PHYSICAL AND PERSONAL CHARACTERISTICS AFFECTING WALKING IN THE COMMUNITY: A CROSS SECTIONAL STUDY OF CHRONIC STROKE SURVIVORS

by

Tanya Chopra

Submitted in partial fulfilment for the requirements for the degree of Master of Science

at

Dalhousie University
Halifax, Nova Scotia
July 2019

THANK YOU GOD FOR YOUR COUNTLESS BLESSINGS.

This thesis is dedicated to my grandfather, parents and my brother
Basant Chopra, Atul Chopra, Nisha Chopra and Akshat Chopra
for always believing in me.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

The transition from walking in clinical to community settings is problematic for many stroke survivors and few report walking in the community without difficulty. Improved walking ability is one of the most often stated goals by stroke rehabilitation participants and community-dwelling stroke survivors.The primary objective of the study was to investigate the relationship between walking in the community (daily step counts) and various physical and personal characteristics. The secondary objective of the study was to find out which factors predict walking in the community in chronic stroke survivors. Thirty-five stroke survivors, mean age 67.6± 8.6 years, 7±6.5 years post-stroke took part in the study.6MWT,10MWT and balance were significantly correlated to daily step counts. The hierarchical regression model we built containing age, sex, time since stroke, severity of stroke, distance walked during the 6MWT, fatigue scores and knee extensor strength predicted 50 % of variance in daily step counts.

LIST OF ABBREVIATIONS USED

BSS- Berg Balance Scale

BBA- Brunel Balance Assessment

BDS- Beck Depression Inventory-II

CESD- Center for Epidemiologic Studies Depression Scale

DALY- Disability-adjusted-life-years

FAS- Fatigue Assessment Scale

FIS- Fatigue Impact Scale

FMA- Fugl-Meyer Motor Assessment

FSS- Fatigue Severity Scale

GDS- Geriatric Depression Scale

HADS- Hospital Anxiety and Depression Scale

ICH - Intracerebral hemorrhage

MAS- Motor Assessment Scale

PASS- Postural Assessment Scale for stroke patients

PHQ-9- Patient Health Questionnaire-9

POMS- Profile of Mood States

PHQ-9- Patient Health Questionnaire-9

PSF- Post-stroke fatigue

PSD- Post-stroke depression

SADQ- Stroke Aphasic Depression Questionnaire

SAH- Subarachnoid hemorrhage

Six- Minute Walk Test- 6MWT

Ten- Meter Walk Test- 10MWT

TIS- Trunk Impairment Scale

GLOSSARY

- Gait- Gait refers to locomotion achieved through movement of limbs[1]. Human gait is defined as bipedal, biphasic forward propulsion of centre of gravity of the human body[1]. Different gait patterns are characterized by differences in limb-movement patterns, overall velocity, forces and changes in the contact with the surface[1].
- Walking- Walking is defined as repetitious sequence of limb motions that move the body forward while simultaneously maintaining stance stability and is a gait which keeps at least one foot in contact with the ground at all times[1].
- Walking in the community- Able to walk a minimum of 3 metres (10 feet) continuously inside the home and in the community with or without assistive devices and/or manual contact of no more than one person.
- Percent inactive: Percent time of the day included for analysis in which no steps were recorded.
- Low cadence- 1-30 steps per minute.
- Medium cadence- 31- 80 steps per minute.
- High cadence- Above 81 steps per minute.
- Low cadence percentage: Percentage of steps relative to all steps in the time included for analysis taken at a low step rate.
- Medium cadence percentage- Percentage of steps relative to all steps in the time included for analysis taken at a medium step rate.
- High cadence percentage- Percentage of steps relative to all steps in the time included for analysis taken at a high step rate.

ACKNOWLEDGEMENTS

I cannot express in words how thankful I am to my supervisor Dr. Marilyn MacKay Lyons for guiding me in this beautiful journey. With me, having no background in research, she has been extremely patient in teaching me everything during my master's degree. I extend my deepest gratitude to her for helping me in every step starting from narrowing down my research interests to giving me every opportunity to grow as a researcher and expand my academic and personal knowledge. She is an epitome of what a supervisor should be. I admire her dedication and all the hard work she has put in to help me in these two years.

I would also like my thank my committee members Dr. Shaun Boe and Dr. Gail Eskes for their insightful feedback and most importantly for their time.

I have a lot of people to thank in this journey. I am very grateful to Paul Curwin, Sue Ehler, Tony, Alyson McDonald, Adria Quigley and Sarah Gaudry for helping in participant recruitment. I am very thankful to all the stroke survivors and their families for agreeing to be a part of my study. This thesis would not have been possible without you.

Beyond school, I would like to thank my friends in Halifax who became my family. Shantanu, Prachi, Astad, Purva, Maninder, your friendship has given me the strength to keep working hard and never lose focus. Thank you for the beautiful times we have had together. I love you guys so much.

I am extremely lucky to have friends back in India. Thank you Paridhi, Pankul, Anu, Bhumika, Aditi, Onika, Jasmine, Aprajita, Jaisleen, Shreya for supporting me and

keeping me sane from miles away. Our text and phone conversations kept me motivated and forever happy.

Lastly, I would like to thank my family. It is because of them I am here today in Dalhousie University. Thank you for sending me 10,944 kilometers away for you to pursue my dreams. Everything I have is because of them and they have given me the strength to be dedicated towards my goals. I miss them every moment here in Halifax and cannot wait to unite with them.

CHAPTER 1: INTRODUCTION

Stroke is the second-ranked cause of mortality in the world and a major cause of disability[2]. Stroke, whether ischemic or hemorrhagic in etiology, leads to deficits in physical, cognitive, psychological and communication functioning[3]. One deficit that is particularly critical to maintaining functional independence, daily activity levels, and health-related quality of life after stroke is walking[4]. In fact, stroke survivors spend more of their time in rehabilitation practicing walking compared to all other activities and improved walking ability is one of the most often stated goals by stroke rehabilitation participants and community-dwelling stroke survivors[5]. Walking is also the preferred mode of physical activity in people with neurological conditions[6]. Walking activity in people with chronic stroke is well below the walking activity of most sedentary adults (<5000 steps per day)[7,8]. A 3 year longitudinal study by Kunkel and colleagues showed that by the 3rd year of recovery, stroke survivors spent only 9 % of their time walking[9].

Recovery of walking ability post-stroke ranges from complete dependence to complete independence[10]. The proportion of stroke survivors who can walk unaided is about 33% by one week after stroke onset and 50-80% by three weeks. By 6 months, 85% of the stroke survivors have the ability to walk independently without physical assistance but out of these 85 % ,only about 7 % of people discharged from inpatient rehabilitation can manage steps, inclines and acquire speeds and distances required for competent walking in the community [10]. Nonetheless, the transition from walking in clinical to community settings is problematic for many stroke survivors,[11] and few report walking in the community without difficulty[4]. While walking in the real-world stroke survivors have to negotiate many different obstacles, including street curbs, ramps, and

crossing the street. Instances like walking while talking to another person, holding bags while walking requires the ability to make adjustments during walking and limits their ability to respond in a safe, timely and effective manner[10,11].

When considering the challenges of transitioning from clinical to community settings the taxonomy of motor tasks developed by Ann Gentile several decades ago is a useful framework[12]. Of particular relevance is the distinction between closed and open tasks[12]. A *closed task* (e.g., pressing a switch) is a relatively stereotypical movement pattern, the performance of which is not greatly affected by contextual factors, which include the setting in which the task is performed. In contrast, an *open task* is influenced by various contextual factors and therefore requires constant adaptation by the performer[12,11]. Although walking is an open task, this motor skill is often approached in stroke rehabilitation as if it were a closed task. Both assessment and retraining of walking are generally conducted in predictable, clinical settings where the layout, therapeutic equipment, and furnishings remain relatively unchanged over time[11,4]. As such, an accurate reflection of the ability to walk in the community may not be garnered over the course of formal stroke rehabilitation[4]. An example of this lack of commensurability is the 6-Minute Walk Test (6MWT) - a walking endurance test performed in clinical settings that is regarded as a proxy measure of the ability to walk in the community[13]. However, the 6MWT explains only 46-54% of the variability in daily step counts of ambulatory stroke survivors[14,15]. Clearly, other personal characteristics and extra-personal (or environmental) contextual factors need to be taken into account when considering the demands of real-world walking after stroke. Gaining a better understanding of the multiplicity of personal characteristics and environmental factors that impact the task of walking in the community will help the patient undergoing stroke

rehabilitation be better prepared for everyday life encounters. This study focussed on physical and personal characteristics as a means to address limitations in the current literature related to variables affecting community ambulation.

Several physical characteristics that may affect walking in the community after stroke have been introduced in the literature but not fully explored. The most studied is *walking endurance*, which has been mentioned above. *Walking speed*, as commonly measured using the 10-Metre Walking Test (10MWT), is moderately (r=0.55-0.65) correlated with daily step counts[14-16]. *Knee extensor strength* of both paretic and non-paretic limbs has been found to be associated with gait pattern and walking speed in stroke survivors[17,18], but its relationship to walking activity in the community has not been established. The potential for *balance* to be a contributing factor is conceptually sound because negotiating real-world environments requires constant postural adjustments [19]. As a result, individuals with limited balance may avoid outdoor walking because of the heightened risk of falls.[10]. Alzahrani et al, 2012 reported a moderate correlation (r=0.52) between balance and daily activity counts, which are not as specific to walking as step counts[20].

In terms of personal characteristics, *depression* is associated with reduced activity levels among adults with limitations in function in activities of daily living and stair climbing following stroke[21,22]. The combination of impaired balance and depression has been reported to explain 40% of the variability in daily activity counts [20]. A strong relationship has been reported between *post-stroke fatigue* and physical activity in neurological conditions but the association of fatigue and walking activity in the community has not been studied[23,24].

The primary objective of the study was to investigate the relationship between walking in the community (daily step counts) and various physical (walking speed, walking endurance, balance, quadriceps strength) and personal (depression, fatigue). The secondary objective of the study was to identify which physical and personal factors predict walking in the community after stroke. We hypothesised that walking speed, walking endurance, balance and quadriceps strength will have a significant positive correlation with daily step counts and depression and fatigue would have a significant negative correlation with daily steps.

CHAPTER 2: REVIEW OF RELEVANT LITERATURE

The literature review serves the purpose of informing all aspects of the methods of my study. The review begins with a brief summary of the different types of stroke, prevalence and clinical presentation of stroke. In the following sections impact of stroke on walking, relationship between walking in the community and various physical and personal characteristics are explained. Attention then turns to frequently used measures for assessing these correlates. Lastly, 'lessons learned' from this literature review in terms of informing the rationale of the study are summarized.

2.1 General Introduction to Stroke

Stroke is defined by World Health Organisation as the clinical syndrome of rapid onset of focal (or global, as in subarachnoid haemorrhage) cerebral deficit, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular one[3]. There are two types of stroke – ischaemic stroke and haemorrhagic stroke. Ischaemic stroke, the most common type of stroke, accounts for 71% of all strokes[25]. It is caused by abrupt and sustained reduction in the regional cerebral blood flow leading to formation of infarct core (irreversible tissue damage and cell death) and penumbra (surrounding zone of damaged tissue that may recover with abrupt restoration of CBF)[26]. Cerebral infarction in classified as cardioembolic, large vessel atherothrombotic and lacunar infarcts[26]. Hemorrhagic stroke is defined as an acute neurological injury occurring as a result of bleeding into the head[11]. Bleeding can occur directly in to brain parenchyma-intracerebral hemorrhage (ICH) or bleeding into the cerebrospinal fluid containing sulci, fissures and cisterns -subarachnoid hemorrhage (SAH). ICH, second most common cause of stroke accounts for 10-15% of all strokes[11]. SAH is slightly less common and

accounts for 3-5% of all strokes. Hypertension, cerebral amyloid angiopathy, vascular malformations, neoplasms, hemorrhagic infarction are the causes for ICH and aneurysm rupture for SAH[11].

2.2 Prevalence of Stroke

According to the most recent data from the Canadian Chronic Surveillance System, the number of adults aged 20 and older who experienced a stroke rose steadily over the decade between 2003-2004 and 2012-2013 with addition of over 215,000 survivors. The age-standardized occurrence of stroke increased by 1% during the same period. Stroke predominantly affects older people with about 10% of adults age 65 years and older having experienced a stroke. Raised awareness, better stroke care and improvements in the management of risk factors have contributed to the decline in first-stroke and all-cause mortality rates over several decades.

Sex differences in stroke are observed across epidemiologic studies, pathophysiology, treatments and outcomes[27]. Prevalence of stroke, mortality and fatality rates increase with age, particularly among women[28]. Premenopausal women experience fewer strokes than men of comparable age whereas the rate of stroke is higher among postmenopausal women compared with age-matched men[27] . Stroke in young is not a rare occurrence .The nature and etiology of stroke in young adults (i.e., age 45 or less) is different from that in older patients which calls for different diagnostic evaluation and treatment plan[29]. Typical causes of stroke in young people include infective diseases (syphilis, tuberculosis meningitis), spontaneous arterial dissection, vasculitis and connective tissue disorders[30]. The incidence of stroke in young people ranges from 60 to 200 new cases per year per million inhabitants with incidence being higher in non-

industrialised countries[30]. Traditional vascular stroke risk factors such as hypertension, dyslipidemia and diabetes still have a significant role in younger patients and their role only increases with age[30]. Smoking, migraine, pregnancy and puerperium, oral contraceptives and illicit drug use are risk factors which are considered minor in the elderly but have a greater impact on etiology of strokes in the young[30].

Stroke is the second leading cause of death and the third leading cause of disability[31]. Stroke leads to approximately 10% of worldwide deaths each year with 44 million disability-adjusted-life-years (DALY) lost [32,33]. In Canada, stroke is the third leading cause of death and tenth largest contributor to DALY. Moreover, healthcare costs related to stroke occurrence continue to escalate. According to the Burden of Ischemic Stroke study, the cost for stroke sufferers and Canada's health care system totals about $2.5 billion, with more than 50,000 new strokes occur each year in Canada [34]. This cost accounts for hospitalizations, physician appointments, medications, diagnostic imaging, home care, rehabilitation and indirect costs such as disability leave, lost wages and caregiver salaries[34]. Stroke in the young has a disproportionately large economic burden as compared to stroke in older people because stroke in young people results in disability during the most productive years [29].

At a global level, a large range has been reported in the prevalence (25-74%) of stroke-related physical, cognitive or emotional deficiencies and require partial or complete assistance to carry out activities of daily living[35], experience mood alterations and social alienation[36]**.** A global focus on reducing mortality and morbidity from stroke is the need of the hour.

2.3 Clinical Presentation of Stroke

During a stroke, body functions controlled by the central nervous system are affected leading to multiple impairments of varying severity – physical involvement (e.g., limb weakness, sensory loss, postural disturbances), perceptual (visual, spatial and visuo-motor organisation deficits), communication and language deficits (aphasia, alexia, agraphia, acalculia, dysarthria)[37],and cognitive impairments (memory and thinking). Challenges with mobility and environmental barriers may lead to activity limitations [11,38] (e.g., self-care activities, walking, stair climbing) which negatively impact participation in societal roles (e.g., home-making ability, employment, leisure and sport)[39, 40-45].

2.4 Impact of Stroke on Walking

Impairments in walking occurs in more than 80% of stroke survivors[46]. Despite undergoing rehabilitation, stroke survivors have residual gait impairments making them dependent on physical assistance before hospital discharge[47]. Walking requires a complex process of neuromusculoskeletal control. To ensure appropriate joint positions to support and advance the body weight in different phases of gait cycle, activation of muscles in lower limbs, trunk and upper limbs in a certain spatiotemporal pattern is required[48]. Walking at a comfortable speed on level surfaces is mediated by brain stem and spinal mechanisms[48]. Supraspinal control adds complexity and flexibility of gait control and gait versatility to meet dynamic environmental needs and challenges[48]. Apart from motor mechanisms, sensory feedback via visual signals, skin receptors, vestibular and proprioceptive signals is crucial for locomotor adaptions[48].

In stroke survivors with walking dysfunction, neural control mechanisms are compromised[48]. Spasticity, a common presentation of stroke leads to synergistic pattern

of activation during standing and walking[48]. Abnormal patterns most commonly observed are flexor synergies in the upper extremity and extensor synergies in the lower extremity[48]. Interactions between muscle weakness, spasticity and spastic activations act on the trunk, pelvis and the legs leading to impairments in walking[48].

Result of the interactions mentioned above is circumductory gait in which stroke survivors hike their hip and circumduct the affected leg during swing phase for foot clearance[48]. Foot drop characterised by lack of voluntary control of dorsiflexors muscles is also exhibited by stroke survivors leading to tripping and falling[48]. Rehabilitation programs to improve walking include muscle strength training, task specific gait training, treadmill training, electromechanical and robot-assisted gait training, functional electrical stimulations, ankle foot orthoses, virtual reality, mental practice with motor imagery and botulinum toxin injection of spastic muscles[48].

2.5 Relationship between walking in the community and physical characteristics

2.5.1 Walking speed and endurance

Walking speed is the most common outcome measure for training walking strategies and reflects the ability to transport the body from one place to another in a timely manner[5]. Perry et al suggested that individuals with stroke who can walk at a speed of 0.4 m/s are more likely to be able to walk in the community[5]. Walking endurance measured by the 6MWT is the second most common walking measure used in clinical trials[5]. Walking after stroke has high energy requirements and walking a certain distance is an important factor for walking and reintegration in the community[14]. The distance walked in the 6MWT by individuals with subacute or chronic, mild-to-moderate stroke usually ranges from 200-300 meters which is far shorter than that of age-matched

adults (400 meters)[14]. Table 1 shows the summary of studies showing the relationship between walking speed, endurance and walking in the community.

