlled trial could be incorporated to avoid potential control group contamination and to maximize the clinical translation of the protocol at all sites (Hemming et al. 2015).

In conclusion, the research conducted for this thesis will makes a significant contribution to both stroke rehabilitation research and clinical practice. It excites me to see how this work may ignite future research and impact clinical practice to maximize the quality of life for those recovering from stroke.

Bibliography

Andersen KK, **Olsen TS**, **Dehlendorff C**, **Kammersgaard LP**. Hemorrhagic and ischemic strokes compared: Stroke severity, mortality, and risk factors. *Stroke* 40: 2068–2072, 2009.

Ashe MC, **Miller WC**, **Eng JJ**, **Noreau L**. Older adults, chronic disease and leisure-time physical activity. *Gerontology* 55: 64–72, 2009.

AVERT Trial Collaboration Group. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): A randomised controlled trial. *Lancet* 6736: 1–10, 2015.

Barak S, **Wu SS**, **Dai Y**, **Duncan PW**, **Behrman AL**. Adherence to Accelerometry Measurement of Community Ambulation Poststroke. *Phys Ther* 94: 101–110, 2014.

Benjamin EJ, **Blaha MJ**, **Chiuve SE**, **Cushman M**, **Das SR**, **Deo R**, **De Ferranti SD**, **Floyd J**, **Fornage M**, **Gillespie C**, **Isasi CR**, **Jimenez MC**, **Jordan L**, **Judd S**, **Lackland D**, **Lichtman J**, **Lisabeth L**, **Liu S**, **Longenecker C**, **Mackey R**, **Matsushita K**, **Mozaffarian D**, **Mussolino M**, **Nasir K**, **Neumar R**, **Palaniappan L**, **Pandey D**, **Thiagarajan R**, **Reeves M**, **Ritchey M**, **Rodriguez C**, **Roth G**, **Rosamond W**, **Sasson C**, **Towfighi A**, **Tsao C**, **Turner M**, **Virani S**, **Voeks J**, **Willey J**, **Wilkins J**, **Wu J**, **Alger H**, **Wong S**, **Muntner S**. Heart Disease and Stroke Statistics—2017 Update. *Circulation* 135: e146–e603, 2017.

Biernaskie J, **Chernenko G**, **Corbett D**. Efficacy of Rehabilitative Experience Declines with Time after Focal Ischemic Brain Injury. *J Neurosci* 24: 1245–1254, 2004.

Billinger SA, **Arena R**, **Bernhardt J**, **Eng JJ**, **Franklin BA**, **Johnson CM**, **MacKay-Lyons M**, **Macko RF**, **Mead GE**, **Roth EJ**, **Shaughnessy M**, **Tang A**. Physical activity and exercise recommendations for stroke survivors: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 45: 2532–2553, 2014.

Blennerhassett J, **Dite W**. Additional task-related practice improves mobility and upper limb function early after stroke: a randomised controlled trial. *Aust J Physiother* 50: 219–224, 2004.

Blum L, **Korner-Bitensky N**. Usefulness of the Berg Balance Scale in stroke rehabilitation: a systematic review. *Phys Ther* 88: 559–66, 2008.

de Boer MR, **Waterlander WE**, **Kuijper LDJ**, **Steenhuis IHM**, **Twisk JWR**. Testing for baseline differences in randomized controlled trials: An unhealthy research behavior that is hard to eradicate. *Int J Behav Nutr Phys Act* 12: 1–8, 2015.

Bohannon RW, **Andrews AW**, **Smith MB**. Rehabilitation goals of patients with hemiplegia. *Int J Rehabil Res* 11: 181–183, 1988.

Bohannon RW, **Kindig J**, **Sabo G**, **Duni AE**, **Cram P**. Isometric knee extension force measured using a handheld dynamometer with and without belt-stabilization. *Physiother Theory Pract* 28: 562–568, 2012.

Boyne P, **Billinger S**, **MacKay-Lyons M**, **Barney B**, **Khoury J**, **Dunning K**. Aerobic Exercise Prescription in Stroke Rehabilitation. *J Neurol Phys Ther* 41: 119–128, 2017.

Burioka N, **Imada A**, **Kiyohiro A**, **Sugitani F**, **Fujii T**, **Hosaka A**, **Nakamoto S**, **Amisaki T**, **Shimizu E**. Modified six-minute walk test: Number of steps per second. *Yonago Acta Med* 57: 61–63, 2014.

Busse ME, **van Deursen RW**, **Wiles CM**. Real-life step and activity measurement: reliability and validity. *J Med Eng Technol* 33: 33–41, 2009.

Carroll SL, **Greig CA**, **Lewis SJ**, **McMurdo ME**, **Sniehotta FF**, **Johnston M**, **Johnston DW**, **Scopes J**, **Mead GE**. The use of pedometers in stroke survivors: Are they feasible and how well do they detect steps? *Arch Phys Med Rehabil* 93: 466–470, 2012.

Chan AW, **Tetzlaff J**, **Altman D**, **Laupacis A**, **Gøtzsche P**, **Krleža-Jerić K**. Research and Reporting Methods Annals of Internal Medicine SPIRIT 2013 Statement : Defining Standard Protocol Items for Clinical Trials. *Ann Intern Med* 158: 200–207, 2013.

Chen G, **Patten C**, **Kothari DH**, **Zajac FE**. Gait differences between individuals with post-stroke hemiparesis and non-disabled controls at matched speeds. *Gait Posture* 22: 51–56, 2005.

Chin J, **Vora N**. The Global Burden of Neurologic Diseases. *Neurology* 83: 349–51, 2014.

Connell L, **Klassen T**, **Janssen J**, **Thetford C**, **Eng J**. Delivering intensive rehabilitation in stroke: factors influencing implementation. *Phys. Ther.*, 2017 (accepted for publication)

Cook DJ, **Thompson JE**, **Prinsen SK**, **Dearani JA**, **Deschamps C**. Functional recovery in the elderly after major surgery: Assessment of mobility recovery using wireless technology. *Ann Thorac Surg* 96: 1057–1061, 2013.

Dobkin BH. Rehabilitation after stroke. *N Engl J Med* 352: 1677–1684, 2005.

Dobkin BH, **Xu X**, **Batalin M**, **Thomas S**, **Kaiser W**. Reliability and validity of bilateral ankle accelerometer algorithms for activity recognition and walking speed after stroke. *Stroke* 42: 2246–2250, 2011.

Dorsch AK, **Thomas S**, **Xu X**, **Kaiser W**, **Dobkin BH**. SIRRACT: An International Randomized Clinical Trial of Activity Feedback During Inpatient Stroke Rehabilitation Enabled by Wireless Sensing. *Neurorehabil Neural Repair* 29: 407–15, 2015.

Doyle L, **MacKay-Lyons M**. Utilization of aerobic exercise in adult neurological rehabilitation by physical therapists in Canada. *J Neurol Phys Ther* 37: 20–6, 2013.

Dromerick AW, **Edwardson MA**, **Edwards DF**, **Giannetti ML**, **Barth J**, **Brady KP**, **Chan E**, **Tan MT**, **Tamboli I**, **Chia R**, **Orquiza M**, **Padilla RM**, **Cheema AK**, **Mapstone ME**, **Fiandaca MS**, **Federoff HJ**, **Newport EL**. Critical periods after stroke study: translating animal stroke recovery experiments into a clinical trial. *Front Hum Neurosci* 9: 231, 2015.

El-Tamawy MS, **Abd-Allah F**, **Ahmed SM**, **Darwish MH**, **Khalifa HA**. Aerobic exercises enhance cognitive functions and brain derived neurotrophic factor in ischemic stroke patients. *NeuroRehabilitation* 34: 209–213, 2014.

Elsworth C, **Dawes H**, **Winward C**, **Howells K**, **Collett J**, **Dennis A**, **Sackley C**, **Wade D**. Pedometer step counts in individuals with neurological conditions. *Clin Rehabil* 23: 171–175, 2009.

English C, **Bernhardt J**, **Crotty M**, **Esterman A**, **Segal L**, **Hillier SL**. Circuit class or seven-day therapy for increasing intensity of rehabilitation after stroke (CIRCIT): a randomized controlled trial. *Int J Stroke* June: 594–602, 2015.

English CK, **Hillier SL**, **Stiller KR**, **Warden-Flood A**. Circuit Class Therapy Versus Individual Physiotherapy Sessions During Inpatient Stroke Rehabilitation: A Controlled Trial. *Arch Phys Med Rehabil* 88: 955–963, 2007.

Feng C, **Wang H**, **Lu N**, **Chen T**, **He H**, **Lu Y**, **Tu XM**. Log-transformation and its implications for data analysis. *Shanghai Arch psychiatry* 26: 105–9, 2014.

Fini NA, **Holland AE**, **Keating J**, **Simek J**, **Bernhardt J**. How Physically Active Are People Following Stroke? Systematic Review and Quantitative Synthesis. *Phys Ther* 97: 707–717, 2017.

French B, **Thomas L**, **Leathley M**, **Sutton C**, **McAdam J**, **Forster A**, **Langhorne P**, **Price C**, **Walker A**, **Watkins C**. Does repetitive task training improve functional activity after stroke? A Cochrane systematic review and meta-analysis. *J Rehabil Med* 42: 9–14, 2010.

Frizzell J. Acute Stroke: Pathophysiology , Diagnosis , and Treatment. *AACN Clin Issues* 16: 421–440, 2005.

Fulk GD, **Combs SA**, **Danks KA**, **Nirider CD**, **Raja B**, **Reisman DS**. Accuracy of Two Activity Monitors in Detecting Steps in People With Stroke and Traumatic Brain Injury. *Phys Ther* 94: 222–229, 2014.

Fulk GD, **Echternach JL**, **Nof L**, **O'Sullivan S**. Clinometric properties of the six-minute walk test in individuals undergoing rehabilitation poststroke. *Physiother Theory Pract* 24: 195–204, 2008.

Go AS, **Mozaffarian D**, **Roger VL**, **Benjamin EJ**, **Berry JD**, **Borden WB**, **Bravata DM**, **Dai S**, **Ford ES**, **Fox CS**, **Franco S**, **Fullerton HJ**, **Gillespie C**, **Hailpern SM**, **Heit JA**, **Howard VJ**, **Huffman MD**, **Kissela BM**, **Kittner SJ**, **Lackland DT**, **Lichtman JH**, **Lisabeth LD**, **Magid D**, **Marcus GM**, **Marelli A**, **Matchar DB**, **McGuire DK**, **Mohler ER**, **Moy CS**, **Mussolino ME**, **Nichol G**, **Paynter NP**, **Schreiner PJ**, **Sorlie PD**, **Stein J**, **Turan TN**, **Virani SS**, **Wong ND**, **Woo D**, **Turner MB**. Heart disease and stroke statistics-2013 update: A Report from the American Heart Association. *Circulation* 127, 2013.

Golicki D, **Niewada M**, **Buczek J**, **Karliska A**, **Kobayashi A**, **Janssen MF**, **Pickard AS**. Validity of EQ-5D-5L in stroke. *Qual Life Res* 24: 845–850, 2015.

Haeuber E, **Shaughnessy M**, **Forrester LW**, **Coleman KL**, **Macko RF**. Accelerometer monitoring of home- and community-based ambulatory activity after stroke. *Arch Phys Med Rehabil* 85: 1997–2001, 2004.

Harris JE, **Eng JJ**. Goal Priorities Identified through Client-Centred Measurement in Individuals with Chronic Stroke. *Physiother Canada* 56: 171–176, 2004.

Hasan SMM, **Rancourt SN**, **Austin MW**, **Ploughman M**. Defining Optimal Aerobic Exercise Parameters to Affect Complex Motor and Cognitive Outcomes after Stroke: A Systematic Review and Synthesis. *Neural Plast* 2016, 2016.

Hashimoto R, **Meguro K**, **Lee E**, **Kasai M**, **Ishii H**, **Yamaguchi S**. Effect of age and education on the Trail Making Test and determination of normative data for Japanese elderly people: The Tajiri Project. *Psychiatry Clin Neurosci* 60: 422–428, 2006.

Hebert D, **Lindsay MP**, **McIntyre A**, **Kirton A**, **Rumney PG**, **Bagg S**, **Bayley M**, **Dowlatshahi D**, **Dukelow S**, **Garnhum M**, **Glasser E**, **Halabi M Lou**, **Kang E**, **MacKay-Lyons M**, **Martino R**, **Rochette A**, **Rowe S**, **Salbach N**, **Semenko B**, **Stack B**, **Swinton L**, **Weber V**, **Mayer M**, **Verrilli S**, **DeVeber G**, **Andersen J**, **Barlow K**, **Cassidy C**, **Dilenge ME**, **Fehlings D**, **Hung R**, **Iruthayarajah J**, **Lenz L**, **Majnemer A**, **Purtzki J**, **Rafay M**, **Sonnenberg LK**, **Townley A**, **Janzen S**, **Foley N**, **Teasell R**. Canadian stroke best practice recommendations: Stroke rehabilitation practice guidelines, update 2015. *Int J Stroke* 11: 459–484, 2016.

Hemming K, **Haines TP**, **Chilton PJ**, **Girling AJ**, **Lilford RJ**. The stepped wedge cluster randomised trial: rationale, design, analysis, and reporting. *Bmj* 350: h391–h391, 2015.

Hesse S, **Werner C**, **Von Frankenberg S**, **Bardeleben A**. Treadmill training with partial body weight support after stroke. *Phys Med Rehabil Clin N Am* 14: 111–123, 2003.

Inoue I, **Takemoto K**, **Miyamoto T**, **Yoshikawa N**, **Taniguchi S**, **Saiwai S**, **Nishimura Y**, **Komatsu T**. Sequential computed tomography scans in acute cerebral infarction. *Radiology* 135: 655–662, 1980.

Jokinen-Salmela H, **Melkas S**, **Ylikoski R**, **Pohjasvaara T**, **Kaste M**, **Erkinjuntti T**, **Hietanen M**. Post-stroke cognitive impairment is common even after successful clinical recovery. *Eur J Neurol* 22: 1288–1294, 2015.

Jorgensen HS, **Nakayama H**, **Raaschou HO**, **Olsen TS**. Recovery of walking function in stroke patients: The Copenhagen stroke study. *Arch Phys Med Rehabil* 76: 27–32, 1995a.

Jorgensen HS, **Nakayama H**, **Raaschou HO**, **Vive-Larsen J**, **Stoier M**, **Olsen TS**. Outcome and time course of recovery in stroke. Part II: Time course of recovery. The Copenhagen Stroke Study. *Arch Phys Med Rehabil* 76: 406–412, 1995b.

Kernan WN, **Viscoli CM**, **Makuch RW**, **Brass LM**, **Horwitz RI**. Stratified randomization for clinical trials. *J Clin Epidemiol* 52: 19–26, 1999.

Klassen T, **Simpson L**, **Lim S**, **Louie D**, **Parappilly B**, **Sakakibara B**, **Zbogar D**, **Eng J**. "Stepping Up" activity poststroke: ankle-positioned accelerometer can accurately record steps during slow walking. *Phys Ther* 96: 355–360, 2015.

Kozlowski DA, **James DC**, **Schallert T**. Use-dependent exaggeration of neuronal injury after unilateral sensorimotor cortex lesions. *J Neurosci* 16: 4776–4786, 1996.

Krakauer JW, **Carmichael ST**, **Corbett D**, **Wittenberg GF**. Getting Neurorehabilitation Right: What Can Be Learned From Animal Models? *Neurorehabil Neural Repair* 26: 923–931, 2012.

Krueger H, **Koot J**, **Hall RE**, **O'Callaghan C**, **Bayley M**, **Corbett D**. Prevalence of Individuals Experiencing the Effects of Stroke in Canada: Trends and Projections. *Stroke* 46: 2226–2231, 2015.

Kugler C, **Altenhöner T**, **Lochner P**, **Ferbert A**. Does age influence early recovery from ischemic stroke? A study from the Hessian Stroke Data Bank. *J Neurol* 250: 676–681, 2003.

Kwakkel G, **Van Peppen R**, **Wagenaar RC**, **Dauphinee SW**, **Richards C**, **Ashburn A**, **Miller K**, **Lincoln N**, **Partridge C**, **Wellwood I**, **Langhorne P**. Effects of augmented exercise therapy time after stroke: A meta-analysis. *Stroke* 35: 2529–2536, 2004.

Lackland DT, **Roccella EJ**, **Deutsch AF**, **Fornage M**, **George MG**, **Howard G**, **Kissela BM**, **Kittner SJ**, **Lichtman JH**, **Lisabeth LD**, **Schwamm LH**, **Smith EE**, **Towfighi A**. Factors influencing the decline in stroke mortality: A statement from the American Heart Association/American Stroke Association. *Stroke* 45: 315–353, 2014.

Lang C, **Strube M**, **Bland M**, **Waddell K**, **Cherry-Allen K**, **Nudo R**, **Dromerick A**, **Birkenmeier R**. Dose-response of task-specific upper limb training in people at least 6 months post stroke: A Phase II, single-blind, randomized, controlled trial. *Ann. Neurol.* (2016). doi: 10.1002/ana.24734.

Lang CE, **MacDonald JR**, **Gnip C**. Counting repetitions: an observational study of outpatient therapy for people with hemiparesis post-stroke. *J Neurol Phys Ther* 31: 3–10, 2007.

Langhammer B, **Lindmark B**, **Stanghelle JK**. Physiotherapy and physical functioning post-stroke: Exercise habits and functioning 4 years later? Long-term follow-up after a 1-year long-term intervention period: A randomized controlled trial. *Brain Inj* 28: 1396–1405, 2014.

Lohse KR, **Lang CE**, **Boyd LA.** Is more better? Using metadata to explore dose-response relationships in stroke rehabilitation. *Stroke* 45: 2053–2058, 2014.

MacKay-Lyons M, **McDonald A**, **Matheson J**, **Eskes G**, **Klus MA**. Dual effects of body-weight supported treadmill training on cardiovascular fitness and walking ability early after stroke: a randomized controlled trial. *Neurorehabil Neural Repair* 27: 644–53, 2013.

MacKay-Lyons MJ, **Makrides L**. Cardiovascular stress during a contemporary stroke rehabilitation program: Is the intensity adequate to induce a training effect? *Arch Phys Med Rehabil* 83: 1378–1383, 2002.

Mackay CP, **Kuys SS**, **Brauer SG**. The Effect of Aerobic Exercise on Brain-Derived Neurotrophic Factor in People with Neurological Disorders: A Systematic Review and Meta-Analysis. *Neural Plast* 2017, 2017.

Mansfield A, **Wong JS**, **Bryce J**, **Brunton K**, **Inness EL**, **Knorr S**, **Jones S**, **Taati B**, **McIlroy WE**. Use of Accelerometer-Based Feedback of Walking Activity for Appraising Progress With Walking-Related Goals in Inpatient Stroke Rehabilitation: A Randomized Controlled Trial. *Neurorehabil Neural Repair* 29: 847–57, 2015.

Martin J, **Krc K**, **Mitchell E**, **Eng J**, **Noble J**. Pedometer accuracy in slow walking older adults. *Int J Ther Rehabil* 19: 1–7, 2012.

Mees M, **Klein J**, **Yperzeele L**, **Vanacker P**, **Cras P**. Predicting discharge destination after stroke: A systematic review. *Clin Neurol Neurosurg* 142: 15–21, 2016.

Mehrholz J, **Wagner K**, **Rutte K**, **Meibner D**, **Pohl M**. Predictive Validity and Responsiveness of the Functional Ambulation Category in Hemiparetic Patients After Stroke. *Arch Phys Med Rehabil* 88: 1314–1319, 2007.

Mittmann N, **Seung SJ**, **Hill MD**, **Phillips SJ**, **Hachinski V**, **Coté R**, **Buck BH**, **Mackey A**, **Gladstone DJ**, **Howse DC**, **Shuaib A**, **Sharma M**. Impact of disability status on ischemic stroke costs in Canada in the first year. *Can J Neurol Sci* 39: 793–800, 2012.

Mudge S, **Stott NS**, **Walt SE**. Criterion Validity of the StepWatch Activity Monitor as a Measure of Walking Activity in Patients After Stroke. *Arch Phys Med Rehabil* 88: 1710–1715, 2007.

Murphy TH, **Corbett D**. Plasticity during stroke recovery: from synapse to behaviour. *Nat Rev Neurosci* 10: 861–872, 2009.

Nasreddine ZS, **Phillips NA**, **Bédirian V**, **Charbonneau S**, **Whitehead V**, **Collin I**, **Cummings JL**, **Chertkow H**. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 53: 695–699, 2005.

National Institute of Neurological Disorders and Stroke. National Institute of Neurological Disorders and Stroke: Stroke Rehabilitation Information [Online]. 2014. https://stroke.nih.gov/documents/Post-Stroke_Rehabilitation_english_brochure.pdf.

Nudo RJ. Adaptive plasticity in motor cortex: Implications for rehabilitation after brain injury. *J Rehabil Med* May: 7–10, 2003.

Nudo RJ, **Plautz EJ**, **Frost SB**. Role of adaptive plasticity in recovery of function after damage to motor cortex. *Muscle and Nerve* 24: 1000–1019, 2001.

Oberlin LE, **Waiwood AM**, **Cumming TB**, **Marsland AL**, **Bernhardt J**, **Erickson KI**. Effects of Physical Activity on Poststroke Cognitive Function: A Meta-Analysis of Randomized Controlled Trials. *Stroke* 48: 3093–3100, 2017.

Outermans JC, **van Peppen RPS**, **Wittink H**, **Takken T**, **Kwakkel G**. Effects of a high-intensity task-oriented training on gait performance early after stroke: a pilot study. *Clin Rehabil* 24: 979–987, 2010.

Page SJ, **Schmid AA**, **Harris JE**. Optimizing Language for Stroke Motor Rehabilitation: Recommendations from the ACRM Stroke Movement Interventions Subcommittee. *Arch Phys Med Rehabil* 93: 1395–1399, 2012.

Pang M, **Eng J**, **Dawson A**, **Gylfadóttir S**. The use of aerobic exercise training in improving aerobic capacity in individuals with stroke: a meta-analysis. [Online]. *Clin Rehabil* 20: 97–111, 2006.

Pang M, **Eng J**, **Dawson AS**, **McKay H**, **Harris JE**. A Community-Based Fitness and Mobility Exercise Program for Older Adults with Chronic Stroke: A Randomized, Controlled Trial. *J Am Geriatr Soc* 53: 1667–1674, 2005.

Paolucci S, **Antonucci G**, **Grasso MG**, **Bragoni M**, **Coiro P**, **De Angelis D**, **Fusco FR**, **Morelli D**, **Venturiero V**, **Troisi E**, **Pratesi L**. Functional Outcome of Ischemic and Hemorrhagic Stroke Patients after Inpatient Rehabilitation: A Matched Comparison. *Stroke* 34: 2861–2865, 2003.

Perera S, **Mody SH**, **Woodman RC**, **Studenski SA.** Meaningful change and responsiveness in common physical performance measures in older adults. *J Am Geriatr Soc* 54: 743–749, 2006.

Perry J, **Garrett M**, **Gronley JK**, **Mulroy SJ**. Classification of walking handicap in the stroke population. *Stroke* 26: 982–989, 1995.

Ploughman M, **Austin MW**, **Glynn L**, **Corbett D**. The effects of poststroke aerobic exercise on neuroplasticity: a systematic review of animal and clinical studies. *Transl Stroke Res* 6: 13–28, 2015.

van de Port IGL, **Wood-Dauphinee S**, **Lindeman E**, **Kwakkel G**. Effects of exercise training programs on walking competency after stroke: a systematic review. *Am J Phys Med Rehabil* 86: 935–951, 2007.

Prabhakaran S, **Ruff I**, **Bernstein RA**. Acute Stroke Intervention: A Systematic Review. *JAMA - J Am Med Assoc* 313: 1451, 2015.

Public Health Agency of Canada. *Tracking Heart Disease and Stroke in Canada, 2009.* 2009.

Rand D, **Eng J**. Disparity between functional recovery and daily use of the upper and lower extremities during subacute stroke rehabilitation. *Neurorehabil Neural Repair* 26: 76–84, 2012.

Salbach NM, **Mayo NE**, **Higgins J**, **Ahmed S**, **Finch LE**, **Richards CL**. Responsiveness and predictability of gait speed and other disability measures in acute stroke. *Arch Phys Med Rehabil* 82: 1204–1212, 2001.

Salbach NM, **Mayo NE**, **Wood-Dauphinee S**, **Hanley JA**, **Richards CL**, **Côté R**. A task-orientated intervention enhances walking distance and speed in the first year post stroke: a randomized controlled trial. *Clin Rehabil* 18: 509–519, 2004.

Seshadri S, **Beiser A**, **Kelly-Hayes M**, **Kase CS**, **Au R**, **Kannel WB**, **Wolf PA.** The lifetime risk of stroke: Estimates from the framingham study. *Stroke* 37: 345–350, 2006.

Silcocks P. How many strata in an RCT A flexible approach. *Br J Cancer* 106: 1259–1261, 2012.

Stoller O, **de Bruin ED**, **Knols RH**, **Hunt KJ**. Effects of cardiovascular exercise early after stroke: systematic review and meta-analysis. *BMC Neurol* 12: 1, 2012.

Sullivan J, **Espe L**, **Kelly A**, **Veilbig L**, **Kwasny M**. Feasibility and Outcomes of a Community-Based, Pedometer-Monitored Walking Program in Chronic Stroke: A Pilot Study. *Top Stroke Rehabil* Mar-Apr: 101–10, 2014.

Sullivan KJ, **Brown DA**, **Klassen T**, **Mulroy S**, **Ge T**, **Azen SP**, **Winstein CJ**. Effects of Task-Specific Locomotor and Strength Training in Adults Who Were Ambulatory After Stroke: Results of the STEPS Randomized Clinical Trial. *Phys Ther* 87: 1580–1602, 2007.

Takacs J, **Pollock CL**, **Guenther JR**, **Bahar M**, **Napier C**, **Hunt MA.** Validation of the Fitbit One activity monitor device during treadmill walking. *J Sci Med Sport* 17: 496–500, 2014.

Tamez E, **Myerson J**, **Morris L**, **White DA**, **Baum C**, **Connor LT**. Assessing executive abilities following acute stroke with the trail making test and digit span. *Behav Neurol* 24: 177–185, 2011.

Teasell R, **Richardson M**, **Allen L**, **Hussein N**. Evidence-Based Review of Stroke Rehabilitation [Online]. *16th Ed.* 2015. http://www.ebrsr.com/.

Toglia J, **Fitzgerald KA**, **O'Dell MW**, **Mastrogiovanni AR**, **Lin CD**. The mini-mental state examination and montreal cognitive assessment in persons with mild subacute stroke: Relationship to functional outcome. *Arch Phys Med Rehabil* 92: 792–798, 2011.

Veerbeek JM, **Van Wegen E**, **Van Peppen R**, **Van Der Wees PJ**, **Hendriks E**, **Rietberg M**, **Kwakkel G**. What is the evidence for physical therapy poststroke? A systematic review and meta-analysis. *PLoS One* 9: e87987, 2014.

Vickers AJ. Parametric versus non-parametric statistics in the analysis of randomized trials with non-normally distributed data. *BMC Med. Res. Methodol.* (2005). doi: 10.1186/1471-2288-5-35.

Victor M, **Ropper AH**. *Adam and Victor's Principles of Neurology*. Seventh. Mc-Graw Hill Medical Publishing Division, 2001.

Ward NS. Restoring brain function after stroke — bridging the gap between animals and humans. *Nat Rev Neurol* 13: 244–255, 2017.

Westfall JM, **Mold J**, **Fagnan L**. Practice-based research--"Blue Highways" on the NIH roadmap. *JAMA* 297: 403–406, 2007.

Williams LS, **Brizendine EJ**, **Plue L**, **Bakas T**, **Tu W**, **Hendrie H**, **Kroenke K**. Performance of the PHQ-9 as a screening tool for depression after stroke. *Stroke* 36: 635–638, 2005.

Winstein CJ, **Stein J**, **Arena R**, **Bates B**, **Cherney LR**, **Cramer SC**, **Deruyter F**, **Eng JJ**, **Fisher B**, **Harvey RL**, **Lang CE**, **MacKay-Lyons M**, **Ottenbacher KJ**, **Pugh S**, **Reeves MJ**, **Richards LG**, **Stiers W**, **Zorowitz RD**. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke* 47: e98–e169, 2016a.

Winstein CJ, **Wolf SL**, **Dromerick AW**, **Lane CJ**, **Nelsen MA**, **Lewthwaite R**, **Cen SY**, **Azen SP**. Effect of a task-oriented rehabilitation program on upper extremity recovery following motor stroke the ICARE randomized clinical trial. *JAMA* 315: 571–581, 2016b.

Wolf SL, **Winstein CJ**, **Miller JP**, **Morris D**. Effect of Constraint-Induced Movement. 296: 2095–2104, 2006.

Zhang C, **Kasner S**. Diagnosis, prognosis, and management of cryptogenic stroke. *F1000Research* 5: 1–6, 2016.

Zinn S, **Bosworth HB**, **Hoenig HM**, **Swartzwelder HS**. Executive Function Deficits in Acute Stroke. *Arch Phys Med Rehabil* 88: 173–180, 2007.