For the purpose of my study, I will use step counts as a measure of walking in the community. Walking speed explains 51% of the variance in daily step counts in older adults supporting the evidence to explore this relationship in older adults with neurological disorders[49]. Alzahrani et al examined the relationship between 6MWT, 10MWT and activity counts measured by Intelligent Device for Energy Expenditure and Physical Activity (IDEEA)[50]. The IDEEA is a small recorder clipped to the belt or waist of the pants that monitors body motion through sensors attached to chest, both thighs and underneath both feet[50]. The study consisted of 42 community-dwelling stroke survivors, aged 70±10 years with 2.8±1.4 years post-stroke[50]. There was a moderate correlation between 10MWT (r=0.66), 6MWT (r=0.60) and activity counts but the 10MWT and 6MWT were not significant predictors of free-living physical activity in a stepwise multiple regression analysis[50]. In a study by Rand et al, 6MWT was moderately correlated with activity counts registered on the paretic hip (r=0.67) and nonparetic hip (r=0.73) in 40 stroke survivors, aged 66.5±9.6 years with 2.9±2.4 years post-stroke. The concern with activity counts is that it does not capture walking in the community specifically and collects data in various transitions (lie to sit, sit to lie, recline to sit, recline to stand, stand to recline, sit to stand and stand to sit) postures (lying, reclining, sitting, standing and leaning) and gait (walking, running, up and down stairs and jumping on both legs)[50].

Table 1. Summary of studies showing relationship between walking speed, endurance and walking in the community.

Author	Study Design	Patient Characteristics	Clinical Measures	Daily Step Counts	Results
Mudge et al[15]	Cross-sectional study	•N=49 stroke survivors •Age=67.4±12.5 years •Time since stroke=5.5±5.0 years	•10MWT=0.67±0.32 m/s •6MWT=230±121 m	Step Watch Activity monitor (SAM) worn for 3 days on the non-paretic ankle.	•6MWT and 10MWT moderately correlated to mean daily step counts (r=0.67, r=0.55 respectively). •In a forward linear regression analysis,6MWT was the only significant predictor for Step Watch daily step counts with 54% of variance in mean daily step counts explained by 6MWT.
Fulk et al[14]	Cross-sectional study	•N=19 chronic stroke survivors •Age=65.7±11.9 years •Time since stroke=3.5±3.0 years	•10MWT=1.01±0.31 m/s •6MWT=348.6±144.4 m	SAM worn for 7 days on the non-paretic ankle.	•6MWT and 10MWT moderately correlated to mean daily step counts (r=0.68, 0.65 respectively). • In a stepwise linear regression analysis, 6MWT was a significant predictor for Step Watch outputs with 46% variance

					in daily step counts
Zalewski et al[16]	Cross-sectional study	N=17 stroke survivors •Age=71.3 ±9.5 years •Time since stroke=2.2 years (note: SD not reported)	•10MWT at comfortable speed=0.8±0.4 m/s •10MWT at fast speed=1.0±0.5 m/s •6MWT=258.5+146 m)	SAM worn for 3 days on the non-paretic ankle, only day 2 data used in analysis.	•6MWT and 10MWT at comfortable walking speed moderately correlated to mean daily step counts (r=0.55,0.59 respectively). •Regression analysis was not done.

2.5.2 Balance

Balance refers to an individual's ability to maintain their line of gravity within their base of support or ability to maintain equilibrium[51]. Static balance is the ability to maintain postural stability and orientation with centre of mass over the base of support and body at rest while in dynamic balance the body parts are in motion[51]. The somatosensory, vestibular and visual systems provide input regarding the body's equilibrium and thus maintain balance[51]. It can be broken down in to three aspects: steadiness (ability to maintain a given posture with minimal extraneous movement), symmetry (equal weight distribution between weight-bearing components) and dynamic ability (ability to move within a given posture without loss of balance)[51]. All these components of balance have been found to be disturbed following stroke. Balance testing of stroke survivors with hemiparesis reveals a greater amount of postural sway during static stance, asymmetry with greater weight on the paretic leg and a decreased ability to move within a weight-bearing posture without loss of balance[51]. Stroke survivors have a large risk of falling at home after they have been discharged from the rehabilitation

center[52]. Therefore, an important objective of rehabilitation care is to regain adequate balance function for walking safely in the community[52]. Thus, it is of significant interest to assess the influence of balance on walking in the community.

Table 2 summarizes studies showing the relationship between balance and walking in the community. However, these studies present with many limitations. In the longitudinal study conducted by Kunkel et al, the study started with 74 stroke survivors but by the end of 3 years, only 15 participants were able to complete full assessments at all time points of the study. Large amounts of missing data and the resulting small sample with complete data limits the generalizability of the study. Michael et al measured walking activity only during a 2-day period, which is not a sufficient time to capture true walking activity in the community for stroke survivors[53].

Table 2. Table summarizing studies showing relationship between balance and walking in the community

Author	**Study Design**	**Patient Characteristics**	**Clinical Measures**	**Daily step counts**	**Results**
Michael et al[54]	Cross-sectional	•N=50 •Age=65 years •Time since stroke=0.8 years	Berg Balance Score=34±9	SAM worn on the non-paretic ankle for 2 days.	•Step per day were associated with scores on the Berg Balance Scale (r=0.58). • In a stepwise linear regression, balance was a significant predictor of daily step counts and explained about 30% of the variance in

					daily step counts.
Fulk et al[14]	Cross-sectional study	•N= 19 chronic stroke survivors •Age=65.7±11.9 years Time since stroke=3.5±3.0 years	BBS=49.3±7.6	SAM worn for 7 days on the non-paretic ankle.	BBS was moderately correlated with daily step counts r=0.54) but was not a significant predictor of daily step counts in stepwise linear regression analysis.
Kunkel et al[9]	Longitudinal study with assessments done in hospital, at 1, 2 and 3 years post-stroke	•N= 74 stroke survivors •Age=76 years	BBS (values not specified)	activPAL worn for 2 days during all assessment points.	Daily step counts were associated with balance scores at year1, 2 and 3 (r=0.609).

2.5.3 Quadriceps strength

Stroke causes muscle weakening in patients due to a decrease in the rate of motor unit recruitment and weakness of selective type II fibers with decreased extension torque in knee joints on the non-paralyzed and paralyzed side when compared to that of healthy individuals of the same age[55]. Among the lower extremity muscles, the quadriceps provides stability in the stance phase during walking and supports normal postural alignment on the knee joint[55]. Studies show a correlation between quadriceps strength of the paretic (r=0.6-0.8) and non-paretic leg (r=0.38) with walking speed and walking endurance measured by 10MWT and 6MWT respectively[56-58]. Walking speed and endurance are considered as measures of walking in the community, there is a high probability that quadriceps strength of the paretic leg might affect ability of the stroke survivors to walk in the community. To date, there are no studies showing the

relationship between steps/ day during walking in the community and quadriceps strength. Therefore, it of interest to us to consider quadriceps strength as one of the factors which is related to walking in the community.

2.6 Relationship between walking in the community and personal characteristics

2.6.1 Post-Stroke Fatigue

Post-Stroke Fatigue is defined as "A feeling of early exhaustion developing during mental or physical activity with weariness, lack of energy and aversion to effort."[59]. Prevalence of PSF ranges between 23-77%[59]. Stroke survivors have described PSF as their "most common invisible impairment"[59]. PSF is associated with functional dependence in activities of daily living and instrumental activities of daily living as well as strained spousal relationships and sexual dysfunction[59]. PSF has also been shown to predict poor health-related quality of life (QOL) at 3 months post-stroke and at long-term follow up[59]. PSF may contribute to and be aggravated by sedentary lifestyle of people suffering from stroke[60]. Many people after stroke enter a vicious cycle of increased sedentary behaviors, leading to further avoidance of activity and persistent fatigue comprising walking in the community[60].

Fatigue may be an important factor associated with reduced physical activity post stroke; however, to date, research is limited. In other neurological conditions such as Parkinson's Disease, fatigue has been found to be strongly linked to deficit severity and functional capacity[24]. Similarly, in Multiple Sclerosis, fatigue has been shown to have a negative effect on the performance of activities of daily living[61]. Michael et al. reported that in patients with chronic stroke, fatigue is associated with cardiovascular deconditioning and results in reduced ambulatory activity at home and in the

community[62]. The association of fatigue with walking in the community following stroke has not been well investigated to date. Robinson et al. found fatigue measured by the Fatigue Severity Scale (FSS) was not associated with Trip activity log(number of trips or walking related activities) recorded by the participant but had a weak correlation (r=0.38)steps per day measured by VKRFitness Twin Step Pedometer in 50 community dwelling stroke survivors, age 65±8.4 years, 85±89.9 months post-stroke[63]. Similarly, Bijleveld-Uitman et al. found that fatigue measured by FSS was not a significant confounder in the relationship between gait speed and walking in the community[64]. While a longitudinal study found significant associations between higher Fatigue Assessment Scale (FAS) scores and lower step counts at 1(r= -0.39), 6 (r=-0.31) and 12 months post-stroke (r= -0.35)[65], a cross sectional study reported no significant relationships between step counts, peak oxygen consumption, and FSS scores at 6 months post-stroke [23,66]. However, these studies are small studies and they used different criteria and definitions of both fatigue and walking in the community, therefore definite conclusions cannot be drawn. Considering the high prevalence of post stroke fatigue and the association of fatigue with ADL performance and physical activity in stroke and other neurological conditions, the relationship between walking in the community and post-stroke fatigue warrants further exploration.

2.6.2 Depression

Post- Stroke Depression (PSD) is a common sequela of stroke. According to Diagnostic and Statistical Manual (DSM) V, PSD is a mood disorder superimposed from another medical condition; i.e. stroke with features of depression, mania or mixed symptoms[67]. The mechanism of post stroke depression is an interplay of psychological,

social and biological factors[68]. It is prevalent in 30-60% stroke patients within the first year of onset[68]. It is the strongest predictor of quality of life in stroke survivors and is associated with poor functional outcome, slow recovery, low quality of life and reduced participation[68]. Post-stroke depression leads to loss of interest in activities or hobbies and fatigue which may prevent the stroke survivors from walking in the community.

A relationship between depression, physical activity and functional ability in patients post stroke has been reported in the literature. A study by Chemerinski et al. examined the effect of post stroke depression on recovery of ADL function in a sample of 55 stroke patients, at three and six months post stroke[21]. The results found post-stroke depression, as measured by the Hamilton Depression Scale (HDS), to be significantly associated with impaired recovery of ADL function[21]. Similarly, a study by Goodwin et al. examined the association of post-stroke depression with functional health outcomes[69]. Depression was measured by Composite International Diagnostic Interview Short Form and to measure functional health-related outcomes they asked the participants a series of questions regarding their inability to walk, climbing stairs, lifting groceries and walking distances. They found a significant association existed between depression and greater limitations in activities of daily living, walking and stair climbing[69]. Post-stroke depression may also result in reduced participation levels. Feibel et al. reported that patients suffering depression at six months post stroke, had greater difficulties in returning to their prior social activities compared with non-depressed patients[70]. Given the association between depression and activity levels post stroke, it is possible that depression may have an influential effect on walking in the community. In a cross-sectional study by Baert et al, 16 stroke survivors aged 61.9 ±11.9 years, one-year post-stroke, depression, measured by the Beck Depression Inventory-II was moderately

correlated to steps/day (r=0.62)[71]. Yamax SW-200 pedometer placed on the lateral side of the non-paretic knee was worn for five consecutive weekdays[71]. Robinson et al studied participation in walking in the community following stroke[63]. They used both subjective and objective measures to measure walking in the community and studied the impact of personal factors (depression, fatigue, falls and balance self-efficacy) on walking in the community[63]. Depression measured by Center for Epidemiologic Studies Depression Scale had a low correlation (r=0.33) with steps day[63]. Objective measurement of walking in the community was done using the Trip activity log and VKRFitness Twin Step Pedometer[63]. However, there are some limitations in these studies. The accuracy of the data of Trip activity log may be affected by recall bias and reliability and validity of VKRFitness Twin Step Pedometer has not been established in the stroke population[63]. Further research is needed to investigate the relationship between walking in the community and post-stroke depression.

2.7 Assessment of clinical correlates

2.7.1 Measurement of walking in the community

Steps are considered as the fundamental unit of human locomotion and the preferred metric for quantifying walking in clinical and community settings[72]. Steps are objective, intuitive, readily understandable to the layperson and are measured easily and accurately[72]. Steps per day has strong associations with physical health variables and are motivational facilitating behavioural change[72]. Tudor-Locke and Bassett proposed a classification scheme for categorizing adults based on their daily steps:[7] <5000 steps/day – sedentary lifestyle, 5000-7499 steps/day- physically inactive lifestyle, 7500-9999-

steps/day moderately active, ≥ 10,000 steps/day- physically active, ≥ 12,500 steps/day- very active[7].

A summary of various step counting devices is presented in Table 3. Variables that affect accuracy of step count include, but are not limited to, type and location of device, body weight, and speed of walking. Klassen and colleagues examined the effect of walking speed and positioning of the accelerometer (non-paretic side of waist versus ankle) on its accuracy in ambulatory individuals post-stroke [73]. The protocol consisted of eight 15m walking trials with one trial performed at a self-selected pace and the other 7 at speeds from 0.3 - 0.9 m/sec, progressed in 0.1 m/sec increments[73]. Findings suggested that the accuracy of the accelerometer was greater as walking speed increased from 0.3 to 0.9 m/s (range of speed typical of hemiplegic gait[74]) and for walking speeds between 0.3-0.6 m/s, when placed at the ankle rather than the wrist[73]. Consistent with the latter result, Giggins and colleagues concluded in a review of step count monitoring in patients with neurological conditions that activity monitors positioned on the ankle were more accurate than wrist or waist-mounted devices, particularly during slow walking conditions[75].

For the purpose of my study, I will use Step Watch Activity Monitor worn on the paretic ankle for 3 days. Total step counts have excellent test-retest reliability with intraclass correlation coefficient of 0.93-9.98 when used for 3 days in stroke survivors, monitoring for less than 3 days is not recommended due to high variability and does not yield reliable data[53].

Table 3. Table summarizing step counting devices.

Device	Mechanism	Reliability/validity
Wrist-mounted (e.g., Nike Fuelband, Fitbit Flex, Fitbit Surge)	• Triaxial accelerometer using a finely tuned algorithm for step counting[72] • Motion size exceeds a set threshold- step count recorded[72].	•Steps not recorded if wrist is stationary (e.g., using a walker, grasping treadmill hand rails)[76] •Invalid steps recorded with arm movements not associated with walking (e.g., folding laundry, gesturing while talking)[76]
Waist-mounted pedometer	•Horizontal, spring-suspended lever arm moves up and down with each step causing opening and closing of an electrical circuit and subsequent registration of steps[72]	•Slow walking speeds and obesity result in underestimation of steps[77]
Waist/pocket-mounted accelerometers (e.g., Fitbit One, Fitbit Zip, Philips Direct Life, Misfit Shine)	Piezoelectric or piezoresistive triaxial accelerometers[72]	•More accurate than spring-levered pedometers because not impacted by body weight •Diminished accuracy at slow walking speeds[77].
Thigh-mounted accelerometers (e.g., ActivPAL)	Uni-axial accelerometer that records gravitational and leg movement accelerations during walking and running[72]	Accurate in counting steps to about 2.4 kph (1.5 mph[78])
Ankle-mounted accelerometers (e.g., Step Watch 3)	Analog accelerometer	•Regarded as the most accurate step counter for walking[79] •High sensitivity and specificity for step counts during walking[72] •Accurate at very slow walking speeds and in obese individuals[80] •Accurate during household activities[81] •Records extra steps during bicycling, heel tapping or stationary leg swinging[82]
Shoe-mounted or shoe lace-mounted pedometers	•Contact of the heel with ground causes a step to be recorded in seconds with a step being counted between pre-swing and initial contact[72]	• More accurate than body-mounted step counters when tested in patients with chronic health conditions and healthy aged-matched volunteers[72]

	• It consists of a sensor and transmitter assembly: a sensor, a microcontroller unit and a wireless transmitter with the microcontroller unit receiving a pair of impulses each time the shoe contacts the ground[83].	

2.7.2 Measurement of various physical characteristics related to walking in the community

2.7.2.1 Balance

Below is a brief description of the scales used for assessing balance in stroke survivors:

Table 4. Table summarizing scales used for assessing balance in stroke survivors.

Scale	Characteristics	Psychometric properties
Berg Balance Scale (BBS)	•Patients maintain positions and complete moving tasks of varying difficulty[84]. •In most items, patients must maintain a given position for a specified time. •Score range: 0-56 [84]. •A score from 0-20 in the BBS indicates high risk of falls, 21-40 indicates medium risk of falls and a score from 41-56 indicates low risk of falls[84].	•Cronbach's alpha: 0.97[85] •Inter-rater reliability: 0.88)[86]
Postural Assessment Scale for Stroke Patients (PAS)	• 12 items of increasing difficulty that measure balance in lying, sitting and standing[87]. •Designed specifically for patients with stroke regardless of postural competence[87]. • 4-point scale where items are scored from 0-3 with a total range of 0-36[87].	•Cronbach's alpha: 0.94[87] •Inter rater reliability: 0.97[87].