Appendices

Appendix A Chapter 2: Study Participant Data Form

Fitbit Study
Participant Data Form #1

Lab Person/Assistant's Initials: __/___(First/Last) Assessment Date: ___ _____(MM/DD/YR)

TO BE COMPLETED BY THE PARTICIPANT:

1. Participant's ID:_____

2. Gender: M□ F□

3. Date of Birth: M____D_____Yr____

4. Date of Stroke: M____D____YR_____

5. Do you have any other known medical conditions: □Yes □No

   If yes, please write down the name(s) of the medical condition:

_____

_____

6. Have you had any surgery in the past 12 months: □Yes □No

   If yes, please write down the type of surgery and date:

_____

_____

STUDY CRITERIA (Lab Person)

1. Participants meets all inclusion criteria: □ Yes □ No
   a) At least 3 months post-stroke
   b) Able to follow 3 step commands
   c) Able to walk independently for at least 100 feet with an orthotic/assistive device
   d) No MAJOR medical conditions (MS, PD, angina, heart attack)
   e) No MAJOR surgery in the past 12 month (hip replacement, heart surgery)
   f) ≥ 19 years of age

2. Participant signed consent form? □ Yes □ No

WALKING ANALYSIS (Assistant)

1. Most Affected Side: □ R □ L □ Weakness on both sides
2. Limb(s) Affected: □ UE □ LE
3. Assistive Device: □ None
   □ Single point cane
   □ Quad cane
   □ 2 wheeled walker
   □ 4 wheeled walker
   □ Other_____
4. Ankle-Foot Orthosis (AFO): □ Yes □ No
5. Walking Pattern (check all that are appropriate):
   □ paretic knee hyperextension in stance
   □ paretic knee flexion in stance
   □ paretic pelvic hike and/or circumduction in swing
   □ minimal paretic hip flexion and knee flexion in swing
   □ paretic foot clearance difficulties during swing (e.g., not wearing AFO)
   □ ataxic gait
   □ paretic arm spasticity/flexion/add/int rotation (limited hemiparetic arm swing)
   □ shuffling gait
   □ normal gait patterns, but slow

Self-Selected Walking Speed (15 m distance):			**(seconds)**		**m/s**
Walking Speed	**Time (Seconds)**	**STEPS: HIP Fitbit Start**	**End**	**STEPS: ANKLE Fitbit Start**	**End**	**Video (Steps)**
0.3 m/s						
0.5 m/s						
0.4 m/s						
0.6 m/s						
0.8 m/s						
0.9 m/s						
0.7 m/s						

Appendix B Chapter 4: Participant Screening Data Form

1. Interviewer's Initials: __ __ (First/Last) Interview Date: M____D_____Yr____
2. Screening ID: _____
3. Participant signed consent form? Yes No
4. Date of Consent: M_____D_____Yr_____ □N/A
5. Sex: M□ F□
6. Date of Birth: M____ Yr____ Age:_____
7. Date of Stroke: M____D_____Yr____
8. Date of Admission to Inpatient Rehabilitation: M_____D_____Yr_____
9. Brain Hemisphere Affected: □R □L
10. Limb(s) affected: □R □L □UE □LE □No paresis
11. Stroke Type: □Infarct □Hemorrhagic
    11a. If infarct, lacunar: □Yes □No
12. Stroke Location: □Cortical □Sub-cortical □Unknown
13. Other co-existing conditions: □Hypertension □Diabetes Mellitus □Arthritis
    □Respiratory Disease □Other
    Comments:_____

14. Inclusion Criteria:
    Participant is included in the study if:
    a) Yes No Within 10 weeks post hemorrhagic or ischemic CVA with hemiparesis (confirmed by medical chart or motor assessment)
    b) Yes No **Pre-stroke** disability <2 (less than 2) on the Modified Rankin Scale.
    0 - No symptoms.
    1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
    2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
    3 - Moderate disability. Requires some help, but able to walk unassisted.
    4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
    5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
    6 - Dead.

    c) Yes No Able to ambulate at least 15 feet (5 m distance). May use assistive and/or orthotic device and maximum one person assist.
    d) Yes No Overground walking speed less than 1.0m/s (over a 5 m distance)
    e) Yes No Able to understand and follow directions
    f) Yes No Greater than or equal to 19 years of age.

15. Exclusion Criteria:

Participant is excluded in the study if:

a) Yes No Pre-stroke health included a gait disorder or disease that affected ambulation (musculoskeletal conditions, amputation, etc.)

b) Yes No Pre-stroke health included a neurological condition (such as Parkinson's disease or Multiple Sclerosis) or other serious medical condition (active cancer)

c) Yes No Current health includes serious medical condition (uncontrolled diabetes, uncontrolled hypertension, active cancer, etc.)

d) Yes No Excessive pain in the body/joint preventing participation in an exercise intervention.

e) Yes No Participating in an experimental drug field study.

f) Yes No Participating in another formal exercise rehabilitation clinical trial.

16. □ Yes □ No Participant meets study criteria and would like to proceed with study.

17. □ Yes □ No Participant meets study criteria, but does not want to proceed with study.
Comment:_____

18. □ Yes □ No Participant does not meet study criteria.
Comment:_____

Other comments:

Appendix C Chapter 4: DOSE Study Evaluation Protocols and Forms

OUTCOME OF EVALUATIONS AND ESTIMATED TIME

- Recommended order (ascending to descending) for Baseline/Post/6 and 12 month evaluations to allow for the participant to be fully rested for walking measures.

Screening Evaluation	Baseline Evaluation	Post Evaluation	6 month Evaluation	12 month Evaluation
Consent	MOCA *8 minutes*	MOCA	MOCA	MOCA
Participant Screening Form	6 minute walk *10 minutes*	6 minute walk	6 minute walk	6 minute walk
Cardiac Stress Test (if participant consents and meets all study criteria)	Trails A+B *10 minutes*	Trails A+B	Trails A+B	Trails A+B
Participant Baseline Information Form	5 meter walk (comfortable) *5 minutes*	5 meter walk (comfortable)	5 meter walk (comfortable)	5 meter walk (comfortable)
Participant Personal Information Form	Berg Balance Scale *15 minutes*	Berg Balance Scale	Berg Balance Scale	Berg Balance Scale
SAM Calibration (or at Baseline)	Isometric Knee Extension *5minutes*	Isometric Knee Extension	Isometric Knee Extension	Isometric Knee Extension
	EQ-5D-5L *5 minutes*	EQ-5D-5L	EQ-5D-5L	EQ-5D-5L
	DSST *3 minutes*	DSST	DSST	DSST
	PHQ-9 *10 minutes*	PHQ-9	PHQ-9	PHQ-9
	NIH Stroke Scale *5 minutes*			
	Godin Leisure Time Exercise Questionnaire *1 minute*			
	Participant Randomization Form	6 and 12 month Follow Up Information Form	6 and 12 month Follow Up Information Form	6 and 12 month Follow Up Information Form
			Step Activity Monitor Form	Step Activity Monitor Form
	Total est. time: 87 minutes	**Total est. time: 81 minutes**	**Total est. time: 71 minutes**	**Total est. time: 71 minutes**

IMPAIRMENT MEASURES

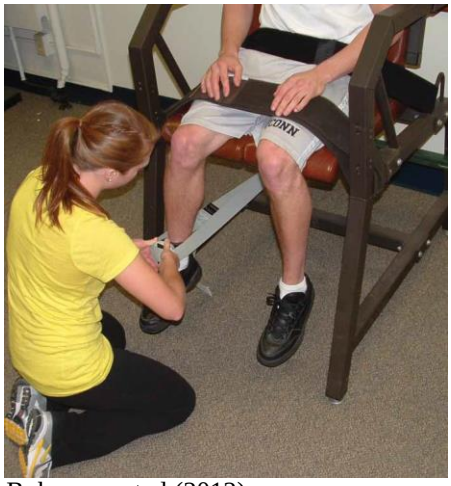
Isometric Knee Extension Using Hand-Held Dynamometry

Protocol

Description: Reliable measure to assess lower extremity strength in individuals post-stroke.

Participant position:

- Have the participant sit on a firm chair with the back of the chair positioned against a wall.
- Ensure the participant's bottom is at the back of the chair so that the thighs are maximally supported. If necessary, put a belt around the participant's waist and attach it behind the chair.
- Position the participant's bilateral hips/knees in 90 degrees flexion, with his/her feet dangling just above the floor. Adjust the participant's position (pillow behind the back, higher or lower chair) to ensure this position is attained.
- The participant's upper extremities should rest comfortably in his/her lap.


Bohannon et al (2012)

Procedure:

1. Assess the participant's NON-PARETIC lower extremity first.
2. Position the testing belt around the participant's distal tibia and chair so that it is taut in the lower extremity testing position (see above photo).
3. Provide manual resistance to the participant's distal anterior tibia, just above the malleoli.
4. With the participant's hip/knee in 90 degrees flexion and arms resting in lap, give the participant the following instructions:
   "Try to straighten your leg. I will resist you from moving it. Hold this for 5 seconds"
   (This is a maximal isometric contraction of knee extension). Do a trial of the contraction without the use of the dynamometer.
5. After the trial contraction, put the hand-held dynamometer anterior, on the distal tibia, just proximal to the malleoli and position the testing belt around it.
6. Provide resistance to permit an ISOMETRIC contraction. Hold for 5 seconds. Allow the participant to rest 30 seconds between trials. Repeat 3 times.
7. Record the information on the data form.
8. Repeat the above procedure on the PARETIC lower extremity.
9. The therapist can provide distal stability to the paretic thigh (just above the knee) to decrease synergistic movements during the contraction.
10. Record as "0" if the participant is unable to obtain the testing position or generate an isometric contraction.

Reference: Pang MY et al. (2005); Bohannon et al. (2012)

Data Form

Isometric Knee Extension

1. Participant's Study ID: _____

2. Evaluation: ___1. Baseline
___2. Post-Treatment
___3. 6 month follow up
___4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___
Month Day Year

4. Evaluator's Initials: __ ___
First/Last

Paretic lower extremity: ☐ R ☐ L Trial 1 __ ___ ___.___ newtons/kg
Trial 2 __ ___ ___.___ newtons/kg
Trial 3 __ ___ ___.___ newtons/kg

Non-paretic lower extremity: ☐ R ☐ L Trial 1 __ ___ ___.___ newtons/kg
Trial 2 __ ___ ___.___ newtons/kg
Trial 3 __ ___ ___.___ newtons/kg

NIH Stroke Scale (NIHSS)

Protocol

- The **National Institutes of Health Stroke Scale**, or **NIH Stroke Scale** (**NIHSS**), is a tool used by healthcare providers to objectively quantify the impairment caused by a stroke.
- The NIHSS is composed of 11 items, each of which scores a specific ability between a 0 and 4.
- For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment.
- The individual scores from each item are summed in order to calculate a patient's total NIHSS score. The maximum possible score is 42, with the minimum score being a 0.
- Assessment of the items in the scale may be obtained from other aspects of the DOSE Baseline evaluation.
- If the scale needs to be completed in its entirety, then:
  - Administer the stroke items in the order listed
  - Record performance on the participant's first attempt. Scores should reflect what the participant does, not what the clinician thinks the participant can do.
  - Follow the instructions for each exam technique.
  - Do not go back and change scores.
- If necessary, use the materials in the Appendix (pages 12-14) to complete the tasks in the "Best Language" and "Dysarthria" Domains

Score	Stroke Severity
0	No Stroke Symptoms
1-4	Minor Stroke
5-15	Moderate Stroke
16-20	Moderate to Severe Stroke
21-42	Severe Stroke

References: http://www.ninds.nih.gov/doctors/NIH_Stroke_Scale_Booklet.pdf
http://en.wikipedia.org/wiki/National_Institutes_of_Health_Stroke_Scale

Data Form

1. **Participant's Study ID: _____**
2. **Evaluation: ___1.** Baseline

3. **Evaluation Date: ___ ___/___ ___/___ ___ ___ ___**
   Month Day Year

4. **Evaluator's Initials: __ ___**
   First/Last

MEASUREMENT INSTRUCTIONS

- Administer the stroke items in the order listed
- Record performance on the patient's first attempt. Scores should reflect what the patient does, not what the clinician thinks the patient can do.
- Follow the instructions for each exam technique.
- Do not go back and change scores.

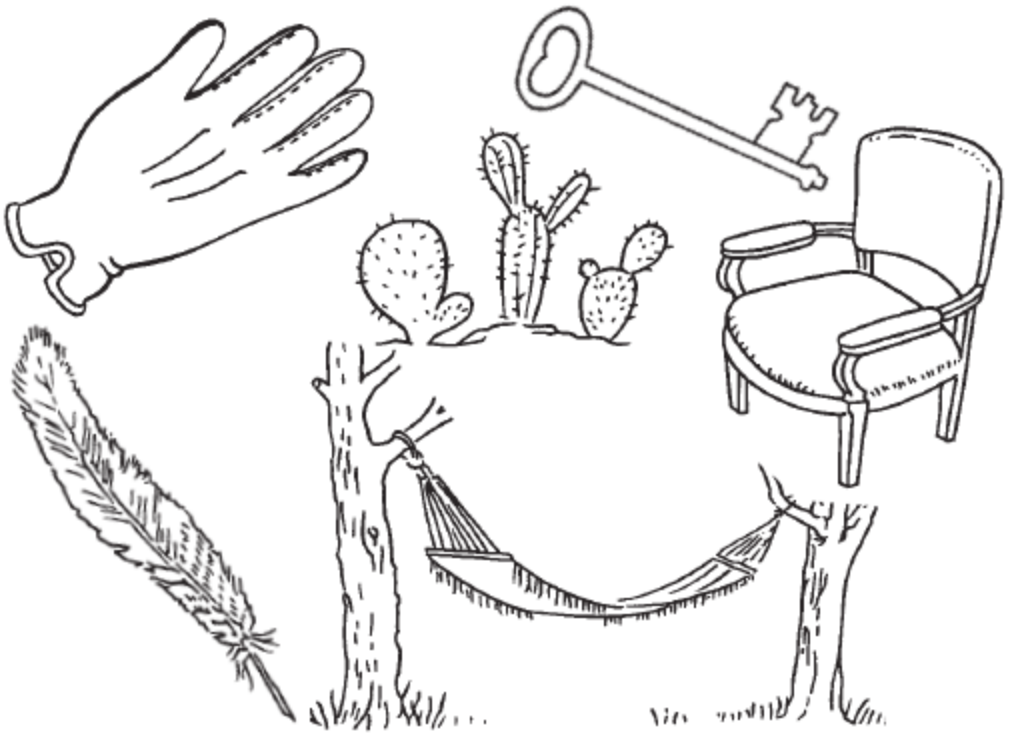
Item	Instructions	Scale (Circle the correct answer)
Level of Consciousness		0: **Alert, keenly responsive** 1: **Not alert;** but arousable by minor stimulation to obey, answer, or respond. 2: **Not alert;** requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements. 3: **Responds only with reflex motor or autonomic effects** or totally unresponsive, flaccid and areflexic.
Level of Consciousness Questions	Ask the patient the month and his/her age. The answer must be correct – there is not partial credit for being close. Aphasic patients will score 2	0: **Answers** both questions correctly 1: **Answers** one question correctly 2: **Answers** neither question correctly
Level of Consciousness	Ask the patient to: 1. Open and close the eyes, then	0: **Performs** both tasks correctly 1: **Performs** one task correctly

Commands	2. Grip and release the non-paretic hand Credit is given if an unequivocal attempt is made but not completed due to weakness	2: **Performs** neither task correctly	
Best Gaze	Test horizontal eye movements	0: **Normal** 1: **Partial gaze palsy;** gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2: **Forced deviation**; or total gaze paresis is not overcome by the oculocephalic maneuver.	
Visual	Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat. Score 1 only if a clear cut asymmetry if found.	0: **No visual loss** 1: **Partial hemianopia** 2: **Complete hemianopia** 3: **Bilateral hemianopia** (blind including cortical blindness)	
Facial Palsy	Ask the patient to: 1. Show teeth, then 2. Close eyes Score symmetry of movement	0: **Normal** symmetrical movements 1: **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling) 2: **Partial paralysis** (total or near-total paralysis of lower face) 3: **Complete paralysis** of one or both sides (absence of facial movement in the upper and lower face).	
Motor Arm	Test both UEs, starting with the non-paretic UE. <u>Choose a position:</u> 1.Sitting with 90 degrees shoulder flexion, palm down OR 2. Supine, 45 degrees shoulder flexion, palm down. Have the patient hold the arm in the position for 10 seconds. Drift is scored if the arm falls before 10 seconds	0: **No drift;** limb holds 45 degrees (or 90) for full 10 seconds 1: **Drift;** limb holds 45 degrees (or 90), but drifts down before full 10 seconds; does not hit bed or other support 2: **Some effort against gravity;** limb cannot get to or maintain (if cued) 45 degrees (or 90), drifts down to bed, but has some effort against gravity. 3: **No effort against gravity;** limb falls 4: **No movement.** 5: **Amputation** or joint fusion; explain.	
		Left UE Score:	**Right UE Score:**

<table>
<tr><td rowspan="2">Motor Leg</td><td rowspan="2">Test both LEs, starting with the non-paretic LE, in SUPINE.
Place the participant’s extended leg in 30 degrees hip flexion.
Have the patient hold the leg in this position for 5 seconds.
Drift is scored if the leg falls before 5 seconds.</td><td colspan="2">0: No drift; leg holds 30 degree position for full 5 seconds
1: Drift; leg falls by the end of the 5 second period, but does not hit the bed.
2: Some effort against gravity; leg falls to bed by 5 seconds but has some effort against gravity
3: No effort against gravity; leg falls to bed immediately.
4: No movement.
5: Amputation or joint fusion; explain.</td></tr>
<tr><td>Left LE Score:</td><td>Right LE Score:</td></tr>
<tr><td>Limb Ataxia</td><td>This item is aimed at finding evidence of a unilateral cerebellar lesion
Do a finger-nose-finger test with both UEs
Ataxia is scored only in proportion to weakness and is absent in the patient who is paralyzed.</td><td colspan="2">0: Absent
1: Present in one limb
2: Present in two limbs
UN: Amputation or joint fusion: explain.</td></tr>
<tr><td>Sensory</td><td>Only sensory loss attributed to stroke is scored as abnormal.
Examiner should test as many body areas (arms-not hands, legs, trunk,face) as needed to accurately check for hemi-sensory loss.</td><td colspan="2">0: Normal; no sensory loss
1: Mild-to-moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched.
2: Severe or total sensory loss; patient is not aware of being touched in the face, arm, and leg.</td></tr>
</table>

Best Language	Have the patient: 1. Describe what is happening in the attached picture. 2. Name the items on the attached naming sheet. 3. Read from the attached list of sentences Comprehension is judged from responses here, as well as to the other commands in the examination.	0: **No aphasia;** normal. 1: **Mild-to-moderate aphasia;** some obvious loss of fluency or facility of comprehension without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2: **Severe aphasia;** all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response.
Dysarthria	If the patient's speech is thought to be normal, have the patient read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated.	0: **Normal** 1: **Mild to Moderate Dysarthria;** patient slurs at le3ast some words and at worst, can be understood with some difficulty. 2: **Severe dysarthria;** patient's speech is so slurred as to be unintelligible in the absence of or out of proporation to any dysphasia, or is mute/anarthric.
Extinction and Inattention (formerly Neglect)	Neglect can be identified during the prior testing.	0: **No abnormality** 1: **Visual, tactile, auditory, spatial or personal inattention**, or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2: **Profound hemi-inattention or extinction to more than on modality;** does not recognize own hand or orients to only one side of space.
TOTAL SCORE:		

Appendix Forms



You know how.

Down to earth.

I got home from work.

Near the table in the dining room.

They heard him speak on the
radio last night.

MAMA

TIP – TOP

FIFTY – FIFTY

THANKS

HUCKLEBERRY

BASEBALL PLAYER

MOBILITY MEASURES

Six-Minute Walk

Protocol

REQUIRED EQUIPMENT

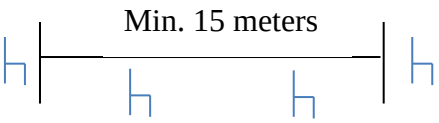
1. Stopwatch
2. Lap counter
3. Measured and marked course
4. Chairs set up along the walking course
5. Data form and 6 minute walk instructions on a clipboard
6. Automatic blood pressure cuff
7. Telephone

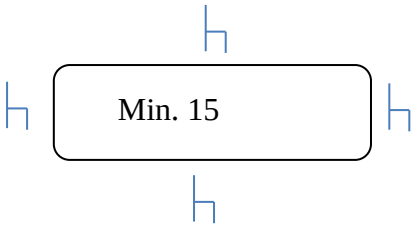
PARTICIPANT PREPARATION

1. Comfortable clothing should be worn.
2. Appropriate shoes for walking should be worn.
3. Participants should use their usual walking aids during the test (cane, walker, orthosis, etc.)
4. The participant's usual medical regimen should be continued.
5. A light meal is acceptable before early morning or early afternoon tests. Participants should not have exercised vigorously within 2 hours of beginning the test.

ADMINISTRATION:

1. A measured course indoors is established with a minimum length of 15 meters in a straightaway. Position chairs around the distance as appropriate.





2. Baseline/post/follow-up testing should be performed about the same time of day to minimize intraday variability.

3. A "warm-up" period before the test is NOT permitted.

4. The 6 minute walk will be completed after the MOCA, so the participant will have rested for about 10 minutes in a chair. At the completion of the MOCA, prior to starting the 6 minute walk, measure the participant's pulse and blood pressure, check for contraindications to testing, and make sure that the participant's clothing and shoes are appropriate. Record this information on the data form.

   CONTRAINDICATIONS to starting the 6 minute walk:
   1. Unstable angina and/or MI during the previous month (ATS guidelines)
      Resting HR > 120 bpm; SBP>180 mm Hg; DBP>100 mm Hg (ATS guidelines)

5. Tell the participant the following instructions:

- "The object of this test is to walk AS FAR AS POSSIBLE in 6 minutes."
  - *If appropriate for the participant:* "You are not allowed to jog or run."
- You will walk back and forth in this hallway around the cones (or around the "track").
- You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall or sit in the chair while resting, then continue walking whenever you feel able as your time will not stop when you are resting.
- I will stay with you as we walk and you are allowed to use your assistive device (walker, cane, etc.).
- We will not talk during the walk as this may affect your performance.
- I will inform you of the time that has passed.
- Please let me know if you are uncomfortable or have pain. The idea is for you to walk at a comfortable pace but cover as much ground as possible in the six minutes. Do you have any questions? I will now show you how you are going to do it."

6. Demonstrate by walking one lap yourself. Walk and pivot around a cone/course briskly. "Are you ready to do that? Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes."

7. Put a transfer belt on the participant if appropriate. Position the participant at the starting line and stand beside him/her.

8. Provide the minimum amount of manual assistance necessary to maintain patient safety.

9. When you instruct the participant to "GO", start the timer. Stay beside the participant for the entire test period. When the participant is walking, walk behind them and on their affected side. The test should be stopped for any of the following reasons:
   a) Participant complains of angina symptoms (eg: chest pain or tightness)

   b) Participant exhibits any of the following symptoms:

      - Light-headedness
      - Confusion
      - Ataxia, staggering unsteadiness
      - Pallor
      - Cyanosis
      - Nausea
      - Marked dyspnea
      - Unusual fatigue
      - Signs of peripheral circulatory insufficiency
      - Claudication or other significant pain
      - Facial expression signifying distress

*If the test is terminated for a) or b), the participant's nurse should be immediately notified.

10. The participant and tester should not be distracted during the test. The tester should use an even tone of voice when providing the standard phrases of encouragement. The tester must watch the participant closely and provide close supervision. The tester should only provide hands-on assistance to the participant if he/she is at risk for a fall/maintain safety.

11. Only the following verbal encouragement can be provided to the participant during the test. Do not use other words of encouragement (or body language to speed up).
    1. At 1 minute: Tell the participant (in even tones): "You are doing well. You have 5 minutes to go."
    2. At 2 minutes: "Keep up the good work. You have 4 minutes to go."
    3. At 3 minutes: "You are doing well. You are halfway done."
    4. At 4 minutes: "Keep up the good work. You have only 2 minutes left."
    5. At 5 minutes: "You are doing well. You have only 1 minute to go."
    6. At 5 minutes, 45 seconds: "In a moment I'm going to tell you to stop. When I do, just stop right where you are."

    When the timer rings (or buzzes), tell the participant to "Stop!" Have a chair available so the participant can sit down. Mark the spot where the participant stopped by placing a bean bag or a piece of tape on the floor. Congratulate the participant on good effort and offer a drink of water.

12. If the participant stops walking during the test and needs a rest, say this:
    "You can stop or sit in the chair if you would like; then continue walking whenever you feel able."

    Do not stop the timer.

    If the participant is resting when it is time to provide encouragement change the encouragement statement to:
    "It's been _____ minute(s). Rest as long as you need to and let me know when we can get started again."

    If the subject continues to rest through the next minute, state:
    "_____minute(s) is/are left in the test. You may continue to rest or resume walking when you feel able."
    Repeat this statement at each minute if the participant continues to rest.

    If the participant stops before the 6 minutes are up and refuses to continue (or you decide that they should not continue), wheel the chair over for the participant to sit on, discontinue the walk, and note on the data form the distance, the time stopped, and the reason for stopping pre-maturely.

13. **Post-test:** Calculate the total distance walked, rounding to the nearest meter, and record it on the data form. Also, record the participant's assistive device/orthotic (if necessary) and FAC.

Reference: ATS Statement: Guidelines for the Six-Minute Walk Test (2002)

Data Form

1. Participant's Study ID: _____

2. Evaluation: ___1. Baseline
___2. Post-Treatment
___3. 6 month follow up
___4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___
Month Day Year

4. Evaluator's Initials: __ ___
First/Last

5. Rest HR: _____ ; Rest BP: _____ / _____

6. Distance covered in 6 minutes: _____meters

7. Assistive Device: ___
□ None
□ Single point cane
□ Quad cane
□ 2 wheeled walker
□ Standard walker
□ Other_____

8. Type of AFO: ___
□ None
□ Rigid Plastic (no joint)
□ Rigid Plastic (with joint)
□ Other_____

9. FAC:___
2 Ambulator – Dependent for Physical Assistance Level II
3 Ambulator – Dependent for Physical Assistance Level I
4 Ambulator – Dependent for Supervision
5 Ambulator – Independent, Level surfaces only
6 Ambulator – Independent, Level and non-level surfaces

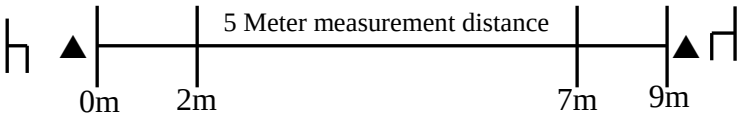
10. Reason for stopping the 6 minute walk:
□Challenging to breathe
□Limb fatigue: L R UE LE
□Feeling of nausea
□Generalized fatigue/whole body
□Mental fatigue
□Feeling of dizziness
□Other (describe):

5 Meter Walk

Protocol

Description: The five meter walk test is a measure of walking speed.
Equipment: Digital stopwatch, tape.
Note: The participant may use an assistive device and/or orthosis for the assessment.
Administration:

1. A measured course indoors is established with a total length of 9 meters. Lines are drawn with tape at 0 meters, 2 meters, 7 meters and 9 meters. Pylon markers can be placed at 0m and 9m.



2. Explain to the participant that he/she is going to walk a distance of 9 meters, two times. Instruct the participant that the two trials will be completed at a "comfortable pace."

3. Explain to the participant that you will be beside him/her while he/she is walking, but will ONLY provide hands-on assistance if his/her safety is a concern. Put a transfer belt on the participant if necessary.

4. Have the participant proceed to the start line (0 meters).
   Instructions:
   - "I am going to measure your comfortable walking speed."
   - "The command will be **"READY, SET, GO…"** and when I say "**GO**", walk in a straight line at a pace which is safe and comfortable for you, until you reach the pylon and I say "**STOP**".
   - "Do you have any questions before we start?"

   If the participant starts before you say **"GO", stop the test and try again.*

5. **START THE STOPWATCH** when the participant's first foot crosses the plane of the **2 meter line** and **STOP THE STOPWATCH** when the participant's first foot crosses the plane of the **7 meter line**. Have the participant continue walking until he/she reaches the chair after the 9 meter line.

6. Record (in seconds – XX.XX) the time it took for the participant to walk the five meter distance between the 2m line and the 7m line.

7. Have the participant sit in the chair at the 9 meter line until he/she feels he/she is adequately rested to repeat the test again.

8. Have the participant repeat the **EXACT SAME procedure** described above for the 2nd trial at a "comfortable pace" - except the participant will be walking from the 9m line to the 0m line. START the stopwatch at the 7m line, and STOP the stopwatch at the 2m line.

9. Record the time (in seconds) for the 2nd trial at a "comfortable pace". The participant can rest in the chair at the 0m line.

10. Record the assistive device, type of AFO (if appropriate) and FAC on the data form.

Reference: Salbach NM et al. (2001)

Data Form

1. Participant's Study ID: _____

2. Evaluation: ___1. Baseline
___2. Post-Treatment
___3. 6 month follow up
___4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___
Month Day Year

4. Evaluator's Initials: __ ___
First/Last

5 METER WALK TEST

Time (in seconds) to walk 5 meters:
"Comfortable" (Self-Selected)Pace:

a. Trial 1: "Comfortable Pace" - Number of seconds: ___ ___ ___.___ ___sec
b. Trial 2: "Comfortable Pace" - Number of seconds: ___ ___ ___.___ ___sec

c. Assistive Device: ___
□ None
□ Single point cane
□ Quad cane
□ 2 wheeled walker
□ Standard walker
□ Other_____

d. Type of AFO: ___
□ None
□ Rigid Plastic (no joint)
□ Rigid Plastic (with joint)
□ Other_____

e) FAC:___
2 Ambulator – Dependent for Physical Assistance Level II
3 Ambulator – Dependent for Physical Assistance Level I
4 Ambulator – Dependent for Supervision
5 Ambulator – Independent, Level surfaces only
6 Ambulator – Independent, Level and non-level surfaces

Functional Ambulation Classification (FAC)

- Rate the participant at the level s/he performs during the 5 meter walk and 6 minute walk.

FAC Level	Ambulation Description	Definition
1	Nonfunctional	Unable to ambulate Ambulates only in parallel bars Requires supervision or physical assistance from > 1 person
2	Dependent, Level II	Requires manual contact of one person during ambulation on level surfaces Manual contact is continuous and necessary to support body weight and/or to maintain balance or assist coordination
3	Dependent, Level I	Requires manual contact of one person during ambulation on level surfaces Manual contact is continuous or intermittent light touch to assist balance or coordination
4	Dependent, Supervision	Ambulation occurs on level surfaces without manual contact of another person Requires stand-by guarding of one person because of poor judgment, questionable cardiac status, or the need for verbal cuing to complete the task
5	Independent, Level Surfaces Only	Ambulate is independent on level surfaces Requires supervision/physical assistance to negotiate stairs, inclines, or unlevel surfaces.
6	Independent, Level and Non-Level Surfaces	Ambulation is independent on unlevel and level surfaces, stairs, and inclines.

(References: Holden et al., 1984; www.rehabmeasures.org)

FUNCTIONAL MEASURES
Berg Balance Scale
Protocol

In most items, the participant is asked to maintain a given position for a specific time. Progressively more points are deducted if the time or distance requirements are not met, if the participant's performance warrants supervision, of if the participant touches an external support or receives assistance from the examiner. Participants should understand that they must maintain their balance while attempting the tasks. The choices of which leg to stand on, which side to transfer to, or how far to reach are left to the participant. Poor judgment will adversely influence the performance and the scoring.

The participant CAN NOT use an assistive device for this test. If the participant wears an orthotic device, this is permitted. The same orthotic device should be worn for all follow-up evaluations on this test.