Sitting balance section of the Motor Assessment Scale (MAS)	•Developed to assess everyday function in patients with stroke. •8 subscales, only one of which related to balance (sitting balance)[88]. •Sitting balance section is scored on a 7-point scale •Patients are assessed on their ability to perform progressively harder sitting balance activities[88]. •Score of 0 indicates a patient is only able to sit with assistance of another person, whereas 6 indicates they can sit on a stool unsupported, reach sideways to touch the floor and return to the starting position[88].	•Inter-rater reliability: 0.97[88]
Balance section of the Fugl-Meyer Motor Assessment (FMA)	•FMA is a stroke-specific, performance-based impairment index[88]. •Designed to assess motor functioning, balance, sensation and joint functioning in patients with post-stroke hemiplegia[88]. •Balance subscale examines static sitting, parachute reactions in sitting, standing and single stance[88]. •7 items are each rated on a 3-point ordinal scale[88].	•Inter-rater reliability: 0.93[88]
Trunk Impairment Scale (TIS)	•TIS aims to measure motor impairment of the trunk after stroke. •17 tasks in three subscales: static sitting balance, dynamic sitting balance and coordination[88]. •Range from sitting on the edge of the bed, sitting on the edge with a narrower base of support and various selective movements of the trunk[88].	•Inter-rater reliability:0.85-0.99[88]
Brunel Balance Assessment (BBA)	•12-point ordinal scale of balance activity with functional performance tests at each level of the ordinal scale[88].	•Cronbach's alpha: 0.92[88]

	•Ordinal scale arranged into three subscales (sitting, standing and stepping balance)[88].	

For the purpose of my study, I will use BBS as it is identified as the most commonly used assessment tool across the continuum of stroke rehabilitation[84]. It has strong reliability, validity and responsiveness to change[84]. The scale is useful and easy to administer without the need for expensive equipment or prolonged assessment time[84].

2.7.2.2 *Walking speed and endurance*

Developed in the 1960s to assess people with cardiovascular and respiratory diseases[89,90] the 6- minute walk test (6MWT) measures the distance that a patient can walk on a hard surface in six minutes[91]. It is a valid and reliable tool commonly used in a wide range of populations (e.g., healthy adults, people undergoing cardiovascular rehabilitation, patients with schizophrenia, fibromyalgia, cancer and trans-tibial amputation)[92]. It has excellent test-retest reliability (ICC= 0.96-0.99) and criterion validity (r= 0.66)[93]. It has been used to monitor changes in walking capacity or following stroke and a significant predictor of community ambulation and integration in stroke survivors [94,95].

The 10-metre walk test (10MWT) has robust psychometric quality in the evaluation of patients with neurological conditions [96] and measures average gait speed at a single pace (comfortable or fast) over a short distance and requires only a few minutes to complete[97]. It has excellent test-retest reliability (ICC= 0.95-0.99)[98] and criterion validity (r= 0.66)[96].The 6 MWT is often used in conjunction with 10MWT because 6MWT is used to investigate walking endurance and the 10MWT is used for testing walking speed[99]. The maximal 10MWT requires a brief, maximal effort and is associated

particularly with muscle strength whereas the 6MWT induces more metabolic stress and is, therefore, more closely associated with aerobic capacity[100].

2.7.2.3 Muscle Strength

Hand-held dynamometer will be used to determine the muscle strength of quadriceps muscle of the paretic leg. A hand held dynamometer is used to quantify maximal strength and offers several advantages over free weights, including ease of transportation, time efficiency and low cost[17]. The ICC used to characterize the reliability of the strength tests by hand-held dynamometer ranges from 0.84 to 0.99 and it is a reliable and valid means of measuring muscle strength in patients with brain damage[17].

2.7.2.4 Level of Ambulation

The Functional Ambulation Categories (FAC) evaluates ambulation ability. It is a 6-point scale which assesses ambulation status by determining the amount of human support a person requires when walking, regardless of their use of personal assistive device[101].

2.7.3 Measurement of various personal characteristics related to walking in the community

2.7.3.1 Depressive symptomatology

A number of self-reported measures, such as questionnaires and surveys have been developed to screen depression. Several articles discuss the use of outcome measures for PSD, many of which conclude that while there are various useful measures, it remains unclear whether one measure is more valid and reliable than the others[102].

Table 5. Table summarizing scales used for assessing depressive symptomatology.

Scale	Characteristics	Psychometric properties
Beck Depression Inventory-II (BDS-II)	•21 items scale each with a 4-point scale indicating degree of severity •Score range- 0-63[103]. •Items that reflect the cognitive, affective, somatic, and vegetative symptoms of depression[103]. •Strengths: time efficiency, simplicity in administration and scoring, availability of translations into several languages, application in many different populations[103]. •Limitations: overlapping symptoms between medical conditions and depression[103].	•Internal validity (0.79 – 0.90) [103]
Centre for Epidemiologic Studies Depression Scale (CES-D)	•20- item scale with 4-point Likert scale ranging from 0 (rarely or none of the time) to 3(most or all of the time). •Score range- 0-60[103]. •Strengths: many available translations, validation with many populations and cost free access[103]. •Limitations: high false positive rate for clinical depression and the original 20-item version can be difficult to follow[103].	•Internal validity: 0.85-0.90[103] •Sensitivity: 0.56[103] •Specificity: 0.91[103] (For post-stroke populations)
Geriatric Depression Scale (GDS)	•Original version contains 30 items. •Shorter 15-item version, GDS-15 was developed to decrease fatigue or lack of selective attention[103]. •Items represent characteristics of depression in the elderly in the affective and cognitive domains[103].	•Reliability: 0.75[103] •Sensitivity: 0.66[103] •Specificity: 0.79[103] (In people with mild-depression)

	•Strengths: time-efficient, simple to administer and score[103] •Limitations: lack of information on the validity of the GDS in those over 85 years of age and concern that it assesses general distress rather than depressive symptoms[103]. •High clinical usability for identifying depression in elderly and aphasic medical patients with a yes/no format makes it easy to use in aphasic patients[103].	
Hospital Anxiety and Depression Scale (HADS)	•Self-report measure to assess anxiety and depressive symptoms in a general medical population aged 16-65 years[103]. •7 items measuring cognitive and emotional aspects of depression and 7 anxiety items focusing on cognitive and emotional aspects of anxiety[103]. •4-point scale, with score range:0-42[103]. •Strengths: time efficiency, use with many populations and many available translations[103].	•Validity:0.67 [103] •Sensitivity: 0.73[104] •Specificity: 0.82[104] (For post-stroke populations)
Patient Health Questionnaire-9 (PHQ-9)	•9 item scale with 4-point Likert scale ranging from 0 (not at all) to 3(nearly every day) •Score ranges-0-27[105]. •Strengths: time efficiency, wide use with many different populations, sensitive to treatment, valid for both diagnosing depressive disorders and depression severity and availability in the public domain[105].	•Test-retest reliability: 0.98[105] •Concurrent validity: 0.7[105] •It performs well as a depression screening tool in patients post-stroke, with 91% sensitivity and 83% specificity for major depression and 78%, and 96% specificity for any depression diagnosis[105].
The Stroke Aphasic Depression Questionnaire (SADQ)	•Self-reported measure to detect depressed mood in community-dwelling	•Reliability: 0.80[106]

	individuals post-stroke with significant aphasia[106]. •21-item questionnaire based on observable behaviors often associated with a depressed mood[106].	

All of the aforementioned measures are commonly used for the purpose of diagnosing depression; however, due to multiple factors influencing depressive symptoms, there is not one perfect measure for all. Given this caveat and the limitations noted above, I have determined that the PHQ-9 is the most appropriate measure for depression for my proposed study. The rationale for selecting the PHQ-9 for the study is that it is easily available to the public, is time efficient, has strong psychometric properties, and can be used in measuring baseline depression severity and responsiveness to treatment.

2.7.3.2 Assessment of PSF

Many tools have been used to measure PSF but all were originally developed to measure fatigue in conditions other than stroke and have not been validated for the stroke population[107 ,108]. Assessment tools for PSF differ in the concept of what they measure as the use of a uniform definition of PSF is lacking[109]. Researchers and clinicians face challenges when comparing data and assessing a patient's condition because currently many different assessment tools and cut-off scores are in use[109]. Measures that include questions about general weakness may not be valid because post-stroke weakness is generally attributed to hemiparesis rather than fatigue[107]. Recently, a few scales specific to stroke have been introduced (e.g. the Dutch Multidimensional Fatigue Scale, the Fatigue Scale for Motor and Cognitive functions (FSMC) and the Neurological Fatigue Index for Stroke) but, as yet, they are not used widely in clinical and research settings[109].

Table 6. Summary of frequently scales used for assessment of PSF.

Scale	Characteristics	Psychometric properties
Fatigue Severity Scale (FSS)	•10-item scale to self-rate fatigue in the past week. •7-point Likert scale ranging from 1(strongly disagree) to 7 (strongly agree)[108]. • Range of scores: 0-63. •Well-accepted cut-off for classifying fatigue (≥4) facilitating prevalence comparisons across studies[110].	•Cronbach's alpha: 0.88-0.93[107] • Intra-class correlation coefficient: 0.76-0.80[107]
Fatigue Impact Scale (FIS)	•40-item instrument evaluates the effect of fatigue on cognitive functioning, physical functioning and psychological functioning.[111] •5-poiny Likert scale ranging from 0 (no problem) to 4 (extreme problem)[111]. •Range of scores: 0-160, higher score indicating higher fatigue[111]. •21-item Modified Fatigue Impact Scale may be used if full scale is toofatiguing[111]	•Internal consistency: 0.93[108]
Fatigue Assessment Scale (FAS)	• 10 fatigue-related questions[112] •5-point Likert scale from 1 (*never*) to 5 (*always*)[112]. •Range of scores: 10-50 points with higher scores indicating greater fatigue [112] •Cut-off of >24 proposed for classification of PSF [110].	•Cronbach alpha: 0.58-0.62[108] •Construct validity: 0.71[108].
Fatigue Subscale of the Profile of Mood States (POMS	•7-item subscale of POMS to evaluate contribution of fatigue to changes in mood. •5- point Likert scale ranging from 0 (not at all) to 4 (extremely)[113].	•Cronbach's alpha: 0.91-0.93[114] •Construct validity: 0.47[114].
Vitality Scale of SF-36	•6- point Likert scale ranging from 1 (*all the time*) to 6 (*none of the time*) [113].	•Cronbach's alpha: 0.88-0.89[108] •Construct validity: 0.75[108]

	•Higher score indicates higher vitality (greater energy, lower fatigue)[115].	

For my study I will use the FSS scale with a cut-off of 4 on 1-7 scale. Nadarajah et al. showed excellent internal consistency of FSS for stroke survivors with Cronbach's alpha >0.90[116]. The scale has excellent test-retest reliability with ICC= 0.93 [116]. The scale demonstrated good concurrent validity with VAS-Fatigue (r> 0.60) and is sensitive to distinguish fatigue in stroke from healthy individuals[116].

2.8 Conclusions from the literature review

A review of the literature shows that walking in the community is of paramount importance to the stroke survivors with many physical and affective characteristics affecting walking in the community. Although the studies mentioned in the literature review provide evidence of relationship between walking in the community and physical and affective characteristics, research is limited in this area and presents with many limitations as mentioned in the literature review. There is a dearth in literature regarding studies focusing on walking in the community. Most studies on stroke survivors focus on the physical activity levels of the population rather than walking. There is a very prominent difference between physical activity and walking where physical activity is defined as "movement produced by the action of skeletal muscles that substantially increases energy expenditure[117]" and walking is defined as "repetitious sequence of limb motions that move the body forward while simultaneously maintaining stance stability"[1]. Studies measuring walking in the community use subjective scales rather than objective measures to measure walking in the community. Community ambulation questionnaire

used in the studies is not an objective measure of walking in the community, it categorizes patients in to different categories of walking in the community [64,118,119]. Use of pedometers and activity counters is not reliable in measuring step counts/day as mentioned in the literature review.

Studies on factors which affect walking in the community are mostly correlational studies. It is important to note that correlation does not equal causation, it is a way of measuring the extent to which two variables are related. Thus, it is critical to interpret the results with great caution. Mudge et al. concluded that 10MWT (r=0.55) and 6MWT (r=0.67) were correlated to mean daily step counts but in a forward linear regression analysis, 6MWT was the only significant predictor for Step Watch daily step counts with 54% of variance in mean daily step counts explained by 6MWT. Therefore, it is not necessary if two variables are correlated, they will also have significant relationship in regression analysis. Regression analysis is important before we reach to conclusion about relationship between two variables as it indicates the change in the dependent (outcome) variable associated with a unit change in the independent (predictor)[120]. The studies mentioned in the literature review use step wise linear regression analysis for data analysis[15,54]. In stepwise regression, the order in which predictors are entered in to the model is based on a purely mathematical criterion[120]. It is not recommended to use stepwise regression method because it relies on computer selecting the variables[120]. Variable selection depends upon only slight differences in the criteria and these slight numerical difference contrast with major theoretical differences[120]. For my study I will use hierarchical method as it is appropriate method for theory testing[120].

This literature review was helpful in identifying key parameters for the study. Based on the findings, it is evident that walking speed and endurance play an important role in ability to walk in the community. However, they don't always accurately predict walking in the community and therefore it is important to establish what other physical and affective characteristics are associated with walking in the community after stroke. Factors such as fatigue, depression, balance and quadriceps strength have been shown to associated with physical performance post-stroke but their relationship to walking in the community requires further investigation.

CHAPTER 3: METHODS

The study was approved by the Nova Scotia Health Authority (NSHA) Research Ethics Board (REB) (ROMEO File No. 1024100). Data collection and recruitment began in January 2019 and proceeded until May 2019. The role of research assistant was taken by the author. The author worked to coordinate and schedule participants and assist with data collection and data processing.

3.1 Study Design

An observational, cross-sectional design was used to examine the relationships between walking activity in the community and various physical and affective characteristics in community-dwelling men and women who were greater than six months post-stroke.

3.2 Participant Selection

The following inclusion and exclusion criteria were used to recruit participants for the study:

Inclusion Criteria

1. Male or female.
2. 18 years or older.
3. Diagnosed with stroke, confirmed by a physician, CT or MRI.
4. At least >6 months post-stroke.
5. Able to walk at least 10 meters with or without assistive devices (Functional Ambulation Classes 2-5) inside or outside the home[121].
6. Medically stable.
7. Able to understand spoken English.

8. Able to provide informed consent.
9. Able to attend assessment session.

Exclusion Criteria

1. Resting heart rate <60 bmp or > 120 bpm[91].
2. Resting systolic blood pressure >170 mmHg[91].
3. Resting diastolic blood pressure >95 mmHg[91].
4. Has a health-related condition that would prevent participation in this study.
5. Participating in another research study that could confound the results of this study.

3.3 Sample size

The study consisted of 35 community-dwelling stroke survivors.

3.4 Participant Recruitment

The following methods were used to recruit participants for the study:

1. Investigators attended community stroke group meetings in the Halifax Regional Municipality and provided a short information session about the study. Investigators asked the group members interested in obtaining more information about the study to complete a form providing their name and preferred contact information.
2. A recruitment poster (Appendix A) approved by the NSHA REB was posted at community centres, church halls and health care centres in the Halifax Regional Municipality.
3. Investigators had access the Dalhousie University Stroke Rehabilitation Database which contains information about the people who have provided

written consent to be contacted about future stroke related projects that have received Research Ethics Board Approval.

The investigators of the study contacted interested participants via telephone to conduct a screening phone interview (Appendix B) to determine preliminarily if they meet the inclusion and exclusion criteria of the study and to provide a brief description of the study. Participants who met the inclusion and exclusion criteria and expressed interest in possible participation in the study received a consent form (Appendix C) by email or mail (as preferred by the participant) for review.

A week after sending the consent form, the same investigator contacted the potential participants again. If after reviewing the consent form, a potential participant continued to be interested in participating, a 2-hour appointment was set up with author at the Rehabilitation lab of the Nova Scotia Rehabilitation Centre at a time convenient to the participant to discuss the study. In preparation for the appointment participant was advised to: (i) have a light meal or snack before the appointment, (ii) continue with their usual medical regimen, (iii) avoid exercising vigorously within the 2 hours before the appointment and (iv) wear comfortable clothing and appropriate shoes, and (v) use their usual walking aids, if any [91].

At the appointment: (i) the study was described, (ii) the consent form was reviewed, (iii) eligibility criteria was confirmed (which included measuring resting heart rate and blood pressure in quiet sitting), (iv) all questions of the participant and/or caregiver were answered to their satisfaction (v) to assesses participant's capacity to provide informed consent, Mini Mental State Examination was administered. (vi) the consent form was signed, dated, and witnessed and a (vii) copy of the signed consent

form was given to the participant. Time to complete the above procedure was approximately 30 minutes.

3.5 Data Collection Procedure

3.5.1 Participant background information

After the participant provided written informed consent, the following demographic information was obtained: age, sex, employment status, marital status. The Functional Ambulation Category and NIHSS scale were administered. Time of stroke (month, year) was obtained from the participant or a caregiver. Time to complete was approximately 20 minutes.

The participant was asked to complete the FSS scale and PHQ -9 for evaluation of fatigue and depression respectively. If required or preferred by the participants, the author assisted the participant in completing the questionnaires.