Equipment required: stopwatch or watch with a second hand, a 30cm (12 inch) measuring tape/ruler that can indicate lengths of 2, 5 and 10 inches (5, 12.5 and 25 cm), chairs used during testing should be of reasonable height. Either a step or a stool height of 6 inches (15cm) may be used for item #12.

- Complete the assessments in the measure. Give instructions as written to the participant for each activity and demonstrate when indicated. See the data form for the instructions.
- The examiner will guard the participant during performance of each task. Assistance will be provided as needed to complete the task and/or prevent a fall.
- Score each activity. If all criteria are not met at a given level, score should be adjusted downward. If physical contact is actually required to keep the participant from falling, then the task would be scored lower (eg: "needs help" or whatever lower category pertains to that particular task).
- **Items should be scored based on the participant's first attempt.** If participant fails the first time but then attempts a 2nd or 3rd time and succeeds, the score corresponding with the first attempt is the score given, unless explicitly indicated otherwise.
- All timing starts when the position for the required task is attained.

Operational definitions:

- **Supervision** refers to standby assistance (no physical contact) that is provided because the person is unsteady and may require physical intervention to keep from falling.
- **Assistance** refers to human contact.
- **Minimal assistance** refers to physical contact in the form of light support or guidance.
- **Moderate-maximal assistance** refers to effort required on the part of the examiner to keep participant from losing balance to help them complete task safely.

References: 1. Smith PS et al (2004)
2. www.rehabmeasures.org (http://www.fallpreventiontaskforce.org/pdf/BergBalanceScale.pdf)

Data Form

1. Participant's Study ID: _____

2. Evaluation: ___1. Baseline
___2. Post-Treatment
___3. 6 month follow up
___4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___
Month Day Year

4. Evaluator's Initials: __ ___
First/Last

1. Sitting to Standing

Instructions: *Please stand up. Try not to use your hands for support*.
4: Able to stand no hands and stabilize independently.
3: Able to stand independently using hands.
2: Able to stand using hands after several tries.
1: Needs minimal assistance to stand or to stabilize.
0: Needs moderate or maximal assistance to stand.

2. Standing Unsupported

Instructions: *Please stand for two minutes without holding*.
4: Able to stand safely 2 minutes.
3: Able to stand 2 minutes with supervision.
2: Able to stand 30 seconds unsupported.
1: Needs several tries to stand 30 seconds unsupported.
0: Unable to stand 30 seconds unassisted.

If a participant is able to stand 2 minutes unsupported, score full points for sitting unsupported. Proceed to item #4.

3. Sitting With Back Unsupported But Feet Supported on Floor or on a Stool

Instructions*: Please sit with arms folded for two minutes*.
4: Able to sit safely and securely 2 minutes.
3: Able to sit 2 minutes under supervision.
2: Able to sit 30 seconds.
1: Able to sit 10 seconds.
0: Unable to sit without support 10 seconds.

4. Standing to Sitting

Instructions: *Please sit down*.
4: Sits safely with minimal use of hands.
3: Controls descent by using hands.
2: Uses back of legs against chair to control descent.
1: Sits independently but has uncontrolled descent.
0: Needs assistance to sit.

5. Transfers

Instructions: *Arrange chair(s) for a pivot transfer. Ask the participant to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs (one with and one without armrests) or a bed and a chair. If a bed/plinth is used, it should be at the chair height.*
4: Able to transfer safely with minor use of hands.
3: Able to transfer safely definite need of hands.
2: Able to transfer with verbal cuing and/or supervision.
1: Needs one person to assist.
0: Needs two people to assist or supervise to be safe.

6. Standing Unsupported with Eyes Closed

Instructions*: Please close your eyes and stand still for 10 seconds*.
4: Able to stand 10 seconds safely.
3: Able to stand 10 seconds with supervision.
2: Able to stand 3 seconds.
1: Unable to keep eyes closed 3 seconds but stays steady.
0: Needs help to keep from falling.

7. Standing Unsupported with Feet Together

Instructions: *Place your feet together and stand without holding*.
4: Able to place feet together independently and stand 1 minute safely.
3: Able to place feet together independently and stand for 1 minute with supervision.
2: Able to place feet together independently but unable to hold for 30 seconds.
1: Needs help to attain position but able to stand 15 seconds with feet together.
0: Needs help to attain position and unable to hold for 15 seconds.

8. Reaching Forward with Outstretched Arm While Standing

Instructions: *Lift arm to 90 degrees. Stretch out your fingers and reach forward as far as you can*. (Examiner places a ruler at end of fingertips when arm is at 90 degrees. Fingers should not touch the ruler while reaching forward. The recorded measure is the distance forward that the fingers reach while the subject is in the most forward lean position. When possible, ask the participant to use both arms when reaching to avoid trunk rotation).
4: Can reach forward confidently more than 10 inches (>25cm)
3: Can reach forward more than 5 inches safely (>12.5cm)
2: Can reach forward more than 2 inches safely (>5cm)
1: Reaches forward but needs supervision.
0: Needs help to keep from falling. * **_____inches**

9. Pick Up Object from the Floor from a Standing Position

Instructions: *Pick up the shoe/slipper which is placed in front of your feet*.
4: Able to pick up slipper safely and easily.
3: Able to pick up slipper but needs supervision.
2: Unable to pick up but reaches 1 to 2 inches (2-5cm) from slipper and keeps balance independently.
1: Unable to pick up and needs supervision while trying.
0: Unable to try/needs assistance to keep from losing balance or falling.

10. Turning to Look Behind Over Left and Right Shoulders While Standing

Instructions: *Turn to look **directly** behind you over your left shoulder. Repeat to the right*.
4: Looks behind from both sides and weight shifts well.
3: Looks behind one side only; other side shows less weight shift.
2: Turns sideways only but maintains balance.
1: Needs supervision when turning.
0: Needs assistance to keep from losing balance or falling.

11. Turn 360 Degrees

Instructions: *Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.*
4: Able to turn 360 degrees safely in less than 4 seconds each side.
3: Able to turn 360 degrees safely one side only – less than 4 seconds.
2: Able to turn 360 degrees safely but slowly.
1: Needs close supervision or verbal cuing.
0: Needs assistance while turning.

12. Placing Alternate Foot on Step or Stool While Standing Unsupported

Instructions: *Place each foot alternately on the step/stool. Continue until each foot has touched the step/stool four times*.

4: Able to stand independently and safely and complete 8 steps in 20 seconds.
3: Able to stand independently and complete 8 steps in more than 20 seconds.
2: Able to complete 4 steps without aid with supervision.
1: Able to complete more than 2 steps – needs minimal assistance.
0: Needs assistance to keep from falling/unable to try.

13. Standing Unsupported One Foot in Front

Instructions: (DEMONSTRATE to subject.) *Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the other foot.* (To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject's normal stride width.)
4: Able to place foot tandem independently and hold 30 seconds.
3: Able to place foot ahead of the other independently and hold 30 seconds.
2: Able to take small step independently and hold 30 seconds.
1: Needs help to step but can hold 15 seconds.
0: Loses balance while stepping or standing.

14. Standing on One Leg

Instructions: *Stand on one leg as long as you can without holding*.
4: Able to lift leg independently and hold more than 10 seconds.
3: Able to lift leg independently and hold 5 to 10 seconds.
2: Able to lift leg independently and hold at least 3 seconds.
1: Tries to lift leg, unable to hold 3 seconds but remains standing independently.
0: Unable to try or needs assistance to prevent fall.

TOTAL SCORE:____/56

COGNITIVE MEASURES

Montreal Cognitive Assessment (MoCA)

Protocol

- The MoCA is a screening instrument to assess for cognitive impairment.
- It assesses several cognitive domains: attention and concentration, executive function, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation.
- The assessment is scored out of a total of 30 points; 26 points is considered normal
- If a participant has expressive aphasia and is getting frustrated in attempting to answer the following verbal questions, then they may be modified in this manner:
  - Naming: The participant can write on a piece of paper the names of the animals.
  - Memory: The participant can write down the words. This piece of paper will then be discarded.
  - Attention:
    Read list of digits: The participant can write down the numbers after the examiner says them.
    Serial 7's: The participant can write down the numbers.
  - Language: The participant can write down the sentences and the words that begin with "F".
  - Abstraction: The participant can write down the similarity between the words.
  - Delayed Recall: The participant can write down the words.
  - Orientation: The participant can write down the answers.
- Record the participant's score on the data form.
- If the participant has expressive aphasia, two scores will be recorded. The total score, with "0" given for every modification made, will be calculated. An "expressive aphasia" score will also be calculated, accounting for the participant's correct responses to the questions that could be modified with written responses. Record this value on the data form under "Expressive Aphasia score".

Adapted from MoCA Version August 18, 2010

Detailed Instructions

1. Alternating Trail Making:

Administration: The examiner instructs the subject: *"Please draw a line, going from a number to a letter in ascending order. Begin here* [point to (1)] *and draw a line from 1 then to A then to 2 and so on. End here* [point to (E)]."

Scoring: Allocate one point if the subject successfully draws the following pattern: 1 –A- 2- B- 3- C- 4- D- 5- E, without drawing any lines that cross. Any error that is not immediately self-corrected earns a score of 0.

2. Visuoconstructional Skills (Cube):

Administration: The examiner gives the following instructions, pointing to the **cube**: *"Copy this drawing as accurately as you can, in the space below".*

Scoring: One point is allocated for a correctly executed drawing.
- Drawing must be three-dimensional
- All lines are drawn
- No line is added
- Lines are relatively parallel and their length is similar (rectangular prisms are accepted)

A point is not assigned if any of the above-criteria are not met.

3. Visuoconstructional Skills (Clock):

Administration: Indicate the right third of the space and give the following instructions: *"Draw a clock. Put in all the numbers and set the time to 10 past 11".*

Scoring: One point is allocated for each of the following three criteria:
- Contour (1 pt.): the clock face must be a circle with only minor distortion acceptable (e.g., slight imperfection on closing the circle);
- Numbers (1 pt.): all clock numbers must be present with no additional numbers; numbers must be in the correct order and placed in the approximate quadrants on the clock face; Roman numerals are acceptable; numbers can be placed outside the circle contour;
- Hands (1 pt.): there must be two hands jointly indicating the correct time; the hour hand must be clearly shorter than the minute hand; hands must be centred within the clock face with their junction close to the clock centre.

A point is not assigned for a given element if any of the above-criteria are not met.

4. Naming:

Administration: Beginning on the left, point to each figure and say: *"Tell me the name of this animal".*

Scoring: One point each is given for the following responses: (1) lion (2) rhinoceros or rhino (3) camel or dromedary.

5. Memory:

Administration: The examiner reads a list of 5 words at a rate of one per second, giving the following instructions: *"This is a memory test. I am going to read a list of words that you will have to remember now and later on. Listen carefully. When I am through, tell me as many words as you can remember. It doesn't matter in what order you say them".* Mark a check in the allocated space for each word the subject produces on this first trial. When the subject indicates that (s)he has finished (has recalled all words), or can recall no more words, read the list a second time with the following instructions: *"I am going to read the same list for a second time. Try to remember and tell me as many words as you can, including words you said the first time."* Put a check in the allocated space for each word the subject recalls after the second trial.
At the end of the second trial, inform the subject that (s)he will be asked to recall these words again by saying, *"I will ask you to recall those words again at the end of the test."*

Scoring: No points are given for Trials One and Two.

6. Attention:

Forward Digit Span: Administration: Give the following instruction: "*I am going to say some numbers and when I am through, repeat them to me exactly as I said them*". Read the five number sequence at a rate of one digit per second.

Backward Digit Span: Administration: Give the following instruction: "*Now I am going to say some more numbers, but when I am through you must repeat them to me in the backwards order.*" Read the three number sequence at a rate of one digit per second.

Scoring: Allocate one point for each sequence correctly repeated, (*N.B.*: the correct response for the backwards trial is 2-4-7).

Vigilance: Administration: The examiner reads the list of letters at a rate of one per second, after giving the following instruction: "*I am going to read a sequence of letters. Every time I say the letter A, tap your hand once. If I say a different letter, do not tap your hand*".

Scoring: Give one point if there is zero to one errors (an error is a tap on a wrong letter or a failure to tap on letter A).

Serial 7s: Administration: The examiner gives the following instruction: *"Now, I will ask you to count by subtracting seven from 100, and then, keep subtracting seven from your answer until I tell you to stop."* Give this instruction twice if necessary.

Scoring: This item is scored out of 3 points. Give no (0) points for no correct subtractions, 1 point for one correction subtraction, 2 points for two-to-three correct subtractions, and 3 points if the participant successfully makes four or five correct subtractions. Count each correct subtraction of 7 beginning at 100. Each subtraction is evaluated independently; that is, if the participant responds with an incorrect number but continues to correctly subtract 7 from it, give a point for each correct subtraction. For example, a participant may respond "92 – 85 – 78 – 71 – 64" where the "92" is incorrect, but all subsequent numbers are subtracted correctly. This is one error and the item would be given a score of 3.

7. Sentence repetition:

Administration: The examiner gives the following instructions: *"I am going to read you a sentence. Repeat it after me, exactly as I say it* [pause]: ***I only know that John is the one to help today."*** Following the response, say: *"Now I am going to read you another sentence. Repeat it after me, exactly as I say it* [pause]: ***The cat always hid under the couch when dogs were in the room."***

Scoring: Allocate 1 point for each sentence correctly repeated. Repetition must be exact. Be alert for errors that are omissions (e.g., omitting "only", "always") and substitutions/additions (e.g., "John is the one who helped today;" substituting "hides" for "hid", altering plurals, etc.).

8. Verbal fluency:

Administration: The examiner gives the following instruction: *"Tell me as many words as you can think of that begin with a certain letter of the alphabet that I will tell you in a moment. You can say any kind of word you want, except for proper nouns (like Bob or Boston), numbers, or words that begin with the same sound but have a different suffix, for example, love, lover, loving. I will tell you to stop after one minute. Are you ready?* [Pause] *Now, tell me as many words as you can think of that begin with the letter F.* [time for 60 sec]. *Stop."*

Scoring: Allocate one point if the subject generates 11 words or more in 60 sec. Record the subject's response in the bottom or side margins.

9. Abstraction:

Administration: The examiner asks the subject to explain what each pair of words has in common, starting with the example: *"Tell me how an orange and a banana are alike"*. If the subject answers in a concrete manner, then say only one additional time: *"Tell me another way in which those items are alike"*. If the subject does not give the appropriate response *(fruit)*, say, *"Yes, and they are also both fruit."* Do not give any additional instructions or clarification. After the practice trial, say: *"Now, tell me how a train and a bicycle are alike"*. Following the response, administer the second trial, saying: *"Now tell me how a ruler and a watch are alike"*. Do not give any additional instructions or prompts.

Scoring: Only the last two item pairs are scored. Give 1 point to each item pair correctly answered. The following responses are acceptable:
Train-bicycle = means of transportation, means of travelling, you take trips in both;
Ruler-watch = measuring instruments, used to measure.
The following responses are **not** acceptable: Train-bicycle = they have wheels; Ruler-watch = they have numbers.

10. Delayed recall:

Administration: The examiner gives the following instruction: *"I read some words to you earlier, which I asked you to remember. Tell me as many of those words as you can remember."* Make a check mark (√) for each of the words correctly recalled spontaneously without any cues, in the allocated space.

Scoring: **Allocate 1 point for each word recalled freely without any cues.**

Optional:
Following the delayed free recall trial, prompt the subject with the semantic category cue provided below for any word not recalled. Make a check mark (√) in the allocated space if the subject remembered the word with the help of a category or multiple-choice cue. Prompt all non-recalled words in this manner. If the subject does not recall the word after the category cue, give him/her a multiple choice trial, using the following example instruction, *"Which of the following words do you think it was, NOSE, FACE, or HAND?"*
Use the following category and/or multiple-choice cues for each word, when appropriate:

FACE:	category cue: part of the body	multiple choice: nose, face, hand
VELVET:	category cue: type of fabric	multiple choice: denim, cotton, velvet
CHURCH:	category cue: type of building	multiple choice: church, school, hospital
DAISY:	category cue: type of flower	multiple choice: rose, daisy, tulip
RED:	category cue: a colour	multiple choice: red, blue, green

Scoring: **No points are allocated for words recalled with a cue.** A cue is used for clinical information purposes only and can give the test interpreter additional information about the type of memory disorder. For memory deficits due to retrieval failures, performance can be improved with a cue. For memory deficits due to encoding failures, performance does not improve with a cue.

11. Orientation:

Administration: The examiner gives the following instructions: "Tell me the date today". If the subject does not give a complete answer, then prompt accordingly by saying: *"Tell me the [year, month, exact date, and day of the week]."* Then say: *"Now, tell me the name of this place, and which city it is in."*

Scoring: Give one point for each item correctly answered. The subject must tell the exact date and the exact place (name of hospital, clinic, office). No points are allocated if subject makes an error of one day for the day and date.

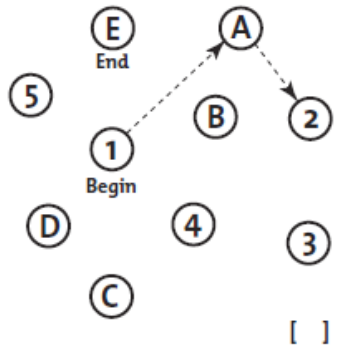
TOTAL SCORE: Sum all subscores listed on the right-hand side. Add one point for an individual who has 12 years or fewer of formal education, for a possible maximum of 30 points. A final total score of 26 and above is considered normal.

Data Form

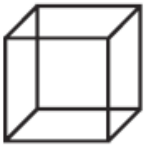
MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE — POINTS



Copy cube



[ ] [ ]

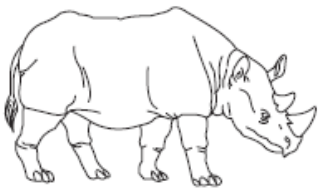
Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING

[ ]



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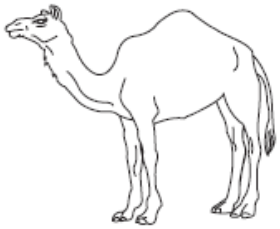

[ ]

__/3

MEMORY — Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION — Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE — Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)

__/1

ABSTRACTION — Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION — [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

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Normal ≥ 26/ 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

MOCA Data Form

1. Participant's Study ID: _____

2. Evaluation: _____1. Baseline

_____2. Post-Treatment

_____3. 6 month follow up

_____4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___

Month Day Year

Visuospatial/Executive ___ /5

Naming ___ /3

Memory No points

Attention

Digits ___ /2
Letters ___ /1
Serial Subtraction ___ /3

Language

Repeat ___ /2
Fluency ___ /1

Abstraction ___ /2

Delayed Recall ___ /5

Orientation ___ /6

Education ___
(add one point if ≤ 12 years)

TOTAL SCORE __ __/30

Expressive Aphasia ☐ Yes ☐ No

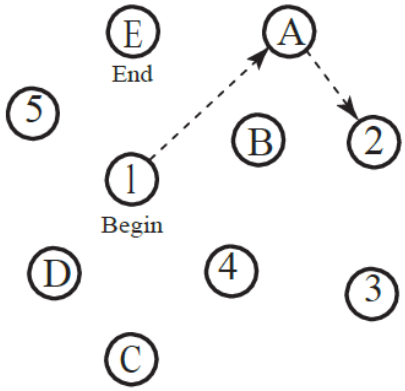
Expressive Aphasia Score: __ __/30

DOSE Participant MOCA Work Sheet

MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
ID :
DATE :

VISUOSPATIAL / EXECUTIVE



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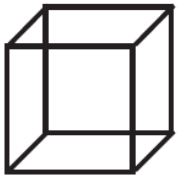


Copy cube

[ ]

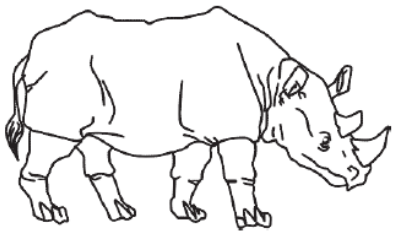
Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS ___/5

NAMING

[ ]



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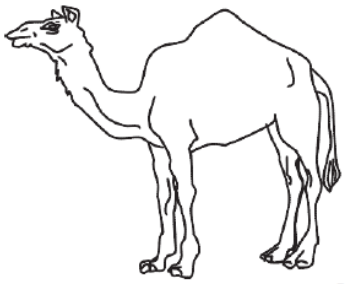


[ ]

___/3

Digit Symbol Substitution Test (DSST)

Protocol

1. Have the participant sit comfortably in a chair at a table with a pen.

2. Put the DSST in front of the participant.

3. Provide the following explanation to the participant:
   "In the top row, there are 9 digit symbol pairs. Each number is associated with its very own symbol. For example, 1 is represented by a horizontal line, 2 is represented by an upside down T and so on. In the next row, I would like you to copy down the corresponding symbol under each number."

4. Give the participant 30 seconds to complete the practice row.

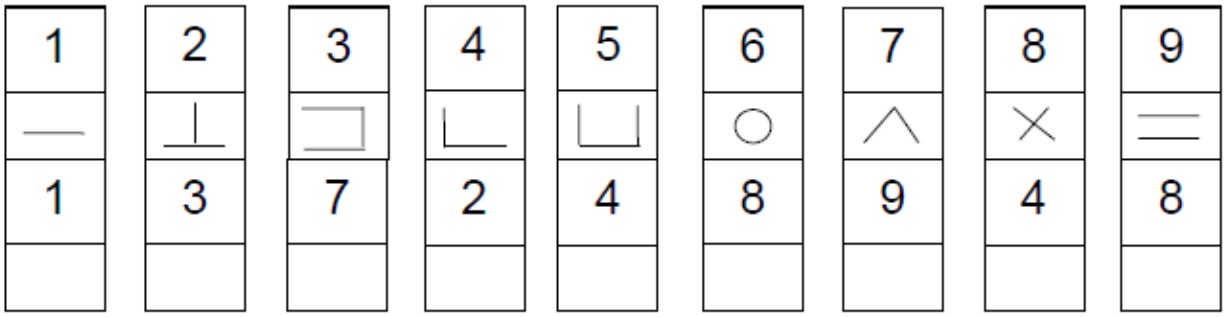
5. Give the participant the following instructions:
   *"Now, I would like you to do the same thing, but this time I will give you **one minute** to fill out as many boxes as you can. Do you understand? On you mark, get so, go!"*

6. Start the time as soon as you say "Go" and tell the participant to stop writing when **one minute** is up.

7. Record on the data form how many correct symbols were completed and how many errors were made in the one minute.

Evaluation Measure

Digit Symbol Substitution Test (DSST)



2	1	3	2	1	4	2	3
5	2	3	1	4	5	6	3
1	4	1	5	4	2	7	6
3	5	7	2	8	5	3	4
6	3	7	9	2	8	1	9

Data Form

DSST DATA FORM

1. Participant's Study ID: _____

2. Evaluation: _____**1.** Baseline

_____**2.** Post-Treatment

_____**3.** 6 month follow up

_____**4.** 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___

Month Day Year

4. Evaluator's Initials: _____ _____

First/Last

5. DSST Results: **___ ___** Number of **correct** symbols in 1 minute

___ ___ Number of **incorrect** symbols in 1 minute

Trail Making A+B

Protocol

Part A Testing Instructions:

1. Place the **Part A warm-up sheet** in front of the participant.

2. Give the participant the following instructions:
   "This is a warm-up test. On this page (point), there are some numbers. Begin with the number one (point to "1") and draw a line from one to two, (point to "2"), two to three (point to "3"), three to four (point to "4"), and so on, in order, until you reach the end (pointing to the circle marked "END"). Draw the lines as fast as you can. Do not lift the pencil from the paper. Ready! Begin!"

3. Start the stopwatch when you say "Begin". The participant has a maximum of **30 seconds** to complete the warm-up. **If the participant makes an error during the tests**, DO NOT stop the timing. Call it to the participant's attention and have him/her proceed from the point at which the mistake occurred (i.e. from the most recent correct number).

4. At 30 seconds, tell the participant to "Stop" and move onto Trail A.

5. Place the **Trail A sheet** in front of the participant.

6. Give the participant the following instructions:
   "On this page, there are numbers from 1 to 25. Do the same thing as you did in the warm-up test. Begin at number one (point) and draw a line from one to two (point), two to three (point), and so on, in order, until you reach the end (point). Remember, work as fast you can and do not lift the pencil from the paper. Ready! Begin!

7. Start the stopwatch when you say "Begin". The participant has a maximum of **8 minutes** to complete the test. **If the participant makes an error during the tests**, DO NOT stop timing. Call it to the participant's attention and have him/her proceed from the point at which the mistake occurred (i.e. from the most recent correct number). Put a star beside where the participant made an error on the Trail sheet.

8. If the participant has not completed the test at 8 minutes, tell the participant to "Stop" and move onto the Part B warm-up. Record the time (in seconds) and number of errors on the data sheet.

Part B Testing Instructions:

1. Place the **Part B warm up sheet** in front of the participant.

2. Give the participant the following instructions:
   "On this page (point), there are some numbers and letters. Begin at number one (point) and draw a line from one to A (point), A to two (point), two to B (point), B to three (point), and so on; in order until you reach the end (point to circle marked "END"). Remember, first you have a number (point to "1"), then a letter (point to "A"), then a number (point to "2"), then a letter (point to "B"), and so on. Draw the lines as fast as you can. Do not lift the pencil from the paper. Ready! Begin!"

3. Start the stopwatch when you say "Begin". The participant has a maximum of **30 seconds** to complete the warm-up. **If the participant makes an error during the tests**, DO NOT stop the timing. Call it to the participant's attention and have him/her proceed from the point at which the mistake occurred (i.e. from the most recent correct number or letter).

4. At 30 seconds, tell the participant to "Stop" and move onto Trail B.

5. Place the **Trail B sheet** in front of the participant.

6. Give the participant the following instructions:
   "On this page, there are both number and letters. Do the same thing you did in the warm-up. Begin with number one (point) and draw a line from one to A (point), A to two (point), two to B (point), B to three (point), and so on, in order; until you reach the end (point to circle marked "END"). Remember, first you have a number (point), then a letter (point), and so on. Draw the lines as fast as you can. Do not lift the pencil from the paper. Ready! Begin!"

7. Start the stopwatch when you say "Begin". The participant has a maximum of **8 minutes** to complete the test. **If the participant makes an error during the tests**, DO NOT stop the timing. Call it to the participant's attention and have him/her proceed from the point at which the mistake occurred (i.e. from the most recent correct number or letter). Put a star beside where the participant made an error on the Trail sheet.

9. If the participant has not completed the test by 8 minutes, tell the participant to "Stop". Record the time (in seconds) and number of errors on the data sheet.