Time to complete all questionnaires was approximately 10 minutes.

3.5.2 Functional Walking Tests

3.5.2.1 Six-Minute Walk Test

On their visit to the Nova Scotia Rehabilitation Centre, the participant performed the 6MWT in presence of the author. The test was performed indoor along a 30 metre long, flat, straight, enclosed corridor with a hard surface which was seldom travelled[91]. Turns were marked with orange traffic cones[91]. The patient was seated in a chair at least 10 minutes before starting of the test and during this time pulse and blood pressure was recorded[91]. The participant started walking from a marked starting line[91]. Before and immediately after the test, rating of perceived exertion$_{0\text{-}10\ scale}$[91] was recorded, together with the heart rate and blood pressure (via an automatic blood pressure monitor). The

participant was given instructions at the start of the test to walk as far as possible for 6 minutes[91]. The participant walked back and forth the hallway around the cones without exerting themselves and was permitted to slow down, to stop and to rest, as necessary[91]. While resting they could lean against the wall or sit, and then resume walking as soon as possible[91]. The timer was not stopped while the patient was resting. A lap counter was used to track the number of laps completed. At the 6-minute mark, a small object was placed on the floor to mark the end location and a measuring wheel was used to measure the distance covered in the last lap. The total distance in metres walked rounded to one decimal point was calculated[91]. Time to complete was approximately 10 minutes.

3.5.2.2 10-Metre Walk Test

The participant was instructed to walk a 10-meter distance marked off in a quiet corridor.[122]. A10-meter walk distance was marked at either end. To accommodate acceleration and deceleration, a 2-metre distance was also marked before the actual starting point and after the end point, for a total distance of 14-metres. The timing of the test was started when the toes of the leading foot crossed the 2-meter mark and the timing was stopped when the toes of the leading foot crossed the 10-meter mark[122]. The participants were allowed to use an assistive device during the test if they used any and it's usage was documented. [122]. The patient was instructed to walk at comfortable (preferred) speed until the investigator said stop[122]. Two trials were collected with a brief rest in between, and the average of the two trials was reported[122].The distance travelled during the test (10 metres) was divided by average time calculated from the three trials to obtain the comfortable walking speed of the participant[122]. Time to complete was approximately 10 minutes.

3.5.3 Daily step counts

Walking in the community was quantified using the Step Watch Activity Monitor. It is small (75x50x20 mm), lightweight (38g) and is worn at the ankle[75]. The monitor contains a custom sensor that uses a combination of acceleration, position and timing to detect steps[80]. The Step Watch was calibrated based on each participant's height and gait pattern and was applied to the non-paretic ankle with adjustable straps[80]. The participant was instructed to wear the monitor for 3 days throughout their daily activities removing them only to bathe or sleep. The Step Watch Activity Monitor was returned to the research team after 3 days either by mail (stamped, addressed envelope provided by the investigator) or in person. The participants were told to contact the investigator through phone or e-mail if they had any doubts regarding the usage of SAM. Time to prepare was approximately 10 minutes.

Walking in the community was described by the mean number of steps taken by the participant (daily step counts) in 3 days. The SAM also measured the percentage inactive (percentage of time of the day included for analysis in which no steps were recorded), percentage steps low, medium and high (percentage of steps relative to all steps in the time included for analysis taken at a low, medium and high step rate respectively). The SAM output provides us with the time in minutes included in the analysis and automatically counts the number of steps that were taken each minute.

3.5.4 Assessment of physical characteristics related to walking in the community

Knee extensor strength of the paretic knee was measured using a hand-held dynamometer[123]. Participants were seated at the edge of the plinth with their hips and knee at 90-degree angle and feet dangling just above the floor. The participant's upper extremities were resting on the lap. The participants were familiarized with the testing

procedure by demonstrating it on their non-paretic limb first. The hand-held dynamometer was place anteriorly on the distal tibia, proximal to the malleoli and the testing belt was positioned around it. Author provided resistance to permit an isometric contraction which was held for 5 seconds. The procedure was repeated twice and the participant was allowed to rest in between the two trials. [123]. The highest reading in newtons was used for analysis[123]. The BBS was administered by the author. Time taken for assessment of knee extensor strength and balance was approximately 20 minutes.

Table 7. Table showing estimated time for different procedures of data collection.

Procedure	Estimated Time
Mini Mental Status Examination	**10 minutes**
Intake form	**20 minutes**
Functional Ambulatory Scale	**5 minutes**
National Institute of Health Stroke Scale	**15 minutes**
Patient Health Questionnaire-9	**5 minutes**
Fatigue Severity Scale	**5 minutes**
Six- Minute Walk Test	**10 minutes**
Ten Meter Walk Test	**10 minutes**
Step Watch activity monitor preparation	**10 minutes**
Berg Balance Scale	**15 minutes**
Knee extensor strength measurement	**5 minutes**

3.6 Statistical Analysis

Descriptive statistics of each variable (means, standard deviations, ranges) was used describe the sample and assumptions of normal distribution of each ratio variable (age, sex, stroke severity, time since stroke, FAC,FSS, PHQ-9, BBS, step counts, quadriceps strength, walking speed attained during the 10 MWT and distance covered during 6 MWT) was assessed using P-P plots and Kolmogorov Smirnov Test. Bivariate relationships between walking activity in the community and other variables (age, sex, stroke severity, time since stroke, FAC, FSS, PHQ-9, BBS scores, quadriceps strength, walking speed attained during the 10 MWT and distance covered during 6 MWT) was assessed using Pearson correlation coefficient for normally distributed variables or the Spearman rank correlation coefficient for variables without a normal distribution. The correlation coefficient of 0–0.25 indicated little correlation, 0.26–0.49 meant low correlation, 0.50–0.69 meant moderate, and 0.70–0.89 and 0.90–1.00 were indicators of high and very high correlation respectively[124]. Hierarchical regression approach was used to build a regression model. Multicollinearity was tested using variance inflation factor to ensure whether the outcome variable (daily step counts) has a strong relationship with other independent variables entered in the multivariate analysis[125]. The value of VIF should be ≥ 10 [125]. Level of significance was set at $p<0.05$ and SPSS 24 was used for analysis.

CHAPTER 4: RESULTS

4.1 Descriptive statistics

Thirty-five stroke survivors, 24 (69%) males and 11 (31%) females, mean age 67.6± 8.6 years, 7± 6.5 years post-stroke took part in the study. 18 participants were diagnosed right ischemic stroke and 17 participants were diagnosed with left ischemic stroke. 28 (80 %) participants were married, 7 (19%) were divorced and 1(3%) participant was single. 34 (97%) participants had taken retirement from employment and 1 (3%) participant was on disability leave. 13 (37%) had no symptoms of stroke, 18 (52%) participants had minor stroke symptoms and 4 (11%) participants had moderate stroke symptoms.

Table 8 describes patient characteristics and the results of the various physical and affective characteristics measured during the study.18 participants (51%) reported fatigue. According to the PHQ-9 scores, 19 (54%) participants were not depressed, 10 (28 %) participants were screened for mild depression and 3 (9%) participants were screened for moderate depression and 3 (9%) were screened for moderately severe depression. Table 9 contains the descriptive statistics of the measures of walking in the community.

Table 8. Descriptive statistics of patience characteristics and various physical and affective characteristics measured during the study.

Participant characteristic (n=35)	**Mean (Standard Deviation)**	**Range**
Age (years)	**67.6 (8.6)**	**49-86**
Time since stroke (years)	**7 (6.5)**	**0.5-27**

Functional Ambulatory Category (1-5)	**4.74 (0.4)**	**4-5**
NIH Stroke Severity Scale (0-42)	**1.8 (1.8)**	**0-6**
Six-Minute Walk Test **(meters)**	**261.1 (107.3)**	**60-440**
Ten-Meter Walk Test **(cm/sec)** **Community ambulator n (% of sample)** **Limited community ambulator** **House-Hold ambulator**	**84.1 (27.8)** **23(66%)** **9 (25%)** **3 (9%)**	**31.7-132**
Berg Balance Score (0-56) **Low risk of fall n (% of sample)** **Medium risk of fall**	**44.4 (7.6)** **25 (72%)** **10 (28%)**	**22-56**
Knee extensor strength (newton)	**80.8 (33.4)**	**0-194.6**
Fatigue Severity Scale (9-63)	**36.3 (11.5)**	**9-58**
Patient Health Questionnaire-9 (0-27)	**5.8 (4.6)**	**0-18**

Table 9. Measures of walking in the community.

Walking activity measure	**Mean (Standard Deviation)**	**Range**
Number of steps	**5284.9 (3342.9)**	**592-13458.7**
Percentage inactive	**84.4 (6.7)**	**70.6-95**
Low cadence percentage	**43.1 (17.9)**	**21.2-92.9**
Medium cadence percentage	**47.1 (15.4)**	**7.3-71.8**
High cadence percentage	**9.8 (13.5)**	**0-51.4**

4.2 Correlational analysis

We did not obtain SAM data from one participant hence he was excluded from analysis. All the variables were tested for normality using histogram and values of skewness and kurtosis. Time since stroke, FAC scores, BBS scores, knee extensor strength and PHQ-9 scores did not have a normal distribution. The non-normally distributed variables had a negative skew. We tried transforming the non-normally distributed variables, only BBS scores were transformed successfully. Bivariate correlations were assessed using the Pearson's correlation coefficient for normally distributed variables. Among age, NIHSS score, 6MWT distance, 10MWT time, FSS scores, only 6MWT distance (r=0.59), 10MWT time (r=0.60) had a moderate significant relationship with daily step counts of the participant. For variables which were not normally distributed, bivariate correlations were assessed using the Spearman's rho correlation coefficient. Among time since stroke, FAC, BBS, knee extensor strength and PHQ-9, only BBS had a moderate significant relationship (r=0.61) with the daily step count of the participant. Refer to Appendix F for the correlational matrix of all the variables.

Table 11 describes the parametric bivariate relationship between daily step counts and the normally distributed variables. Table 12 describes the non-parametric bivariate relationship between daily step counts and the variables which were not normally distributed. Figure 1- Figure 6 shows scatter plots for the various independent variables and it is association with daily step count.

Table 10. Correlation between steps per day and normally distributed variables.

Clinical Outcome Measures	Relationship with steps per day Pearson's r (P)
Age	**-0.22 (0.218)**
NIH Stroke Severity Scale	**-0.29 (0.091)**
Six-Minute Walk Test	**0.59*(0.000)**
Ten-Meter Walk Test	**0.60 *(0.000)**
Fatigue Severity Scale	**-0.08 (0.661)**

*. Correlation is significant at the 0.01 level(2-tailed)

Table 11. Correlation between steps per day and variables having a non-normal distribution.

Clinical Outcome Measures	Relationship with steps per day Spearman's rho (P)
Time since stroke	**-0.290 (0.094)**
Functional Ambulatory Category	**0.20 (0.262)**
Berg Balance Scale	**0.61* (0.000)**
Knee extensor strength	**0.17 (0.330)**
Patient Health Questionnaire-9	**-0.06 (0.745)**

*. Correlation is significant at the 0.01 level(2-tailed)

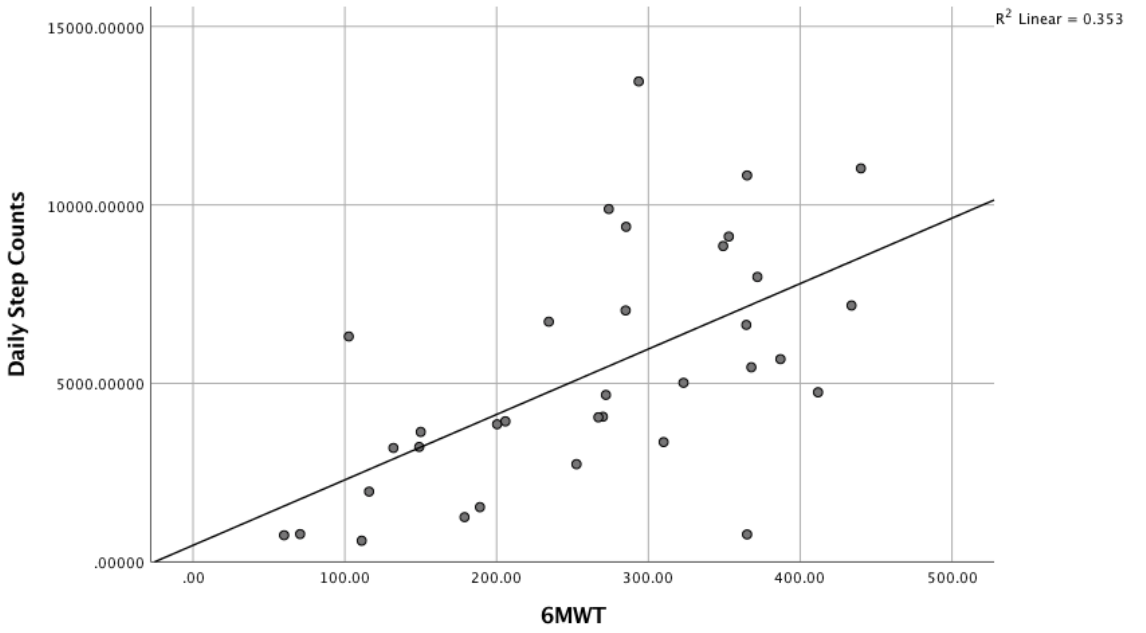


Figure 1. Scatterplot showing moderate correlation between daily step counts and 6MWT.

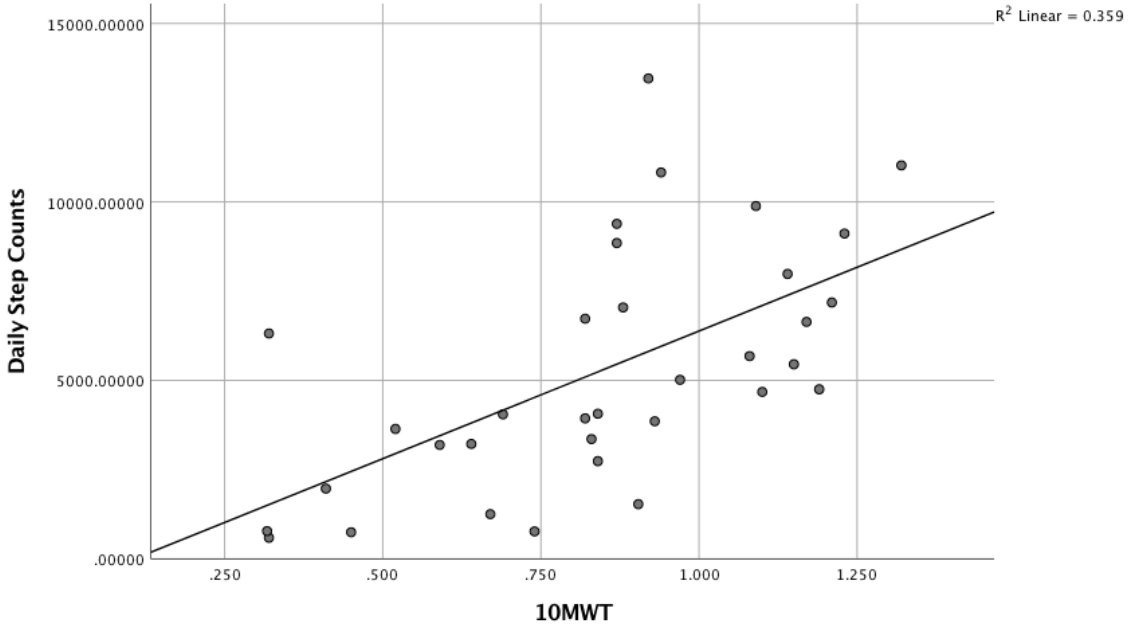


Figure 2. Scatterplot showing moderate correlation between daily step counts and 10MWT.

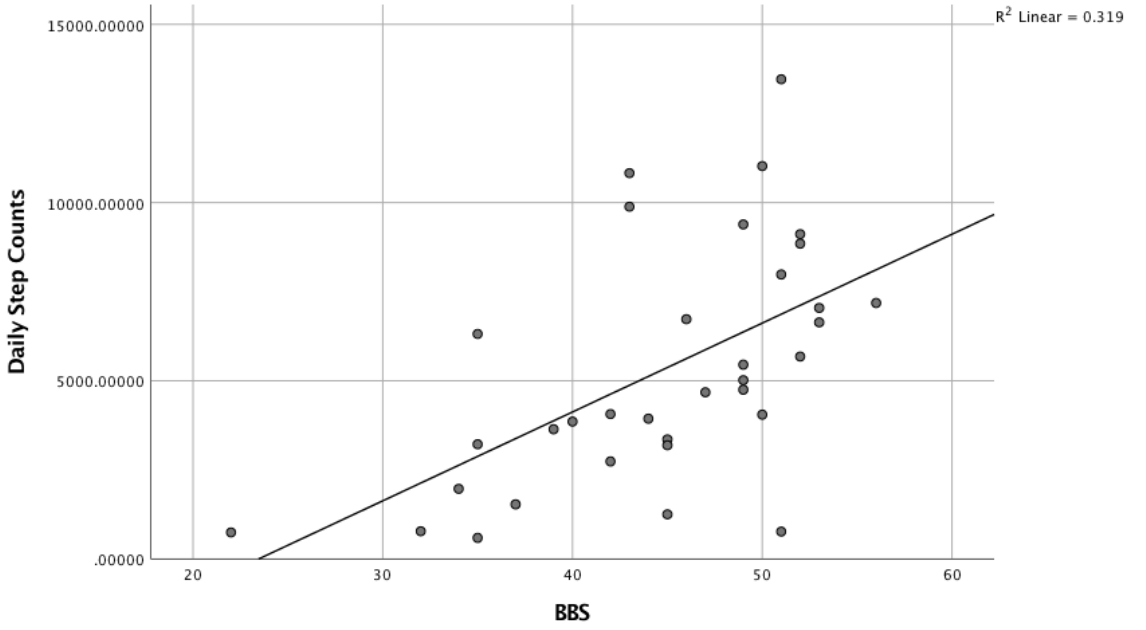


Figure 3. Scatterplot showing moderate correlation between daily step counts and Berg Balance scale scores.

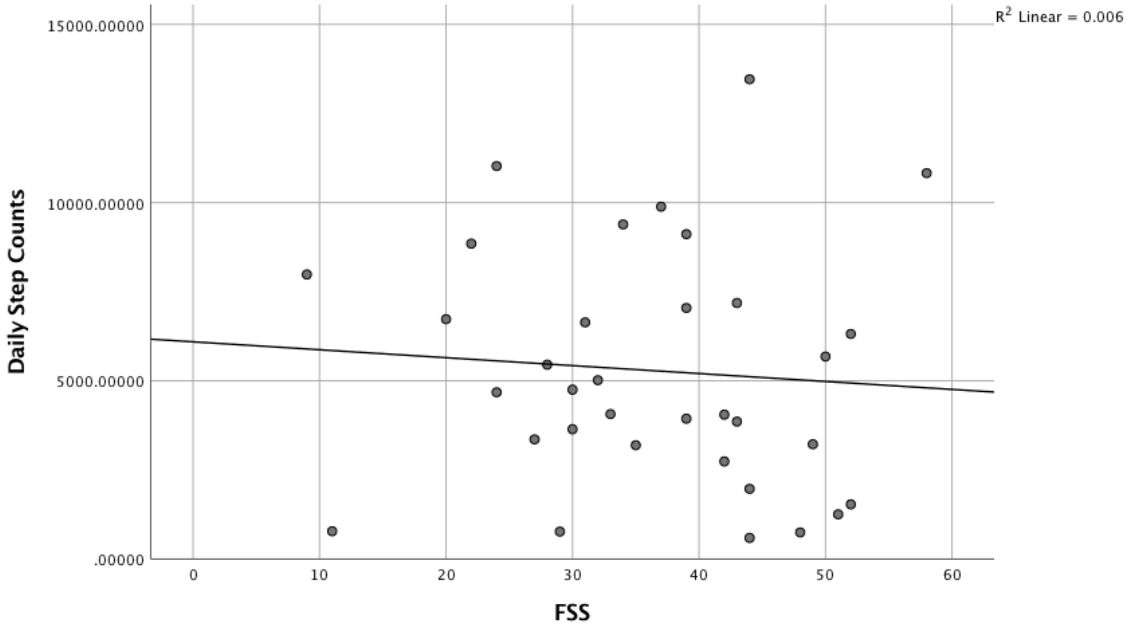


Figure 4. Scatterplot showing relationship between daily step counts and Fatigue Severity scale scores.

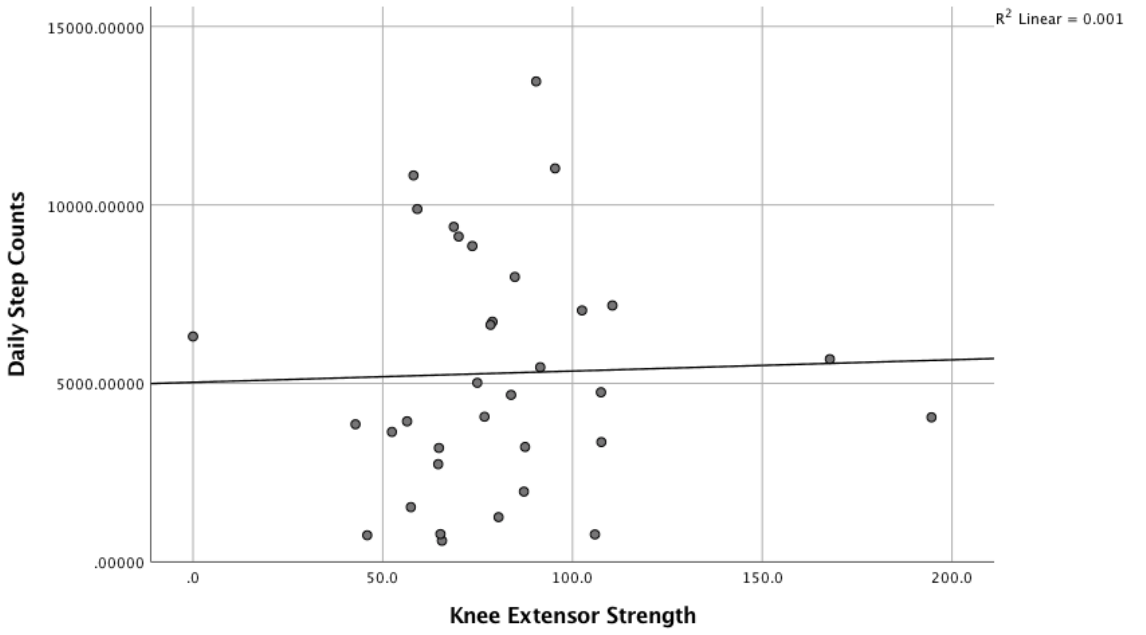


Figure 5. Scatterplot showing relationship between daily step counts and knee extensor strength.

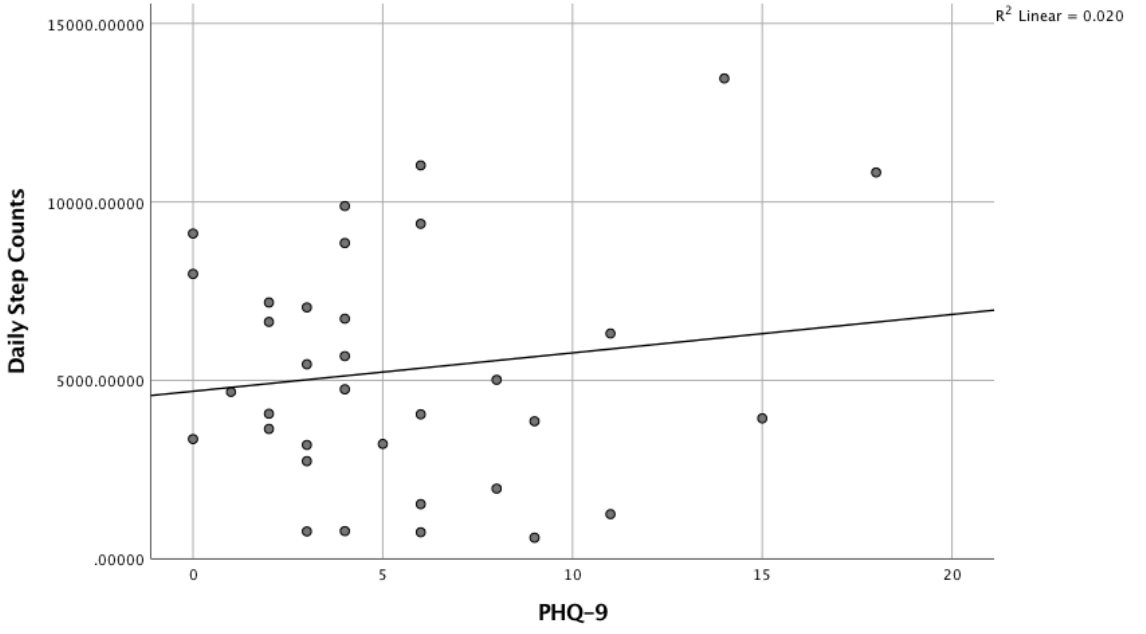


Figure 6. Scatterplot showing relationship between daily step counts and Patient Health Questionnaire-9 scores.

4.3 Regression analysis

Prior to conducting a hierarchical multiple regression, the relevant assumptions of multiple regression were tested. The assumption of singularity was also met as the independent variables were not a combination of other independent variables. An examination of correlations revealed that no independent variables were highly correlated and collinearity statistics (i.e. Tolerance and VIF) were all within accepted limits, the assumption of multicollinearity was met. Residual and scatter plots indicated the assumptions of homoscedasticity was met and variance of error terms was not completely constant but close to constant.

We built a hierarchical regression model with daily step counts as the dependent variable. We built three regression models as the variables. 6MWT, 10MWT and BBS were highly correlated in our study. Refer to table 12 for the correlation matrix for these variables. So, we decided to put these variables in different models.

Table 12. Correlation matrix for 6MWT, 10MWT and BBS.

	6MWT	**10MWT**	**BBS**
6MWT	**1**	**0.88* (0.000)**	**0.85* (0.000)**
10MWT	**0.88* (0.000)**	**1**	**0.75* (0.000)**
BBS	**0.85* (0.000)**	**0.75* (0.000)**	**1**

*. Correlation is significant at the 0.01 level(2-tailed)

A 3-stage hierarchical multiple regression was conducted. In the first block we controlled for possible confounding variables- age, sex, time since stroke and stroke severity. In the second block we added 6MWT/10 MWT/BBS scores in different models. In the third block we added FSS scores and knee extensor strength were added. The

independent variables were entered in this order based of theoretical reasoning. In the first block we added age, sex, time since stroke and stroke severity as these variables have been found to be confounding variables in stroke research. By controlling their effect, we would be able to explore the independent contribution of variables of interest. In the second block, 6MWT/10MWT and BBS were added in separate models because it has been shown to predict daily step counts in stroke survivors as mentioned in the literature review. In the third block we added FSS scores and knee extensor strength together to explore its effect on daily steps counts as it has not been established in the literature before. We decided to exclude FAC from the regression analysis as our study population showed no variation in scores. Similarly, PHQ-9 was not included in the analysis as more than half of our study population (54%) did not report depression. Thus we can not expect PHQ-9 scores to predict daily step counts in our study population.

The regression statistics for model with 6MWT as independent variable are reported in Table 13. The hierarchical multiple regression revealed that at stage one, the confounding variables did not have a significant contribution to the regression model, $F(4,30) = 1.36$, $p= 0.271$ and accounted for 15.4 % of the variation in daily step counts. Introducing 6MWT explained an additional 24.1% of variation in daily step counts and this change in R^2 was significant, $F(5,29) = 3.78$, $p= 0.009$. Adding FSS and knee extensor strength to the regression model, explained an additional variance of 10.5% in daily step counts and this change in R^2 was not significant, $F(7,27) = 3.85$, $p= 0.005$. Based on the model, the equation that predicts steps per day would be:

Daily step count= 2936.62 – 20.70 (Age) + 1345.95 (Sex) – 19.84 (Time since stroke) – 205.05 (NIHSS) + 23.24 (6MWT) + 22.06 (FSS) – 37.56 (Knee extensor strength).

Table 13. Summary of hierarchical regression analysis predicting daily step counts.

Variable	β	t	p	R	R^2	ΔR^2
Step 1				**0.39**	**0.15**	**0.15**
Age	**-97.80**	**-1.42**	**0.17**			
Sex	**159.68**	**0.13**	**0.90**			
Time since stroke	**-20.14**	**-0.21**	**0.83**			
NIHSS	**-569.18**	**-1.68**	**0.103**			
Step 2				**0.63**	**0.39**	**0.24**
Age	**-21.43**	**-0.34**	**0.738**			
Sex	**1321.08**	**1.20**	**0.241**			
Time since stroke	**-11.87**	**-0.15**	**0.884**			
NIHSS	**-21.45**	**-0.07**	**0.949**			
6MWT	**18.54**	**3.40**	**0.002**			
Step 3				**0.71**	**0.50**	**0.11**
Age	**-20.70**	**-0.34**	**0.734**			
Sex	**1354.95**	**1.30**	**0.207**			
Time since stroke	**-19.84**	**-0.25**	**0.807**			
NIHSS	**-205.05**	**-0.63**	**0.531**			
6MWT	**23.24**	**4.16**	**0.000**			
FSS	**22.06**	**0.52**	**0.609**			

Knee extensor strength	**-37.56**	**-2.34**	**0.027**			

The regression statistics for model with 10MWT as independent variable are reported in Table 14. The hierarchical multiple regression revealed that at stage one, the confounding variables did not have a significant contribution to the regression model, F (4,30) = 1.36, p= 0.271 and accounted for 15.4 % of the variation in daily step counts. Introducing 10MWT explained an additional 24.6% of variation in daily step counts and this change in R^2 was significant, F (5,29) = 3.86, p= 0.008. Adding FSS and knee extensor strength to the regression model, explained an additional variance of 3.9% in daily step counts and this change in R^2 was not significant, F (7,27) = 3.01, p= 0.018. Based on the model, the equation that predicts steps per day would be:

Daily step count= 4532.48 – 51.85 (Age) + 929.96 (Sex) – 23.03 (Time since stroke) – 231.25 (NIHSS) + 7195.43 (10MWT) + 7.41 (FSS) – 21.94 (Knee extensor strength).

Table 14. Summary of hierarchical regression analysis with 10MWT as independent predictor.

Variable	**β**	**t**	**p**	**R**	**R^2**	**ΔR^2**
Step 1				**0.39**	**0.15**	**0.15**
Age	**-97.80**	**-1.42**	**0.167**			
Sex	**159.68**	**0.13**	**0.897**			
Time since stroke	**-20.14**	**-0.21**	**0.832**			

NIHSS	**-569.18**	**-1.69**	**0.103**			
Step 2				**0.63**	**0.40**	**0.25**
Age	**-43.48**	**-0.71**	**0.484**			
Sex	**1042.57**	**0.97**	**0.340**			
Time since stroke	**-14.36**	**-0.18**	**0.860**			
NIHSS	**-76.99**	**-0.24**	**0.813**			
10MWT	**6855.67**	**3.45**	**0.002**			
Step 3				**0.66**	**0.44**	**0.04**
Age	**-51.85**	**-0.84**	**0.410**			
Sex	**929.96**	**0.86**	**0.398**			
Time since stroke	**-23.03**	**-0.27**	**0.789**			
NIHSS	**-231.25**	**-0.67**	**0.508**			
10MWT	**7195.43**	**3.53**	**0.002**			
FSS	**7.41**	**0.17**	**0.869**			
Knee extensor strength	**-21.94**	**-1.35**	**0.188**			

The regression statistics for model with BBS scores as independent variable are reported in Table 15. The hierarchical multiple regression revealed that at stage one, the confounding variables did not have a significant contribution to the regression model, F (4,30) = 1.36, p= 0.271 and accounted for 15.4 % of the variation in daily step counts. Introducing BBS explained an additional 18% of variation in daily step counts and this change in R^2 was significant, F (5,29) = 2.91, p= 0.030. Adding FSS and knee extensor

strength to the regression model, explained an additional variance of 11.8% in daily step counts and this change in R^2 was not significant, F (7,27) = 3.17, p= 0.014. Based on the model, the equation that predicts steps per day would be:

Daily step count= -4427.80 – 21.09 (Age) + 696.32 (Sex) – 5.81 (Time since stroke) – 332.16 (NIHSS) + 309.99 (BBS) + 29.74 (FSS) – 40.74 (Knee extensor strength).

Table 15. Summary of hierarchical regression analysis with BBS as independent predictor.

Variable	**β**	**t**	**p**	**R**	**R^2**	**ΔR^2**
Step 1				**0.39**	**0.15**	**0.15**
Age	**-97.80**	**-1.42**	**0.167**			
Sex	**159.68**	**0.13**	**0.897**			
Time since stroke	**-20.14**	**-0.21**	**0.832**			
NIHSS	**-569.18**	**-1.68**	**0.103**			
Step 2				**0.58**	**0.33**	**0.18**
Age	**-28.50**	**-0.425**	**0.674**			
Sex	**754.63**	**0.673**	**0.506**			
Time since stroke	**-4.40**	**-0.052**	**0.959**			
NIHSS	**-141.44**	**-0.415**	**0.681**			
BSS	**221.99**	**2.800**	**0.009**			
Step 3				**0.67**	**0.45**	**0.12**
Age	**-21.09**	**-0.33**	**0.743**			
Sex	**696.32**	**0.66**	**0.515**			

Time since stroke	**5.81**	**0.07**	**0.946**
NIHSS	**-332.16**	**-1.00**	**0.324**
BBS	**309.99**	**3.66**	**0.001**
FSS	**29.74**	**0.65**	**0.519**
Knee extensor strength	**-40.74**	**-2.36**	**0.026**

CHAPTER 5: DISCUSSION

5.1 Walking in the community

With a mean daily step count of the sample of 5284 ± 3342, the overall study sample would be described as "physical inactive" using the classification by Tudor and colleagues [7]. A systemic review with 32 studies concluded that 7000-13000 per day could be expected for relatively healthy, younger adults; 6000-8500 steps per day for healthy older adults and 3500- 5500 steps per day for people living the disabilities and chronic illnesses[126]. Our study sample is representative of the steps per day taken by people living with disabilities and chronic illnesses, but our sample is far below the recommended 10000 steps per day for optimal health promotion and reduction of cardiovascular risk factors[127]. In our study sample, the daily step count of a participant was 13458 steps which meets the recommended steps per day count for optimal health promotion. The participant had minimal stroke symptoms and was 6 years post-stroke. Walking speed (0.92 m/s) and balance (51/56) of the participant were representative of his walking ability. However, he reported significant fatigue and moderate depression which is counterintuitive of his daily step counts. One possible reason might be that he felt fatigued because of his increased walking activity and decreased walking endurance (6MWT distance was 44% of normative value for adults of the same age group). According to our regression equation for daily step counts, this participant should walk 6049 steps per day which is less than half of his actual step count, which limits the generalizability of our results. The most sedentary participant of our study, whose daily step count was 778 steps was 10 years post-stroke. According to his walking speed (0.32 m/s), he was classified as household ambulator, with a medium risk of falls (32/56) and

decreased walking endurance (6MWT distance was 12% of normative value for adults of the same age group). All these factors are reflective of his low step count. However, he did not report significant fatigue and depression.