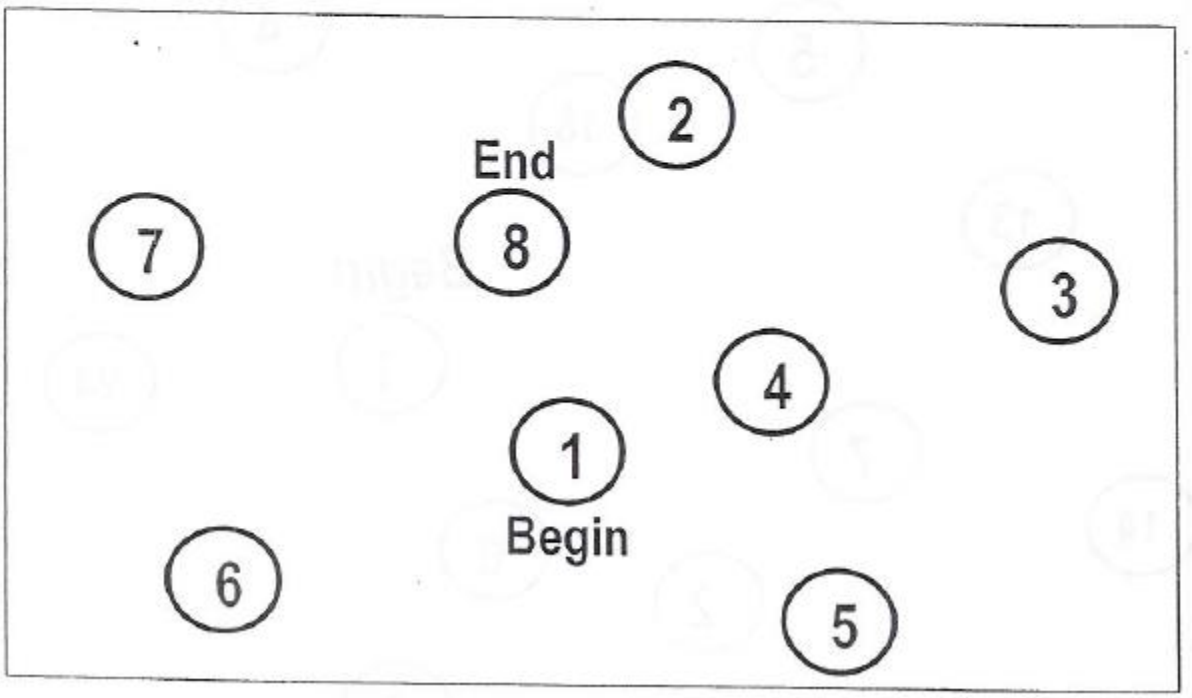
Evaluation Form – Part A

Warm Up Test

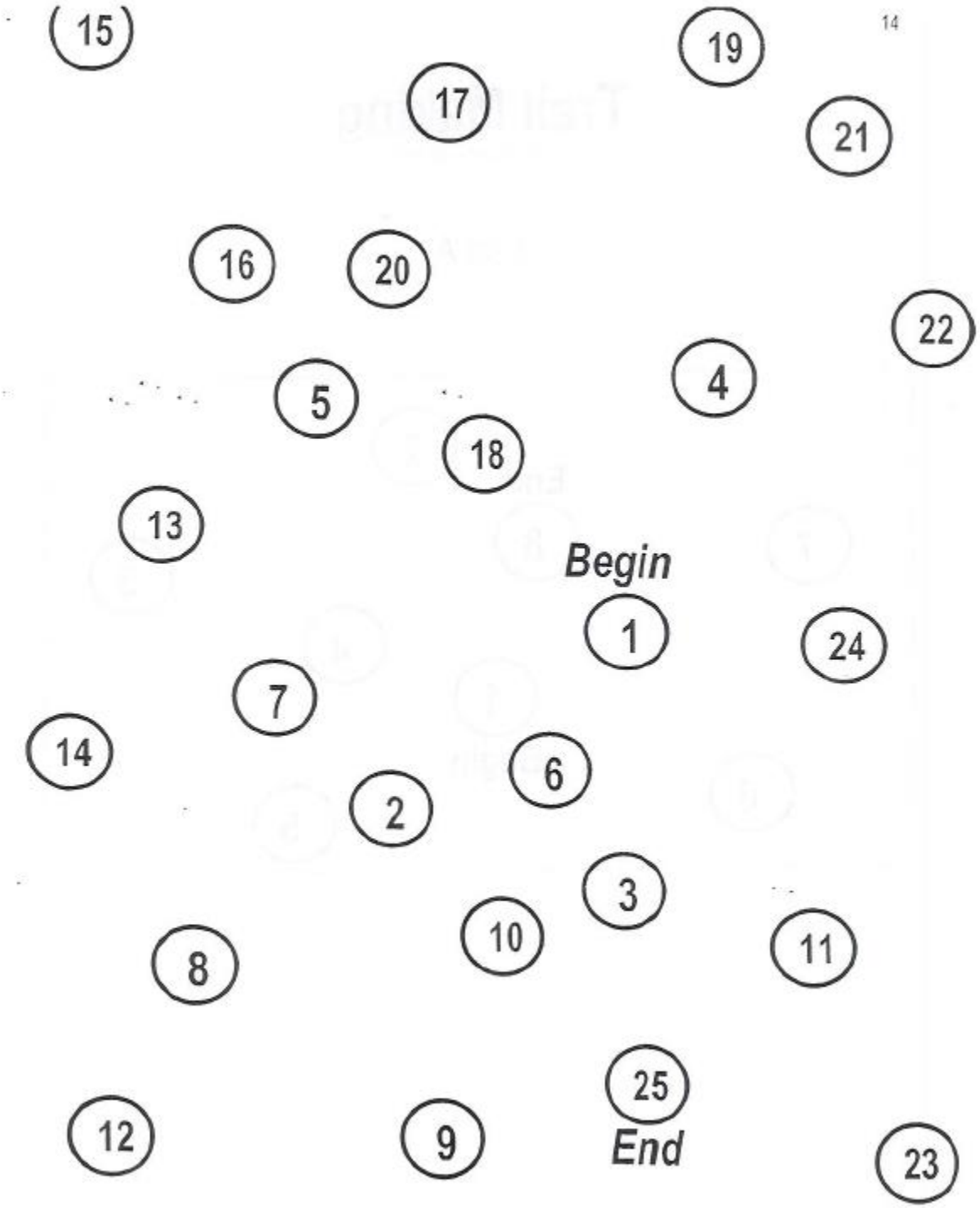
Trail Making

Version November 19, 2002

Part A



Trail Making – Part A



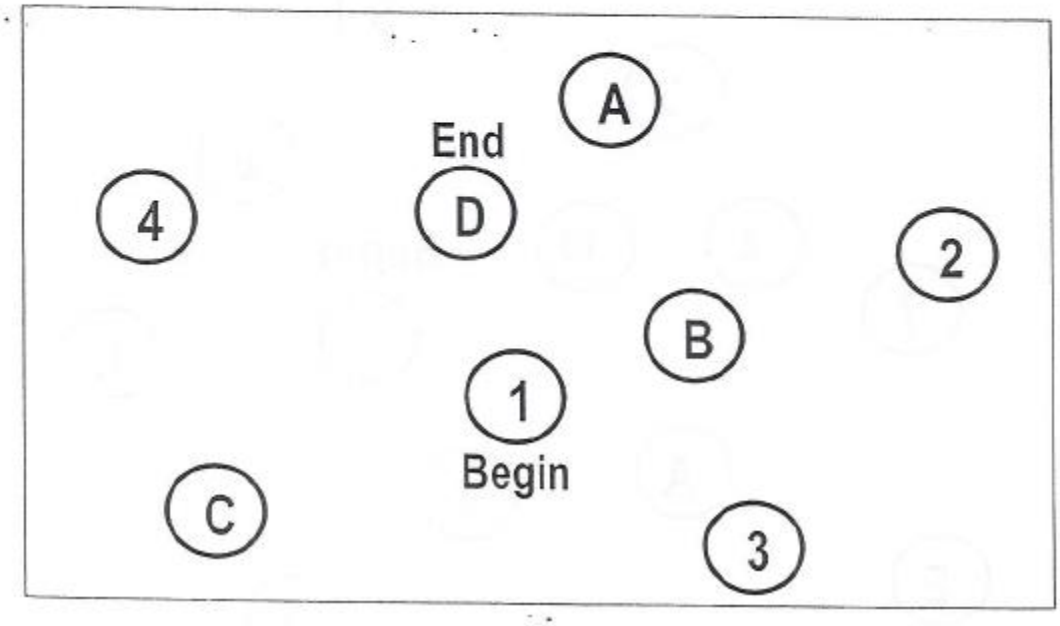
Evaluation Form – Part B

Warm Up Test

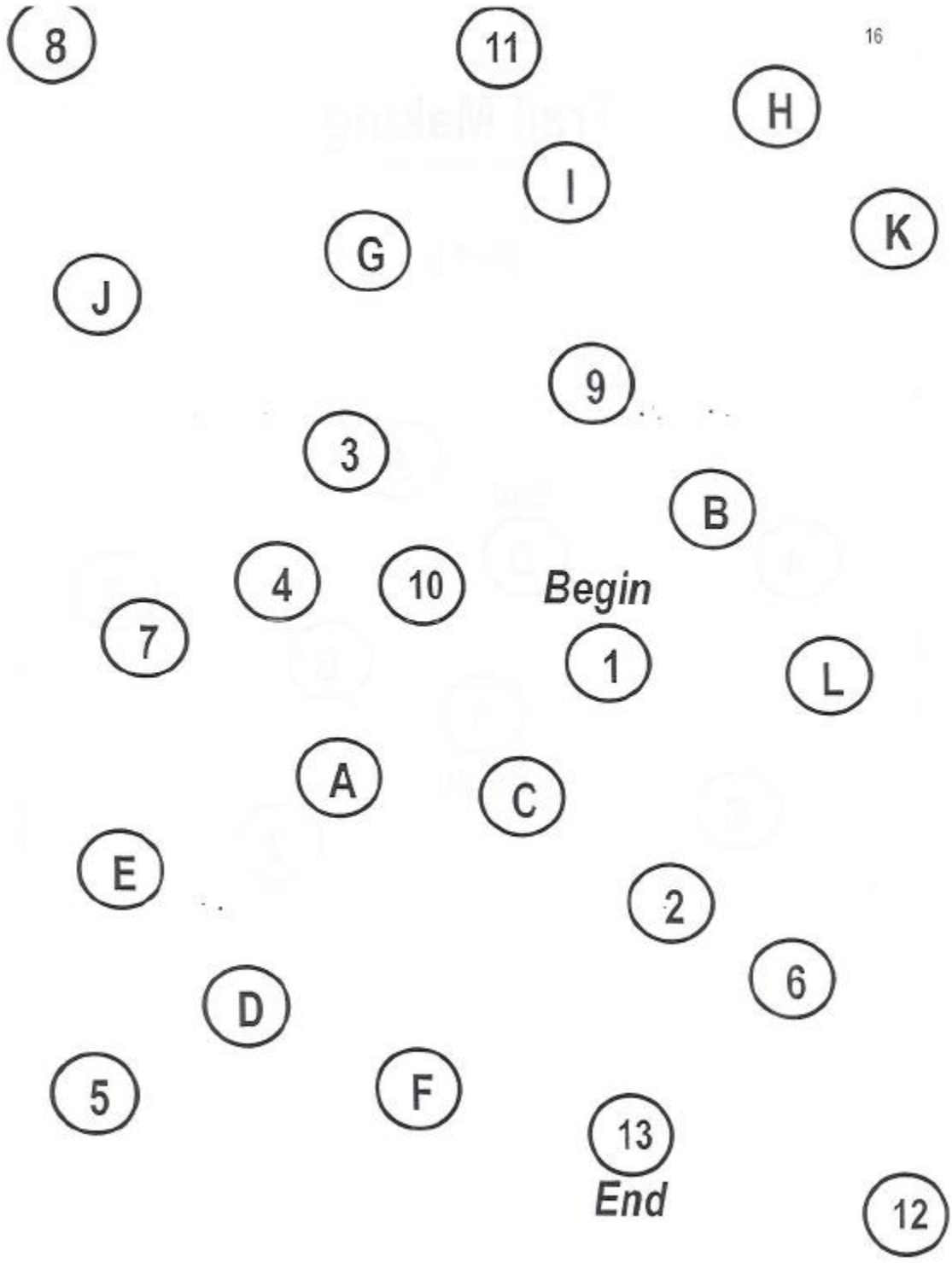
Trail Making

Version November 19, 2002

Part B



Trail Making – Part B



Data Form

1. Participant's Study ID: _____

2. Evaluation: _____1. Baseline

_____2. Post-Treatment

_____3. 6 month follow up

_____4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___

Month Day Year

4. Evaluator's Initials: _____ _____

First/Last

5. Trail Making Results:

TRAIL	**Completion Number / Letter**	**Time (Seconds (xxx.xx))**	**Number of Errors (__ __ __)**
A			
B			

WELL-BEING MEASURES

EQ-5D-5L

Protocol

- This assessment is designed to be completed independently by the participant. Please ensure that the participant is seated comfortably at a chair with the assessment and a pen.

- The evaluator can assist the participant by reading the instructions at the top of each section:

  1. **Part A:** "Under each heading, please tick the ONE box that best describes your health TODAY"

  2. **Part B:** "We would like to know how good or bad your health is **TODAY**. This scale is numbered from 0 to 100. 100 means the **BEST** health you can imagine. 0 means the **WORST** health you can imagine. Mark an X on the scale to indicate how your health is **TODAY**. Now, please write the number you marked on the scale in the box below.

Data Form

1. Participant's Study ID: _____

2. Evaluation: _____1. Baseline
___2. Post-Treatment
___3. 6 month follow up
___4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___
Month Day Year

4. Evaluator's Initials: ___ ___
First/Last

PART A:
Instructions: Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

- ☐ I have no problems in walking about
- ☐ I have slight problems in walking about
- ☐ I have moderate problems in walking about
- ☐ I have severe problems in walking about
- ☐ I am unable to walk about

SELF-CARE

- ☐ I have no problems washing or dressing myself
- ☐ I have slight problems washing or dressing myself
- ☐ I have moderate problems washing or dressing myself
- ☐ I have severe problems washing or dressing myself
- ☐ I am unable to wash or dress myself

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

- ☐ I have no problems doing my usual activities
- ☐ I have slight problems doing my usual activities
- ☐ I have moderate problems doing my usual activities
- ☐ I have severe problems doing my usual activities
- ☐ I am unable to do my usual activities

PAIN / DISCOMFORT

- ☐ I have no pain or discomfort
- ☐ I have slight pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have severe pain or discomfort
- ☐ I have extreme pain or discomfort

ANXIETY / DEPRESSION

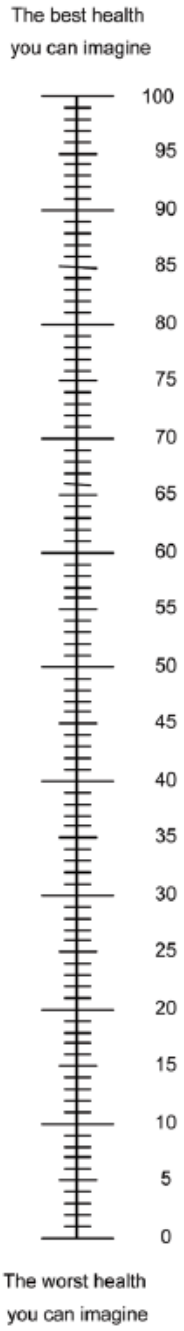
- ☐ I am not anxious or depressed
- ☐ I am slightly anxious or depressed
- ☐ I am moderately anxious or depressed
- ☐ I am severely anxious or depressed
- ☐ I am extremely anxious or depressed

PART B:

Instructions:

- We would like to know how good or bad your health is **TODAY**.
- This scale is numbered from **0** to **100**.
- **100** means the best health you can imagine.
- **0** means the worst health you can imagine.
- Mark an **X** on the scale to indicate how your health is **TODAY**.
- Now, please write the number you marked on the scale in the box below.

PART B: Health Value: ___ ___ ____ (/100)



PHQ-9

Protocol

- This assessment is designed to be completed independently by the participant. Please ensure that the participant is seated comfortably at a chair with the assessment and a pen.

- The evaluator can assist the participant by reading the instructions at the beginning of the assessment:
  "Over the *last 2 weeks*, how often have you been bothered by any of the following problems?"

- The evaluator can orient the participant to the listed problems on the left side of the table, and then instruct the participant to select an answer that reflects his/her feelings **over the last 2 weeks.**

Interpreting the PHQ-9:

- If the evaluation therapist has concern about the study participant's well-being and personal safety, then the evaluation therapist should express his/her concern to the participant and ask permission to share the results with the participant's nurse and medical team.

- A major depressive disorder is suggested if:
  1. Of the 9 items, 5 or more are checked as at least 'more than half the days'
  2. Either item 1 or 2 is positive, that is, at least 'more than half the days'

- Other depressive syndrome is suggested if:
  1. Of the 9 items, 1, 2, or 3, are checked as at least 'more than half the days'
  2. Either item 1 or 2 is positive, that is, at least 'more than half the days'.

- Also, PHQ-9 scores can be used to plan and monitor treatment. To score the instrument, tally each response by the number value under the answer headings, (not at all=0, several days=1, more than half the days=2, and nearly every day=3). Add the numbers together to total the score on the bottom of the questionnaire. Interpret the score by using the guide listed below.

- <u>Guide for Interpreting PHQ-9 Scores</u>
  <u>Score Action</u>

0-4:	The score suggests the patient may not need depression treatment
5-14:	Mild major depressive disorder. Physician uses clinical judgment about treatment, based on patient's duration of symptoms and functional impairment.
15-19:	Moderate-major depressive disorder. Warrants treatment for depression, using anti- depressant, psychotherapy or a combination of treatment.
20 or higher:	Severe major depressive disorder. Warrants treatment with antidepressant, with or without psychotherapy, follow frequently.

Data Form

1. Participant's Study ID: _____

2. Evaluation: ___1. Baseline
___2. Post-Treatment
___3. 6 month follow up
___4. 12 month follow up

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___
Month Day Year

4. Evaluator's Initials: __ ___
First/Last

Over the *last 2 weeks*, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	**0**	**1**	**2**	**3**
2. Feeling down, depressed, or hopeless	**0**	**1**	**2**	**3**
3. Trouble falling or staying asleep, or sleeping too much	**0**	**1**	**2**	**3**
4. Feeling tired or having little energy	**0**	**1**	**2**	**3**
5. Poor appetite or overeating	**0**	**1**	**2**	**3**
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	**0**	**1**	**2**	**3**
7. Trouble concentrating on things, such as reading the newspaper or watching television	**0**	**1**	**2**	**3**
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	**0**	**1**	**2**	**3**
9. Thoughts that you would be better off dead, or of hurting yourself in some way	**0**	**1**	**2**	**3**
	Add columns:	_____ +	_____ +	_____
	TOTAL:			
10. If you checked off *any* problems, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?		**Not difficult at all** _____ **Somewhat difficult** _____ **Very difficult** _____ **Extremely difficult** _____		

Godin Leisure-Time Exercise Questionnaire

Protocol

- The participant is asked to complete a self-explanatory, brief, four-item query of usual leisure-time exercise habits.