The time period for which the participants were asked to wear the SAM differed (2-7 days)[128] and thus drawing conclusions from direct comparisons with the studies is inappropriate. Mudge et al. measured walking activity in community in 58 stroke survivors, median age 71.5 (39-89) years, 3.9 (0.5-18.7) years post stroke[129]. The stroke survivors wore SAM for 3 days and took 4616 ± 2618 steps per day which is close to the steps per day taken by participants in our study [129]. In a recent systemic review and quantitative synthesis, stroke survivors took 4078 step per day (n=1280) in the chronic phase of stroke[130],our study sample being above this average given the participants had minor stroke with no significant disability.

The study sample had low level of walking activity in the community both in terms of quantity and intensity. The stroke survivors were inactive 84.4 % of the time i.e. no steps were recorded during this time. The percentage of time spent inactive was similar in a study by Mudge et al., 49 participants, age 67.4 ± 12.5 years and 66 ± 61 months post- stroke were inactive 83 % of time as recorded by SAM worn for 3 days. One study with small sample size (n=8) reported stroke survivor's sedentary time (time not on feet) as 81 % of the average 24 hour monitored period and another study (n=42) demonstrated that stroke survivors spend 63 % of the average 10- hour monitored period either sitting or lying down [128]. In our study, the percentage of time spent walking with a low cadence (43.1 %) was similar to the previously reported value of 45% in a study involving 79 chronic stroke survivors[131].

According to the recommendations of the American Heart Association, stroke survivors should be involved in aerobic exercise three to seven days a week, for 20-60 minutes, depending on fitness level. However, regular brisk walking is also found to be beneficial for stroke survivors and improves physical fitness, mobility and quality of life. Extrapolating from the recent finding that brisk walking occurs at a cadence of 100 steps per minute, about 2,150 steps per day should be devoted to aerobic activity alone[131]. Considering the vicious cycle of disability and inactivity that occurs after stroke and its relation to development of comorbidities and risk of second stroke, the small amount of time spent in walking activities by stroke survivors is a cause of concern[132].

5.2 Relationship between walking in the community and physical characteristics

5.2.1 Walking speed and endurance

In a systemic review and meta- analysis on 6MWT performance of stroke survivors, the pooled distance walked across 64 studies was 285 meters (95 %CI, 252-318 meters)[94], with our sample walking a shorter distances. Differences in distribution of age, gender or time since stroke did not have a significant influence on distance walked[94]. The 6MWT was moderately correlated with steps per day (r=0.59) with similar correlations seen in other studies (r= 0.68[14], r=0.55[15,16]). All the studies tested 6MWT according to ATS guidelines and did not deviate from the typical protocol. The correlation is justified as 6MWT is a measure of walking endurance and the ability to walk a certain distance is an importance factor for community walking and reintegration[14].

In our study, 6MWT was a significant predictor of steps per day and explained 24.1 % variation in daily step counts. Other studies using stepwise multiple regression have shown 6MWT as a predictor of steps per day explaining 46 %[13] and 54%[14] variation in daily step counts. People post stroke have increased energy requirements because of their impaired walking pattern with peak oxygen consumption of stroke survivors being less than energy expenditure required for performance of basic ADL's[14]. As stroke survivors are severely deconditioned, rehabilitation programs focusing on endurance training should aim to improve cardiovascular and neuromuscular endurance of stroke survivors[14] thus improving their walking performance in the community.

The mean walking speed of our study sample was 0.84 m/s, classifying them as unlimited community ambulators. However, this speed is not sufficient to accomplish some tasks in the community like crossing a street which requires a walking speed of 1m/s[50]. Perry et al. have established walking speed as a valid predictor of community walking in stroke survivors classifying stroke survivors with walking speed of <0.4 m/s as house hold ambulators, 0.4- 0.8 m/s as limited community ambulators and >0.8 m/s as unlimited community ambulators[130]. No study has shown that 10MWT predicts daily step counts. Our study showed significant moderate correlation between walking speed and steps per day (r= 0.60). Our results are similar to other studies showing moderate correlations (r= 0.65[14], r= 0.55 [15,54], r= 0.56[71]). All the studies used homogenous method (10MWT) to measure the walking speed. The correlation has been validated by Bowden et al. The aim of their study to validate the speed based classification of poststroke function given by Perry et al. by examining the relationship by using a quantitative measure (SAM) of walking in the home and community [133].The sample consisted of 59 participants, age 61.9±10.8 years with 4.1± 3.7 years post- stroke with 0.74 m/s as their

average walking speed[131]. Walking speed was significantly correlated with steps per day (r=0.68) and they concluded that number of steps per day were lowest in those who were limited to household walking and greatest in those who were able to achieve unlimited community walking[133].

5.2.2 Balance

The mean BBS score in our study (44.4 out of 56) placed the sample in the category of low risk of falls[134]. The moderate correlation of BBS with daily step counts (r= 0.61) was similar to that reported in the literature (r= 0.58[54], r= 0.54[14]). In a study by Michael and colleagues, 50 stroke survivors, mean age 65 years and 1.1 years post-stroke, balance measured by BBS predicted 30 % of variance in daily step counts in a stepwise linear regression[53]. However, in our study the proportion of variance explained by BBS in daily step counts was very less (18%). The possible explanation of this would be the differences in level of functioning of stroke survivors. In the study by Michael et al., stroke survivors had a BBS score of 34± 9 which is less than the BBS score of our sample. Also, the study sample had very low ambulatory activity. The daily step counts for stroke individuals was 2837± 1503 steps. Our study sample was higher functioning than this study sample. There is a possibility that in different groups of stroke survivors classified on the basis of level of functioning, different factors predict daily step counts.

Given that balance performance is associated with fear of falling and balance related self-efficacy, having a good balance increases the level of self- efficacy to perform daily activities and participate in social life which can lead to increase in walking in the community[135]. Focussing on exercises and functional tasks to improve

balance should be goal for rehabilitation interventions for regaining walking ability in the community for stroke survivors[136].

5.2.3 Knee extensor strength

Knee extensor strength did not have a significant correlation with daily step counts. The reason for this could be the variable nature of our study sample data demonstrated in the scatterplot in Figure 5.

Knee extensor strength was a significant predictor in predicting daily step counts and with FSS, it explained a variance of 10.5 % in daily step counts. Contrary to what we had expected, according to the regression equation predicting steps per day, every unit of increase in knee extensor strength decreased the steps per day taken by the participant by 37 times. A possible explanation would be that knee extensor strength was significantly correlated (Appendix F) with 6MWT and BBS (although there was not any problem with the multicollinearity diagnostics of the model) and the sample size was not enough given the number of predictors in our model, thus giving contrary results. We tried running a step wise regression analysis with age, sex, time since stroke, stroke severity, knee extensor strength and FFS to see if it changes the negative beta value of knee extensor strength. The model was not significant and knee extensor strength did not significantly predict steps per day but the beta value for the knee extensor strength was positive. Other reason for unexpected findings could be that knee extensor strength could be a collider variable. When a variable is casually influenced by two or more variables, it leads to the distortion of association between the desired variables of interest and lead to selection bias[137] .

There are no studies in literature looking at the relationship between knee extensor strength and walking in the community (daily step counts). However, the

relationship between knee extensor strength and gait performance has been explored extensively. In a study by Gerritis and colleagues, 18 stroke survivors, 54±10 years and 22±18 months post-stroke, isometric knee extensor strength (80±10 newton meter) measured by isokinetic dynamometer was significantly related to BBS (r= 0.64), 6MWT (r=0.48) and Rivermead Mobility Index (0.44)[138]. Kobyashi and colleagues also explored correlations between knee extensor strength measured by a hand held dynamometer and functional performance in patients with stroke[139]. 10 stroke survivors, 54.3±8.4 years old, 8.7±4.5 years post stroke participated in their study[139]. Knee extensor strength (102.9±16.6 N) was significantly correlated to walking velocity measured by the 5-meter walk test (r= 0.46), walking distance covered in 5 minutes (r= 0.41), BBS (r=0.76)[139]. There is a need of future studies looking at the correlation between knee extensor strength and daily step counts.

A recent study by Fedrick and colleagues looked at strength training for skeletal muscle endurance after stroke[140]. Stroke survivors were randomized to either a strength training group (n=14, age 57±12 years and 5±4 years post-stroke) or stretching group (n=16, age 55±9, 6±5 years post-stroke) [140]. The strength training group consisted of three sessions per week of bilateral training for lower extremities[140]. Each participant performed leg extension, leg curl and leg press exercises, 2 sets of 20 repetitions on each leg and each machine allowing for development of muscle strength and muscle endurance[140]. The control stretch group completed 45 minutes of supervised stretching exercises on raised padded tables[140]. The exercise and stretching sessions were done for 3 months. The strength training group had significantly greater skeletal muscle endurance gain compared to the stretching group ($p<0.001$)[140]. They also studied the

effect of training sessions on distance walked during the 6MWT and 10MWT[140]. Changes in 6MWT for the strength training group and stretching group were statistically different (p= 0.011) implying that strength training significantly improved walking endurance[140]. It is of significant interest to explore whether strength changes in knee muscles can transfer gains to walking ability in real-world given that this training program improved their skeletal muscle endurance.

5.3 Relationship between walking in the community and affective characteristics

5.3.1 Post-Stroke Fatigue

In our study, fatigue measures by FSS did not have a significant correlation with steps per day. Although the mean FSS score for our study sample was 36.3 and 51 % of participants reported fatigue, we did not see any significant relationship. Our study demonstrated similar results as shown by Michael et al[23,62] . In the study, 53 participants age 66 (45-84) years, 10.3 (6-1660) months post stroke, fatigue as measured by FSS was not correlated to walking activity measured by SAM worn for 2 days[23]. However, contradictory results were seen in a study by Duncan and colleagues. In a longitudinal study design, they studied the associations of fatigue and daily step counts of stroke survivors[65]. The assessments were conducted on participants, median age 71.8 years at 1 (n=132),6 (n=105) and 12 months (n=91) after stroke onset[65]. Fatigue measured by the FAS had a significant correlation with the steps per day recorded by ActivPAL at 1 (r= -0.39) month, 6 months (r= -0.31) and 12 months (r= -0.35)[65]. They also reported that lower daily step count at 1 month predicted higher FAS at 6 and 12 months after controlling for age, sex, prestroke and anxiety explaining [65]. The model explained 31%

and 27% variance in FAS scores at 6 months and 12 months respectively[65]. The possible reason for conflicting results from our study would be large sample size recruited by Duncan et al and the time for which the steps were recorded (7 days as opposed to 3 days in our study and 2 days in study by Michael and colleagues).

In the regression model we built, FSS along with knee extensor strength only explained a variance of 10.5 % in daily step counts and was not a significant predictor. According to the regression equation, a unit change in fatigue scores could lead to 22 times increase in steps which is counterintuitive given that there is a negative correlation between steps per day and fatigue in literature. A possible explanation of this could be that the group of participants who did not have significant fatigue took 5393 steps on an average and group of participants who had fatigue took more steps (5419) steps on an average. The fatigue group walked more and experienced more fatigue.

Future studies with large sample size should explore the relationship between walking in the community and fatigue as it credible that reduced activity because of fatigue may be related of deconditioning, decrease in muscle strength and worsening of balance and ability to walk[23]. Fatigue could also affect motivation thus decreasing walking activity in stroke survivors[23]. The author has submitted a narrative review titled "Post-Stroke Fatigue - An overlooked concern that negatively impacts stroke recovery and function: A Narrative Review" (Appendix H)

5.3.2 Depressive Symptomatology

In our study depression scores did not have a significant correlation with daily step counts. Previous literature has shown moderate ($r= 0.62$[71]) and low correlation ($r= 0.33$[63]) with daily step counts. The discrepancy in results could be due to device used to

quantify walking activity. Pedometers were used in these studies which were worn for a longer period of time (5 days[71] and 7 days[63]). The mean score of the PHQ-9 for our sample (5.8) which is representative of mild depression and 54 % of our population did not report depression, so we cannot expect a significant correlation with depression and steps per day. As mentioned in the literature review, post-stroke depression can lead to decreased participation in social activities and problems in walking and stair climbing. In our study, participants with moderate and moderately severe depression took more steps (13458 and 10826 steps per day respectively) as compared to the rest of the sample (Figure 6). Such variations in the data can account for non-significant correlation between depression and steps per day.

A meta-analysis of 8 randomized controlled trials found that walking is an effective intervention for depression with effect size -0.86 (-1.12, -0.61)[141]. However, literature does not exhibit effect of walking on depression in stroke survivors. Walking is a form of physical activity and many potential mechanisms (endorphin and monoamine hypothesis, cardiovascular fitness, sleep improvement hypothesis, self-efficacy and enhance of self-esteem) have been suggested to prove that physical activity might reduce depressive symptoms[141]. More exploration of this relationship with large sample size and uniform assessment tools is required.

5.4 Limitations

There are several limitations associated with our research study so the results should be interpreted with caution. The first is the small sample size of the study limiting the statistical power of the study. There is a high possibility of sample selection bias as the participants of our study were community dwelling stroke survivors. Majority of the

participants were recruited from community stroke clubs suggesting they were able to access the stroke community meetings without any difficulty. The stroke severity of our study sample showed that they had minor stroke symptoms and were at a higher functional level than the chronic stroke population living in the community thus limiting the generalizability of our results. This deters us from drawing conclusions about walking ability of chronic stroke survivors living in the community with significant disability and lower level of functioning.

Another limitation of our study was that the diagnosis of stroke was self-reported and not confirmed through medical records. There is a high possibility that wearing an activity monitor may have motivated the participants to walk more. The days during which the activity monitor was worn by the participants differed (mostly week days and not weekends). These two factors might have led to overestimation of their overall walking ability thereby altering the strength of the correlations. On the contrary, we collected data during winter time of the year that might have affected walking in the community of stroke survivors. Snow and slippery walkways could have led them to avoid walking outside. Another limitation of the study is that regression is complex correlational analysis. Lastly our study design was cross-sectional, exploratory and not confirmatory in nature warranting caution during interpretation[63].

CHAPTER 6: CONCLUSIONS AND FUTURE IMPLICATIONS

The study explored relationship between various physical and personal factors affecting walking in the community in chronic stroke survivors. We found that distance walked during the 6MWT, walking speed measured by 10MWT and balance measured by BBS were significantly correlated to daily step counts. The hierarchical regression model we built containing age, sex, time since stroke, severity of stroke, distance walked during in the 6MWT, fatigue scores and knee extensor strength predicted 50 % of variance in daily step counts. However, the results of the study should be interpreted with caution given the small sample size and limitations of the study. In literature, the importance of training endurance and knee muscle strength for improving the walking activity in stroke survivors has been highlighted. As only 50% of the variance was accounted by our model, there are definitely other factors affecting the walking activity of stroke survivors. Literature has shown other factors like self-efficacy regarding walking and balance, cardiovascular capacity to be related to walking in the community which were not measured in this study[142]. The study will help clinicians to predict accurately stroke survivors who would be able to return to walking in the community as well as inform interventional strategies for walking in the community leading to focused and specific treatment interventions targeting on training endurance and muscle strength, thus maximizing patient outcomes post-stroke.

Future studies with large sample size and longitudinal study design should be conducted to explore this relationship. For exploring robust associations between walking in the community, fatigue and depression, inclusion criteria of the studies should

be stroke survivors who have been depressed and have significant fatigue. The role of knee extensor strength should be explored on walking in the community given its association with walking measures used clinically (6MWT, 10MWT, FAC). Future pilot studies testing interventions comprising of muscle strength and endurance training combined with behavioural therapies for depression and fatigue and looking its effect on walking in the community would be valuable.

REFERENCES

1 Walter Johnson , O. O., Mayowa Owolabi , Sonal Sachdev. *Stroke: a global response is needed*, <http://www.who.int/bulletin/volumes/94/9/16-181636.pdf> (2016).

2 Warlow, C., Sudlow, C., Dennis, M., Wardlaw, J. & Sandercock, P. Stroke. *Lancet* **362**, 1211-1224, doi:10.1016/S0140-6736(03)14544-8 (2003).

3 Oh, D. Community ambulation: clinical criteria for therapists' reasoning and decision-making in stroke rehabilitation. *Int J Phys Med Rehabil* **1**, 2 (2013).

4 Eng, J. J. & Tang, P.-F. Gait training strategies to optimize walking ability in people with stroke: a synthesis of the evidence. *Expert review of neurotherapeutics* **7**, 1417-1436 (2007).

5 Elsworth, C. *et al.* A study of perceived facilitators to physical activity in neurological conditions. *International Journal of Therapy and Rehabilitation* **16**, 17-24 (2009).

6 Tudor-Locke, C. & Bassett, D. How many steps are enough? Pedometer-determined physical activity indices. *Sports Med* **34**, 1-8 (2004).

7 Roos, M. A., Rudolph, K. S. & Reisman, D. S. The structure of walking activity in people after stroke compared with older adults without disability: a cross-sectional study. *Physical therapy* **92**, 1141-1147 (2012).

8 Kunkel, D., Fitton, C., Burnett, M. & Ashburn, A. Physical inactivity post-stroke: a 3-year longitudinal study. *Disability and rehabilitation* **37**, 304-310 (2015).

9 Balasubramanian, C. K., Clark, D. J. & Fox, E. J. Walking adaptability after a stroke and its assessment in clinical settings. *Stroke research and treatment* **2014** (2014).

10 Gillen, G. *Stroke rehabilitation: a function-based approach*. (Elsevier Health Sciences, 2015).

11 Shumway-Cook, A. & Woollacott, M. H. *Motor control: translating research into clinical practice*. (Lippincott Williams & Wilkins, 2007).

12 Lord, S. E. & Rochester, L. Measurement of community ambulation after stroke: current status and future developments. *Stroke* **36**, 1457-1461 (2005).

13 Fulk, G. D., Reynolds, C., Mondal, S. & Deutsch, J. E. Predicting home and community walking activity in people with stroke. *Archives of physical medicine and rehabilitation* **91**, 1582-1586 (2010).

14 Mudge, S. & Stott, N. S. Timed walking tests correlate with daily step activity in persons with stroke. *Archives of physical medicine and rehabilitation* **90**, 296-301 (2009).

15 Zalewski, K. R. & Dvorak, L. Barriers to physical activity between adults with stroke and their care partners. *Topics in Stroke Rehabilitation* **18**, 666-675 (2011).

16 Watanabe, M. *et al.* The relationship between bilateral knee muscle strength and gait performance after stroke: the predictive value for gait performance. *Journal of physical therapy science* **27**, 3227-3232 (2015).

17 Hsu, A.-L., Tang, P.-F. & Jan, M.-H. Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke1. *Archives of physical medicine and rehabilitation* **84**, 1185-1193 (2003).

18 Barbeau, H. Locomotor training in neurorehabilitation: emerging rehabilitation concepts. *Neurorehabilitation and Neural Repair* **17**, 3-11 (2003).

19 Alzahrani, M. A., Dean, C. M., Ada, L., Dorsch, S. & Canning, C. G. Mood and balance are associated with free-living physical activity of people after stroke residing in the community. *Stroke research and treatment* **2012** (2012).

20 Chemerinski, E., Robinson, R. G. & Kosier, J. T. Improved recovery in activities of daily living associated with remission of poststroke depression. *Stroke* **32**, 113-117 (2001).

21 Patten, S. B., Williams, J. V., Lavorato, D. H. & Eliasziw, M. A longitudinal community study of major depression and physical activity. *General hospital psychiatry* **31**, 571-575 (2009).

22 Michael, K. M., Allen, J. K. & Macko, R. F. Fatigue after stroke: relationship to mobility, fitness, ambulatory activity, social support, and falls efficacy. *Rehabil Nurs* **31**, 210-217 (2006).

23 Garber, C. E. & Friedman, J. H. Effects of fatigue on physical activity and function in patients with Parkinson's disease. *Neurology* **60**, 1119-1124 (2003).

24 Feigin, V. L. *et al.* Update on the Global Burden of Ischemic and Hemorrhagic Stroke in 1990-2013: The GBD 2013 Study. *Neuroepidemiology* **45**, 161-176, doi:10.1159/000441085 (2015).

25 Meschia, J. F. & Brott, T. Ischaemic stroke. *Eur J Neurol* **25**, 35-40, doi:10.1111/ene.13409 (2018).

26 Haast, R. A., Gustafson, D. R. & Kiliaan, A. J. Sex differences in stroke. *J Cereb Blood Flow Metab* **32**, 2100-2107, doi:10.1038/jcbfm.2012.141 (2012).

27 Appelros, P., Stegmayr, B. & Terent, A. Sex differences in stroke epidemiology: a systematic review. *Stroke* **40**, 1082-1090, doi:10.1161/STROKEAHA.108.540781 (2009).

28 Smajlovic, D. Strokes in young adults: epidemiology and prevention. *Vasc Health Risk Manag* **11**, 157-164, doi:10.2147/VHRM.S53203 (2015).

29 Katsnelson, M. J., Della-Morte, D. & Rundek, T. Stroke in young. *Periodicum biologorum* **114**, 347-353 (2012).

30 Lozano, R. *et al.* Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet* **380**, 2095-2128 (2012).

31 Deresse, B. & Shaweno, D. Epidemiology and in-hospital outcome of stroke in South Ethiopia. *J Neurol Sci* **355**, 138-142, doi:10.1016/j.jns.2015.06.001 (2015).

32 Mukherjee, D. & Patil, C. G. Epidemiology and the global burden of stroke.

World Neurosurg **76**, S85-90, doi:10.1016/j.wneu.2011.07.023 (2011).

33 Mittmann, N. *et al.* Impact of disability status on ischemic stroke costs in Canada in the first year. *Can J Neurol Sci* **39**, 793-800 (2012).

34 Miller, E. L. *et al.* Comprehensive overview of nursing and interdisciplinary rehabilitation care of the stroke patient: a scientific statement from the American Heart Association. *Stroke* **41**, 2402-2448, doi:10.1161/STR.0b013e3181e7512b (2010).

35 Tennant, A., Geddes, J. M., Fear, J., Hillman, M. & Chamberlain, M. A. Outcome following stroke. *Disabil Rehabil* **19**, 278-284 (1997).

36 Sinanović, O., Mrkonjić, Z., Zukić, S., Vidović, M. & Imamović, K. Post-stroke language disorders. *Acta Clin Croat* **50**, 79-94 (2011).

37 Tipping, B. Issues in the long-term management of stroke: main article. *CME: Your SA Journal of CPD* **26**, 70-74 (2008).

38 Cawood, J., Visagie, S. & Mji, G. Impact of post-stroke impairments on activities and participation as experienced by stroke survivors in a Western Cape setting. *South African Journal of Occupational Therapy* **46**, 10-15 (2016).

39 Maleka, M., Stewart, A. & Hale, L. The experience of living with stroke in low urban and rural socioeconomic areas of South Africa. *South African Journal of Physiotherapy* **68**, 25-29 (2012).

40 Rhoda, A. Limitations in activity and participation experienced by stroke patients: A qualitative inquiry. *South African Journal of Physiotherapy* **68**, 20-24 (2012).

41 Mudzi, W., Stewart, A. & Musenge, E. Community participation of patients 12 months post-stroke in Johannesburg, South Africa. *African journal of primary health care & family medicine* **5** (2013).

42 Viscogliosi, C. *et al.* Differences in participation according to specific cognitive deficits following a stroke. *Applied Neuropsychology* **18**, 117-126 (2011).

43 Spitzer, J., Tse, T., Baum, C. M. & Carey, L. M. Mild impairment of cognition impacts on activity participation after stroke in a community-dwelling Australian cohort. *OTJR: occupation, participation and health* **31**, S8-S15 (2011).

44 Beaudoin, A. J. *et al.* Visuoperceptual deficits and participation in older adults after stroke. *Australian occupational therapy journal* **60**, 260-266 (2013).

45 Duncan, P. W. *et al.* Management of adult stroke rehabilitation care: a clinical practice guideline. *stroke* **36**, e100-e143 (2005).

46 Hendricks, H. T., Van Limbeek, J., Geurts, A. C. & Zwarts, M. J. Motor recovery after stroke: a systematic review of the literature. *Archives of physical medicine and rehabilitation* **83**, 1629-1637 (2002).

47 Li, S., Francisco, G. E. & Zhou, P. Post-stroke hemiplegic gait: new perspective and insights. *Frontiers in physiology* **9**, 1021 (2018).

48 Middleton, A., Fulk, G. D., Beets, M. W., Herter, T. M. & Fritz, S. L. Self-selected walking speed is predictive of daily ambulatory activity in older adults. *Journal of aging and physical activity* **24**, 214-222 (2016).

49 Alzahrani, M. A., Dean, C. M. & Ada, L. Ability to negotiate stairs predicts free-living physical activity in community-dwelling people with stroke: an observational study. *Australian Journal of Physiotherapy* **55**, 277-281 (2009).

50 Nichols, D. S. Balance retraining after stroke using force platform biofeedback. *Physical therapy* **77**, 553-558 (1997).

51 van Meulen, F. B. *et al.* Analysis of balance during functional walking in stroke survivors. *PloS one* **11**, e0166789 (2016).

52 Mudge, S. & Stott, N. S. Test—retest reliability of the StepWatch Activity Monitor outputs in individuals with chronic stroke. *Clinical Rehabilitation* **22**, 871-877 (2008).

53 Michael, K. M., Allen, J. K. & Macko, R. F. Reduced ambulatory activity after stroke: the role of balance, gait, and cardiovascular fitness. *Archives of physical medicine and rehabilitation* **86**, 1552-1556 (2005).

54 Yang, D. J. *et al.* The correlation between muscle activity of the quadriceps and balance and gait in stroke patients. *Journal of physical therapy science* **28**, 2289-2292 (2016).

55 Hyun, C. W. *et al.* Hemiparetic knee extensor strength and balance function are predictors of ambulatory function in subacute stroke patients. *Annals of rehabilitation medicine* **39**, 577-585 (2015).

56 Patterson, S. L. *et al.* Determinants of walking function after stroke: differences by deficit severity. *Archives of physical medicine and rehabilitation* **88**, 115-119 (2007).

57 Pradon, D., Roche, N., Enette, L. & Zory, R. Relationship between lower limb muscle strength and 6-minute walk test performance in stroke patients. *Journal of Rehabilitation Medicine* **45**, 105-108 (2013).

58 Staub, F. & Bogousslavsky, J. Fatigue after stroke: a major but neglected issue. *Cerebrovascular Diseases* **12**, 75-81 (2001).

59 Billinger, S. A. *et al.* 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, doi:10.1161/STR.0000000000000022 (2014).

60 Krupp, L. B., LaRocca, N. G., Muir-Nash, J. & Steinberg, A. D. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of neurology* **46**, 1121-1123 (1989).

61 Michael, K. M., Allen, J. K. & Macko, R. F. Fatigue after stroke: relationship to mobility, fitness, ambulatory activity, social support, and falls efficacy. *Rehabilitation Nursing* **31**, 210-217 (2006).

62 Robinson, C. A., Shumway-Cook, A., Ciol, M. A. & Kartin, D. Participation in community walking following stroke: subjective versus objective measures and the impact of personal factors. *Physical therapy* **91**, 1865-1876 (2011).

63 Bijleveld-Uitman, M., van de Port, I. & Kwakkel, G. Is gait speed or walking distance a better predictor for community walking after stroke? *Journal of rehabilitation medicine* **45**, 535-540 (2013).

64 Duncan, F. *et al.* Exploratory longitudinal cohort study of associations of fatigue after stroke. *Stroke* **46**, 1052-1058, doi:10.1161/STROKEAHA.114.008079 (2015).

65 Michael, K. & Macko, R. F. Ambulatory activity intensity profiles, fitness, and fatigue in chronic stroke. *Top Stroke Rehabil* **14**, 5-12, doi:10.1310/tsr1402-5 (2007).

66 Diagnostic, D. (American Psychiatric Publishing, 2013).

67 Gbiri, C. A., Akinpelu, A. O. & Odole, A. C. Prevalence, pattern and impact of depression on quality of life of stroke survivors. *International Journal of Psychiatry in Clinical Practice* **14**, 198-203 (2010).

68 Goodwin, R. D. & Devanand, D. P. Stroke, depression, and functional health outcomes among adults in the community. *Journal of geriatric psychiatry and neurology* **21**, 41-46 (2008).

69 Feibel, J. H. & Springer, C. J. Depression and failure to resume social activities after stroke. *Archives of physical medicine and rehabilitation* **63**, 276-277 (1982).

70 Baert, I., Feys, H., Daly, D., Troosters, T. & Vanlandewijck, Y. Are patients 1 year post-stroke active enough to improve their physical health? *Disability and rehabilitation* **34**, 574-580 (2012).

71 Bassett, D. R., Toth, L. P., LaMunion, S. R. & Crouter, S. E. Step counting: a review of measurement considerations and health-related applications. *Sports Medicine* **47**, 1303-1315 (2017).

72 Klassen, T. D. *et al.* "Stepping Up" activity poststroke: ankle-positioned accelerometer can accurately record steps during slow walking. *Physical therapy* **96**, 355-360 (2016).

73 Gronley, J. K. & Mulroy, S. J. Classification of walking handicap in the stroke population. *Stroke* (1995).

74 Giggins, O. M., Clay, I. & Walsh, L. Physical activity monitoring in patients with neurological disorders: a review of novel body-worn devices. *Digital Biomarkers* **1**, 14-42 (2017).

75 Chen, M.-D., Kuo, C.-C., Pellegrini, C. A. & Hsu, M.-J. Accuracy of Wristband Activity Monitors during Ambulation and Activities. *Medicine and science in sports and exercise* **48**, 1942-1949 (2016).

76 Crouter, S. E., Schneider, P. L. & Bassett, J. D. Spring-levered versus piezo-electric pedometer accuracy in overweight and obese adults. *Medicine and science in sports and exercise* **37**, 1673-1679 (2005).

77 Grant, P. M., Dall, P. M., Mitchell, S. L. & Granat, M. H. Activity-monitor accuracy in measuring step number and cadence in community-dwelling older adults. *Journal of aging and physical activity* **16**, 201-214 (2008).

78 Foster, R. C. *et al.* Precision and accuracy of an ankle-worn accelerometer-based pedometer in step counting and energy expenditure. *Preventive medicine* **41**, 778-783 (2005).

79 Mudge, S., Stott, N. S. & Walt, S. E. Criterion validity of the StepWatch Activity Monitor as a measure of walking activity in patients after stroke. *Archives of physical medicine and rehabilitation* **88**, 1710-1715 (2007).

80 Hickey, A., John, D., Sasaki, J. E., Mavilia, M. & Freedson, P. Validity of activity monitor step detection is related to movement patterns. *Journal of Physical Activity and Health* **13**, 145-153 (2016).

81 Karabulut, M., Crouter, S. E. & Bassett, D. R. Comparison of two waist-mounted and two ankle-mounted electronic pedometers. *European journal of applied physiology* **95**, 335-343 (2005).

82 Zhu, S. & Huang, S. S. (Google Patents, 2015).

83 Blum, L. & Korner-Bitensky, N. Usefulness of the Berg Balance Scale in stroke rehabilitation: a systematic review. *Physical therapy* **88**, 559-566 (2008).

84 Berg, K., Wood-Dauphinee, S. & Williams, J. The Balance Scale: reliability assessment with elderly residents and patients with an acute stroke. *Scandinavian journal of rehabilitation medicine* **27**, 27-36 (1995).

85 Flansbjer, U.-B., Blom, J. & Brogårdh, C. The reproducibility of Berg Balance Scale and the Single-leg Stance in chronic stroke and the relationship between the two tests. *PM&R* **4**, 165-170 (2012).

86 Mao, H.-F., Hsueh, I.-P., Tang, P.-F., Sheu, C.-F. & Hsieh, C.-L. Analysis and comparison of the psychometric properties of three balance measures for stroke patients. *Stroke* **33**, 1022-1027 (2002).

87 Tyson, S. & Connell, L. How to measure balance in clinical practice. A systematic review of the psychometrics and clinical utility of measures of balance activity for neurological conditions. *Clinical rehabilitation* **23**, 824-840 (2009).

88 Butland, R., Pang, J., Gross, E., Woodcock, A. & Geddes, D. Two-, six-, and 12-minute walking tests in respiratory disease. *British medical journal (Clinical research ed.)* **284**, 1607 (1982).

89 McGavin, C., Gupta, S. & McHardy, G. Twelve-minute walking test for assessing disability in chronic bronchitis. *Br Med J* **1**, 822-823 (1976).

90 Laboratories, A. C. o. P. S. f. C. P. F. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* **166**, 111-117 (2002).

91 Kubo, H. *et al.* Safety and Feasibility of the 6-Minute Walk Test in Patients with Acute Stroke. *Journal of Stroke and Cerebrovascular Diseases* **27**, 1632-1638 (2018).

92 Dunn, A. *et al.* Protocol variations and six-minute walk test performance in stroke survivors: a systematic review with meta-analysis. *Stroke research and treatment* **2015** (2015).

93 Ng, S. S. *et al.* Walkway length, but not turning direction, determines the six-minute walk test distance in individuals with stroke. *Archives of physical medicine and rehabilitation* **92**, 806-811 (2011).

94 Tyson, S. & Connell, L. The psychometric properties and clinical utility of measures of walking and mobility in neurological conditions: a systematic review. *Clinical rehabilitation* **23**, 1018-1033 (2009).

95 Flansbjer, U.-B., Holmbäck, A. M., Downham, D., Patten, C. & Lexell, J. Reliability of gait performance tests in men and women with hemiparesis after stroke. *Journal of rehabilitation medicine* **37**, 75-82 (2005).

96 Daniel, C. R. & Battistella, L. R. Using the six minute walk test to evaluate walking capacity in patients with stroke. *Acta Fisiátrica* **21**, 195-200 (2016).