- The assessment is designed to be completed independently by the participant. Please ensure that the participant is seated comfortably at a chair with the assessment and a pen.

- There are 2 questions in the questionnaire. Question 1 is comprised of 3 separate questions and question 2 has a single question.

INSTRUCTIONS to the participant:

1. "**Prior to your stroke**, during a typical 7-Day period (a week), how many times on the average did you do the following kinds of exercise for **more than 15 minutes** during your free time? *Ask this question for each component and write on each line the appropriate number.*

2. "**Prior to your stroke**, during a typical 7-Day period (a week), in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

CALCULATIONS:
1. For the first question, weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. Total weekly leisure activity is calculated in arbitrary units by summing the products of the separate components, as shown in the following formula:
Weekly leisure activity score = (9 × Strenuous) + (5 × Moderate) + (3 × Light)

EXAMPLE:
Strenuous = 3 times/wk
Moderate = 6 times/wk
Light = 14 times/wk
Total leisure activity score = (9 × 3) + (5 × 6) + (3 × 14) = 27 + 30 + 42 = 99

2. For the second question, please put a "check mark" in the box corresponding to the participant's answer.

REFERENCE:
Godin, G., Shephard, R. J.. (1997) Godin Leisure-Time Exercise Questionnaire. Medicine and Science in Sports and Exercise. 29 June Supplement: S36-S38.

Data Form

1. Participant's Study ID: _____

2. Evaluation: _____1. Baseline

3. Evaluation Date: ___ ___/___ ___/___ ___ ___ ___

Month Day Year

Godin Leisure-Time Exercise Questionnaire

1. During a typical **7-Day period** (a week) **before your stroke**, how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

	Times Per Week	**Score**
a) STRENUOUS EXERCISE (HEART BEATS RAPIDLY) (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)	_____	**x9=** _____
b) MODERATE EXERCISE (NOT EXHAUSTING) (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)	_____	**x5=**_____
c) MILD EXERCISE (MINIMAL EFFORT) (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)	_____	**x3=**_____

Total Leisure Activity Score _____

2. During a typical **7-Day period** (a week) **before your stroke**, in your leisure time, how often do you engage in any regular activity **long enough to work up a sweat** (heart beats rapidly)?

☐ **Often**	☐ **Sometimes**	☐ **Never/Rarely**
5-7 days/week	2-4 days/week	0-1 days/week

Appendix D Chapter 4: DOSE Study - Intervention Intensity, Progression, and Cardiovascular Safety Guidelines

Exercise Intensity and Cardiovascular Safety

- The exercise program intensity will be individualized for each participant and aerobic training parameters will be calculated by the DOSE site coordinator incorporating the participant's response to the DOSE cardiac exercise stress test and established exercise prescription formulas.

- The DOSE site coordinator will provide you with the following data to use during the intervention program to establish and appropriately progress the participant's aerobic training parameters:
  - The participant's age predicted HR maximum.
  - The participant's aerobic training parameters (40-80% of HRR; 4-7/10 RPE)

- The goal for the aerobic aspect of the intervention program is that the participant will start exercising at a minimum of 40% HRR (RPE 4/10) and progress over the 4 week program, not exceeding a maximum of 80% HRR (RPE 7/10).

- The DOSE cardiac exercise stress test (administered prior to the participant starting intervention), will assist in assessing the participant's cardiac safety for exercising at the prescribed HR parameters. It will provide an initial screen, however, it is likely that over the course of the 4 week treatment program, the participant will potentially reach HR values during exercise that are greater than those obtained during the exercise stress test (but still below their 80% HRR).
  In this situation, you will use clinical monitoring (HR/BP/RPE) and observation (pallor, sweating, dizziness) to determine your ability to safely progress the participant's exercise intensity up to their 80% HRR.

- Exercise intensity parameters may be implemented in all aspects of the intervention program (Weight Bearing Gait Related Activities, Functional Mobility/Sitting Balance, and UE/LE Activation/Strengthening).

- Please see *Progression of Intervention Sessions (page 14)* for information on how to progress the exercise intensity during the study.

Exercise Intensity	DOSE Training Parameters	Rating of Perceived Exertion (10 point Scale)
< 45% HRR		0 = Nothing at all
		1 = Very Light
		2 = Light
	DOSE Training Zone (40-80% HRR)	3 = Moderate
45-60% HRR		4 = Somewhat Hard
		5 = Hard
		6
		7 = Very Hard
>60% HRR		8
		9
		10 = Very, Very Hard (Absolute Maximum)

Adapted from AEROBICS guidelines (2012) and BORG CR-10 Scale (1998)

Heart Rate Intensity Information Form

DOSE Participant ID:_____

Peak HR from exercise test:_____
Age-predicted maximum HR:_____

Zone	Exercise Intensity		HR		RPE Scale		Talk Test
	Description	%HRR	Stress Test	Age-Pred Max	Rating	Description	
1	Light	40			3	Light	Easy – can converse with almost no effort
2	Moderate	45			4	Light	
		50			5	Somewhat Hard	Moderate – conversation requires some effort
		55					
3	Hard	60			5	Somewhat Hard	
		65					
		70			6	Hard (Heavy)	Moderately hard – conversation requires quite a bit of effort
		75					
		80					

***Fitbit goal = at least 2000 steps/session**

I = Intensity Training (Zone 2-3)

- Goal is to complete at least 3 days/week of Intensity Training from Week 1-4.
- Increase %HRR by 5-10% <u>each week.</u>
- Progress bouts of interval/rest over the 4 weeks, preparing the participant to ultimately achieve 30 minutes of continuous weight-bearing activity at 60-80% HRR in his/her rehabilitation future.
- Average HR (from watch) in 30 minute or greater gait re-education time should demonstrate %HRR increase each week.

E = Endurance Training (Zone 1-2)

- Complete 2-3 days/week of Endurance Training.
- Increase %HRR by 5-10% <u>every week or two weeks</u>
- Progress bouts of interval/rest so the participant is able to complete 30 minutes of continuous weight-bearing activity at 40-55% HRR by the end of the 4th week.
- Average HR (from watch) in 30 minute or greater gait re-education time should demonstrate %HRR increase each week.

SAMPLE SCHEDULE (Lower level client)

Week	Program	Intensity (%HRR)		Monday	Tues	Wed	Thurs	Friday
1	Monitoring	I=50%	E=40%	I	E	I	E	I
	+Supplementary			E	I	E	I	E
2	Monitoring	I=55%	E=40%	I	E	I	E	I
	+Supplementary			E	I	E	I	E
3	Monitoring	I=60%	E=45%	I	E	I	E	I
	+Supplementary			E	I	E	I	E
4	Monitoring	I=65%	E=45%	I	E	I	E	I
	+Supplementary			E	I	E	I	E

SAMPLE SCHEDULE (Higher level client)

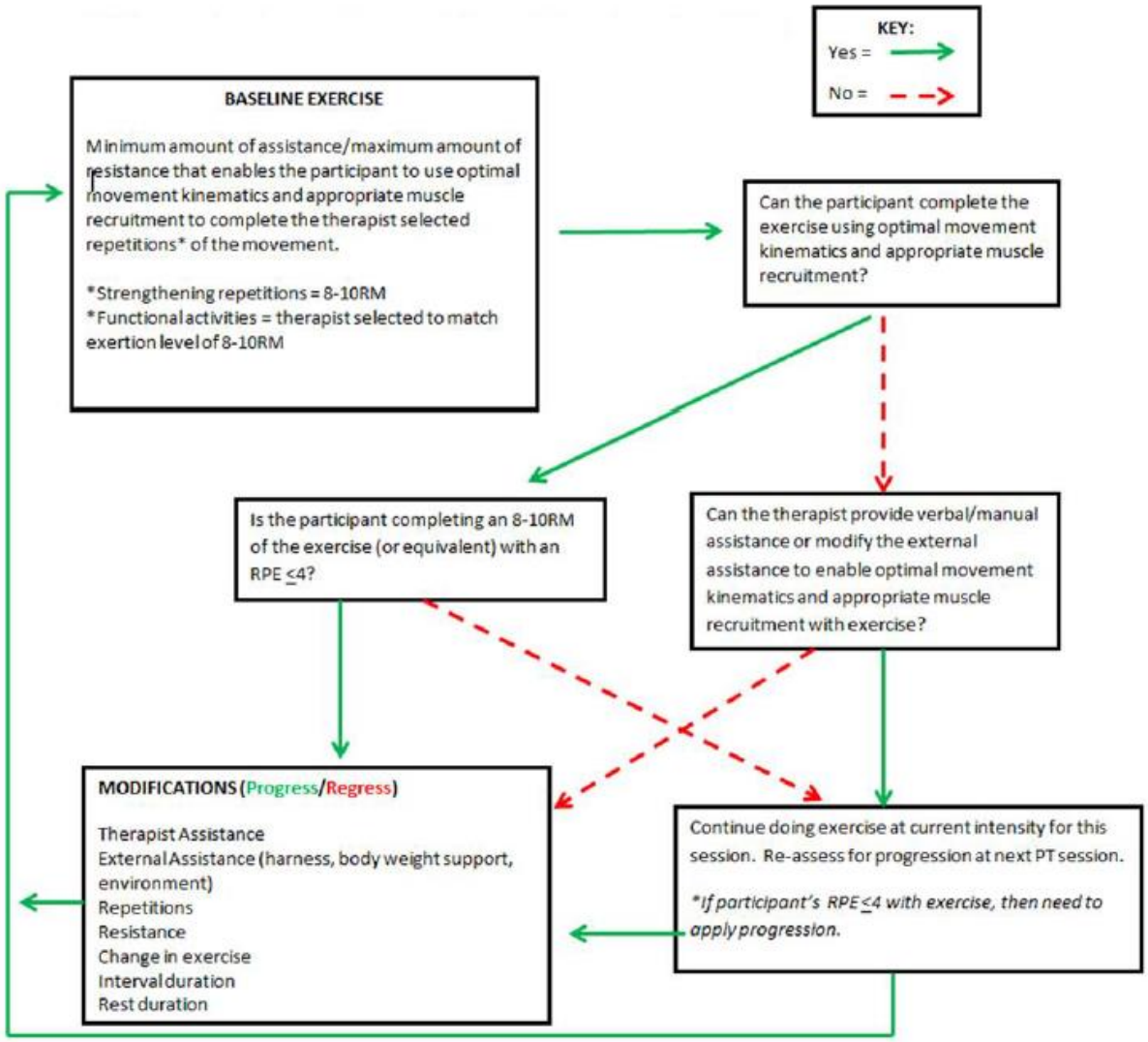
Week	Program	Intensity (%HRR)		Monday	Tues	Wed	Thurs	Friday
1	Monitoring	I=50%	E=40%	I	E	I	E	I
	+Supplementary			E	I	E	I	E
2	Monitoring	I=60%	E=45%	I	E	I	E	I
	+Supplementary			E	I	E	I	E
3	Monitoring	I=70%	E=50%	I	E	I	E	I
	+Supplementary			E	I	E	I	E
4	Monitoring	I=80%	E=55%	I	E	I	E	I
	+Supplementary			E	I	E	I	E

Sample Intervention Session

Sample Participant #1: 63 y.o. female, 3 weeks post-stroke, BBS = 40, 5m walk = 0.45m/s
Peak HR (from exercise stress test) = 120bpm
HR exercises ranges (40-80% HRR) = 105-145bpm

Exercise Domain	Sample #1 – Session 1	Sample #2 – Session 1
Weight Bearing Gait Related Activities	**BWSTT** • Start with a 5 minute interval at 1.5x overground walking velocity (0.7m/s = 2.5km/hr), 30% BWS (max 40%) • HR should be above 105, less than 145bpm • Participant can rest when s/he wants during the 5 minutes. • Take 2 minutes rest at end of 5 minute interval. • Repeat 4x • Practice overground walking x 10 minutes reinforcing gait re-education principles from treadmill • Total session length = **20 minutes walking**, about **45 minutes** to complete with rests, set-up, take-down.	**Overground Gait Re-education** • Participant walking overground with appropriate assistance (PT+RA +/- orthosis / walking aid) • Safely encourage overground walking velocity GREATER than comfortable walking velocity. • Start with 5 minute walk warmup (as many rests as necessary). May include forward walking, sideways walking, etc. • Do 5 repetitions at 1.5x her comfortable walking velocity for 2 minutes →0.45m/s x 1.5 = 0.7m/s x 120 seconds = 84m. • **Participant should try to cover 84 meters in 2 min.** • Take a 1 minute break at the end of each interval. • Repeat 5 times (total of 15 minutes walking) • Cool down walking (forwards/ backwards/ sideways, stairs, etc.) for the remaining time to = **30 minutes** of overground gait re-education.
LE Strengthening / Postural Control	**Exercises** For remaining **15 minutes**: • Likely have time to complete 3 exercises from this domain. • Select three exercises • Complete 2-3 sets, 8-10RM for each exercise.	**Exercises** **30 minutes circuit training:** • Pick 10 exercises (or 5 exercises x 2 loops) • Participant spends 2 minutes at each station. Maximum 30 sec. of each station may be a rest break. • 1 minute transition between each station. • Total = **30 minutes.**
Potential Progressions for Future Sessions	**BWSTT (in no particular order – clinical judgment determines progression selection):** • Increase speed of treadmill • Decrease BWS • Decrease therapist assistance • Decrease rest time • Increase interval time **Exercises:** • Increase resistance/sets/repetitions • Modify environment to challenge participant • Decrease therapist assistance	**Overground Gait Re-education (in no particular order – clinical judgment determines progression selection):** • Increase walking velocity • Decrease therapist assistance • Decrease rest time • Increase interval time • Increase interval repetitions • Decrease warm-up/cool down time **Exercises:** • Increase resistance/sets/repetitions • Modify environment/therapist assistance to challenge participant • Decrease rest time at each station • Increase distance between each station (therefore making participant walk further to each station in same amount of time)

LE Strengthening and Postural Control Exercise Progression Algorithm



Exercise List

Use the Strengthening and Functional Activities Progression Algorithm (page 14) to determine baseline / progression/regression of the exercise

1. **Weight Bearing Gait Related Activities:**
   - Walking indoors, forward, backward and sideways
   - Walking on the treadmill (+/- body weight support)
   - Walking up and down stairs
   - Walking through obstacle courses
   - Sit to stand

2. **LE Strengthening/Postural Control:**
   - Step taps on/off a step/stool
   - Step ups on step/stool (forward and lateral)
   - Eccentric quads over edge of step/stool
   - Standing Balance exercises (dynamic)
     - Touch marks or trace a spiral shape on a white board. Use different stance positions (ie: feet together and tandem stance)
     - Stepping grid: Participants stand with feet in marked areas, then tap 1 foot out to touch marks on floor, repeating with the other foot.
     - Picking up objects from low surfaces or the floors. May be performed in pairs by having participants pass objects to each other.
     - Throwing/catching a ball
     - Kicking a ball
     - Standing on one leg
     - Walking with heel/toe gait
   - Sitting Balance exercises (dynamic)
     - Reaching in various directions outside of base of support to activate paretic leg muscles
   - Squats (+/- Shuttle with resistance)
   - Transfers (bed to chair, floor to chair activating paretic limb)
   - Kneeling activities (split stance kneeling, floor to chair transfer)
   - Lunges
   - Heel raises
   - Leg Ergometer
   - Open/closed chain strengthening for LE muscles (pelvis, gluts, quadriceps, hamstrings, gastroc/soleus, foot/ankle)