97 Dalgas, U., Severinsen, K. & Overgaard, K. Relations between 6 minute walking distance and 10 meter walking speed in patients with multiple sclerosis and stroke. *Archives of physical medicine and rehabilitation* **93**, 1167-1172 (2012).

98 Kang, H.-J. *et al.* Comparative validity of depression assessment scales for screening poststroke depression. *Journal of affective disorders* **147**, 186-191 (2013).

99 Smarr, K. L. & Keefer, A. L. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). *Arthritis care & research* **63**, S454-S466 (2011).

100 Aben, I., Verhey, F., Lousberg, R., Lodder, J. & Honig, A. Validity of the beck depression inventory, hospital anxiety and depression scale, SCL-90, and hamilton depression rating scale as screening instruments for depression in stroke patients. *Psychosomatics* **43**, 386-393 (2002).

101 Williams, L. S. *et al.* Performance of the PHQ-9 as a screening tool for depression after stroke. *stroke* **36**, 635-638 (2005).

102 Leeds, L., Meara, R. & Hobson, J. The utility of the Stroke Aphasia Depression Questionnaire (SADQ) in a stroke rehabilitation unit. *Clinical rehabilitation* **18**, 228-231 (2004).

103 Mead, G. *et al.* Evaluation of fatigue scales in stroke patients. *Stroke* **38**, 2090-2095 (2007).

104 Hinkle, J. L. *et al.* Poststroke fatigue: emerging evidence and approaches to management: a scientific statement for healthcare professionals from the American Heart Association. *Stroke*, STR. 0000000000000132 (2017).

105 Zedlitz, A., Van, M. M., Van, E. M., Geurts, A. & Fasotti, L. Psychometric properties of FSS and CIS-20r for measuring post-stroke fatigue. *International Journal of Psychology* **2**, 27 (2016).

106 Cumming, T. B. & Mead, G. Classifying post-stroke fatigue: Optimal cut-off on the Fatigue Assessment Scale. *Journal of psychosomatic research* **103**, 147-149 (2017).

107 Shahid, A., Wilkinson, K., Marcu, S. & Shapiro, C. M. in *STOP, THAT and One Hundred Other Sleep Scales* (eds Azmeh Shahid, Kate Wilkinson, Shai Marcu, & Colin M. Shapiro) 163-165 (Springer New York, 2012).

108 Brråndal, A., Eriksson, M., Wester, P. & Lundin-Olsson, L. Reliability and validity of the Swedish Fatigue Assessment Scale when self-administrered by persons with mild to moderate stroke. *Topics in stroke rehabilitation* **23**, 90-97 (2016).

109 Fink, A. M. *et al.* Psychometric properties of three instruments to measure fatigue with myocardial infarction. *Western journal of nursing research* **32**, 967-983 (2010).

110 Fisk, J. D. *et al.* Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. *Clinical Infectious Diseases* **18**, S79-S83 (1994).

111 Neuberger, G. B. Measures of fatigue: the fatigue questionnaire, fatigue severity scale, multidimensional assessment of fatigue scale, and short form-36 vitality (energy/fatigue) subscale of the short form health survey. *Arthritis Care & Research: Official Journal of the American College of Rheumatology* **49**, S175-S183 (2003).

112 Nadarajah, M., Mazlan, M., Abdul-Latif, L. & Goh, H.-T. Test-retest reliability, internal consistency and concurrent validity of Fatigue Severity Scale in measuring post-stroke fatigue. *European journal of physical and rehabilitation medicine* **53**, 703-709 (2017).

113 Howard, V. J. & McDonnell, M. N. Physical activity in primary stroke prevention: just do it! *Stroke* **46**, 1735-1739 (2015).

114 Kharb, A., Saini, V., Jain, Y. & Dhiman, S. A review of gait cycle and its parameters. *IJCEM International Journal of Computational Engineering & Management* **13**, 78-83 (2011).

115 Durcan, S. An Investigation Of The Factors Associated With Community Ambulation In Chronic Stroke. (2014).

116 van de Port, I. G., Kwakkel, G. & Lindeman, E. Community ambulation in patients with chronic stroke: how is it related to gait speed? *Journal of Rehabilitation Medicine* **40**, 23-27 (2008).

117 Field, A. *Discovering statistics using SPSS*. (Sage publications, 2009).

118 Gouelle, A. Use of functional ambulation performance score as measurement of gait ability. *Journal of Rehabilitation Research & Development* **51**, 665 (2014).

119 Bohannon, R. W., Andrews, A. W. & Thomas, M. W. Walking speed: reference values and correlates for older adults. *Journal of Orthopaedic & Sports Physical Therapy* **24**, 86-90 (1996).

120 Wiles, C. & Karni, Y. The measurement of muscle strength in patients with peripheral neuromuscular disorders. *Journal of Neurology, Neurosurgery & Psychiatry* **46**, 1006-1013 (1983).

121 Domholdt, E. Physical therapy research. *Principles and applications* (1993).

122 Field, A. *Discovering statistics using IBM SPSS statistics*. (sage, 2013).

123 Tudor-Locke, C. E. & Myers, A. M. Methodological considerations for researchers and practitioners using pedometers to measure physical (ambulatory) activity. *Research quarterly for exercise and sport* **72**, 1-12 (2001).

124 Iwane, M. *et al.* Walking 10, 000 steps/day or more reduces blood pressure and sympathetic nerve activity in mild essential hypertension. *Hypertension Research* **23**, 573-580 (2000).

125 English, C., Manns, P. J., Tucak, C. & Bernhardt, J. Physical activity and sedentary behaviors in people with stroke living in the community: a systematic review. *Physical therapy* **94**, 185-196 (2014).

126 Mudge, S., Barber, P. A. & Stott, N. S. Circuit-based rehabilitation improves gait endurance but not usual walking activity in chronic stroke: a randomized controlled trial. *Archives of physical medicine and rehabilitation* **90**, 1989-1996 (2009).

127 Fini, N. A., Holland, A. E., Keating, J., Simek, J. & Bernhardt, J. How physically active are people following stroke? Systematic review and quantitative synthesis. *Physical therapy* **97**, 707-717 (2017).

128 Michael, K. & Macko, R. F. Ambulatory activity intensity profiles, fitness, and fatigue in chronic stroke. *Topics in stroke rehabilitation* **14**, 5-12 (2007).

129 Members, W. g. *et al.* Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* **119**, 480-486 (2009).

130 Perry, J., Garrett, M., Gronley, J. K. & Mulroy, S. J. Classification of walking handicap in the stroke population. *Stroke* **26**, 982-989 (1995).

131 Bowden, M. G., Balasubramanian, C. K., Behrman, A. L. & Kautz, S. A. Validation of a speed-based classification system using quantitative measures of

walking performance poststroke. *Neurorehabilitation and neural repair* **22**, 672-675 (2008).

132 Kwong, P., Ng, S., Chung, R. & Ng, G. A structural equation model of the relationship between muscle strength, balance performance, walking endurance and community integration in stroke survivors. *PloS one* **12**, e0185807 (2017).

133 Hessam, M. *et al.* Relationship between functional balance and walking ability in individuals with chronic stroke. *Journal of physical therapy science* **30**, 993-996 (2018).

134 Gerrits, K. H. *et al.* Isometric muscle function of knee extensors and the relation with functional performance in patients with stroke. *Archives of physical medicine and rehabilitation* **90**, 480-487 (2009).

135 Kobayashi, T., Leung, A. K. & Hutchins, S. W. Correlations between knee extensor strength measured by a hand-held dynamometer and functional performance in patients with chronic stroke. *Isokinetics and exercise science* **19**, 33-37 (2011).

136 Robertson, R., Robertson, A., Jepson, R. & Maxwell, M. Walking for depression or depressive symptoms: a systematic review and meta-analysis. *Mental health and physical activity* **5**, 66-75 (2012).

APPENDIX A: RECRUITMENT POSTER

Has a stroke affected your walking ability?

We are conducting a study that considers the factors that affect walking after a stroke.

Why take part in our study?

The study will help us gain valuable insight of how a stroke affects walking ability.

Each study participant will receive an assessment of their walking abilities based on measured testing.

Who can participate?

People who are 18 years or older, who have been discharged to home after stroke and can walk short distances with or without assistance.

Contact Tanya Chopra
Tel: (438)-873-0567
Email : tanya.chopra @ dal.ca

nova scotia health authority

DALHOUSIE UNIVERSITY
FACULTY OF HEALTH
School of Physiotherapy

Romeo File No. 1024100

Version 3, February 4, 2019

APPENDIX B: SCREENING FORM

SCREENING FORM		
Physical and affective characteristics associated with walking in the community: A cross-sectional study of chronic stroke survivors		
Potential Participant's Name	**Date**	
Inclusion Criteria	**Comments**	√
≥18 years of age	**Date of birth:**	
Diagnosed with stroke, confirmed by a physician, CT or MRI		
>6 months post-stroke	**Event date: (/ /)**	
Able to walk 10 meters with or without assistive devices		
Oriented to time, place & person; able to follow simple 3-step commands		
Ability & willingness to provide informed consent		
Able to understand spoken English		
Able to attend NSRC for assessment session		
Medically stable		
Exclusion Criteria	**Comments**	**X**
Resting heart rate <60bpm or >120 bpm		
Resting systolic blood pressure >170 mmHg		
Resting diastolic blood pressure > 95 mmHg		
Health-related condition preventing safe participation in study		
Currently participating in another research project that could confound the results of this study		

APPENDIX C: CONSENT FORM

Informed Consent Form Non-Interventional Study

STUDY TITLE:	Physical and affective characteristics associated with walking in the community: a cross-sectional study of chronic stroke survivors.
PRINCIPAL INVESTIGATOR:	Dr. Marilyn MacKay Lyons Professor School of Physiotherapy Dalhousie University Tel: 902-494-2632 M.MacKay-Lyons@dal.ca

Introduction

You have been invited to take part in a research study. A research study is a way of gathering information on a treatment, procedure or medical device or to answer a question about something that is not well understood. Taking part in this study is voluntary. It is up to you to decide whether to be in the study or not. Before you decide, you need to understand what the study is for, what risks you might take and what benefits you might receive. This consent form explains the study.

Please ask the research team to clarify anything you do not understand or would like to know more about. Make sure all your questions are answered to your satisfaction before deciding whether to participate in this research study.

The researchers will:

- Discuss the study with you
- Answer your questions
- Be available during the study to deal with problems and answer questions

If you decide not to take part or if you leave the study early, your usual health care will not be affected.

2. Why is there a need for this study?

Stroke survivors prefer walking as a form of physical activity but have trouble walking in the community. It appears that walking practice during physiotherapy sessions in hospitals and outpatient clinics may not fully prepare them for walking in the community. Unexpected things can happen while walking in the 'real world' which can limit walking ability and safety. We are doing this study to identify factors that affect walking in the community. The findings of this study will be help us to learn more about how to better prepare stroke survivors for walking in everyday life situations.

3. How Long Will I Be In The Study?

You will be asked to attend an assessment session that will take 2 hours. The entire study is expected to take about 8 months to complete and the results should be known in one year.

4. How Many People Will Take Part In This Study?

It is anticipated that about 40 people from the Halifax Regional Municipality will participate in this study.

5. How Is The Study Being Done?

If you are eligible to participate in this study and sign this consent form, a 2-hour appointment will be set up with one of the investigators at the Nova Scotia Rehabilitation Centre at a time convenient for you.

In preparation for the appointment you will be advised to:

1. Have a light meal or snack before the appointment.
2. Continue with your usual medical regimen.
3. Avoid exercising vigorously within the 2 hours before the appointment.
4. Wear comfortable clothing and appropriate shoes.
5. Use your usual walking aids, if any.

First your age, use of prescription drugs, marital status, employment situation (working, unemployed, retired), severity of your stroke and overall walking ability will be recorded. You will be asked to complete 2 questionnaires that ask if you feel you are fatigued or depressed. If you require or prefer help in filling in the questionnaires, an investigator will assist. Then, your balance and strength of your thigh muscles will be assessed. To measure your walking endurance, you will be asked to walk for 6 minutes, with rest breaks as needed. To assess your walking speed, the time it takes to walk 10 metres will be measured. We will offer you a summary of your scores on these tests at the end of the session.

We are also interested in measuring your ability to walk in the community. To do so you will be given a small, lightweight device called an accelerometer or step counter that is to be worn around the ankle of your stronger leg. We ask that the step counter be worn at all times throughout the day and night, including while bathing and sleeping, for a total of 3 days. For comfort, the step counter may be worn over a sock. We will ask you

to return the step counter in person or by mail in a pre-paid, addressed envelope that we will give you. You can contact the investigator through phone or e-mail if any doubt arises regarding the usage of the Step Watch Activity Monitor.

It is important that you tell the research team about any drugs or medicines you are taking or wish to take. You must also tell the research team about anything unusual that is happening with your health. This includes any medical problems that seem to be getting worse. If you have to see another doctor or have to go to a hospital, you should let the doctors know that you are in a research study. You should also tell your own doctor as quickly as possible, for your safety.

6. Are There Risks to the Study?

- Breach of confidentiality: As with all research, there is a chance that confidentiality could be compromised; however, we are taking precautions to minimize this risk. In order to protect your privacy and keep your participation in the study confidential, your name will be replaced by a 4-digit code. The file indicating participant names and codes will be stored in a password-protected laptop computer. Scores will be entered in to the computer and stored in a locked filing cabinet along with all the other information related to the study. All information will be stored in the Rehabilitation Research Lab of the Nova Scotia Rehabilitation Centre for the duration of the study and in the long term, will be store in a locked cabinet in the office of Dr. Marilyn MacKay-Lyon on the fourth floor of the Forrest Building of Dalhousie University. Although no one can absolutely guarantee confidentiality, using a code number makes the chance much smaller that someone other than the research staff or other authorized groups or persons (discussed later in the consent form) will ever be able to link your name to any test results.
- Emotional discomfort: You may find questionnaires you are asked to complete upsetting or distressing. You may feel anxious or sad. You may not like all of the questions that you will be asked. You do not have to answer those questions you find too distressing. If you are found to be depressed from your responses to the questionnaires, we will take the responsibility to let your family doctor know. If you do not have a family doctor, we will arrange for an appointment with a physician if you agree.
- Risk of fall: As falling is one of the most common complications of stroke survivors, there is a risk of fall while walking during the 6MWT and 10MWT. We will make sure there is always a person besides you while you perform walking tests to reduce the chances to fall.

7. Are There Benefits of Participating In This Study?

We cannot guarantee or promise that you will receive any benefits from this research. Your participation may help other people with stroke in the future. This study has the potential to benefit society through the generation of knowledge regarding factors associated with walking in the community of stroke survivors. The study will

help clinicians to predict accurately stroke survivors who would be able to return to walking in the community as well as inform interventional strategies for walking in the community leading to focused and specific treatment interventions and thus maximizing patient outcomes post-stroke.

8. What Happens At The End Of The Study?

It is expected that the results of this study will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your express permission.

9. What Are My Responsibilities?

As a study participant you will be expected to:

- Follow the directions of the research team.
- Report all medications being taken or that you plan on taking.
- Report any changes in your health to the research team.
- Report any problems that you experience that you think might be related to participating in the study.

10. Can My Participation In This Study End Early?

Yes. If you chose to participate and later change your mind, you can say no and stop the research at any time. If you wish to withdraw your consent, please inform the research team. If you choose to withdraw from this study, your decision will have no effect on your current or future medical treatment and healthcare

Also, the Nova Scotia Health Authority Research Ethics Board and the principal investigator have the right to stop patient recruitment or cancel the study at any time.

Lastly, the principal investigator may decide to remove you from this study without your consent for any of the following reasons:

- You do not follow the directions of the research team;
- You are experiencing side effects that are harmful to your health or well-being;

If you are withdrawn from this study, the principal investigator and the research coordinator will discuss the reasons with you.

11. What About New Information?

You will be told about any other new information that might affect your health, welfare, or willingness to stay in the study and will be asked whether you wish to continue taking part in the study or not.

12. Will It Cost Me Anything?

Compensation

It will not cost you anything to participate in this study. You will not be paid to take part in the study and you will not be reimbursed for any expenses related to the study.

Research Related Injury

If you become ill or injured as a direct result of participating in this study, necessary medical treatment will be available at no additional cost to you. Your signature on this form only indicates that you have understood to your satisfaction the information regarding your participation in the study and agree to participate as a subject. In no way does this waive your legal rights nor release the principal investigator, the research staff, the study sponsor or involved institutions from their legal and professional responsibilities.

13. What About My Privacy And Confidentiality?

Protecting your privacy is an important part of this study. Every effort to protect your privacy will be made. If the results of this study are presented to the public, nobody will be able to tell that you were in the study.

However, complete privacy cannot be guaranteed.

If you decide to participate in this study, the research team will look at your personal health information and collect only the information they need for this study. "Personal health information" is health information about you that could identify you because it includes information such as your;

- Name
- Address
- Telephone number
- Age
- Information from questionnaires

Access to Records

Other people may need to look at your personal health information to check that the information collected for the study is correct and to make sure the study followed the required laws and guidelines. These people might include:

- The Nova Scotia Health Authority Research Ethics Board (NSHA REB) and people working for or with the NSHA REB because they oversee the ethical conduct of research studies within the Nova Scotia Health Authority

Use of Your Study Information

Any study data about you that is sent outside of the Nova Scotia Health Authority will have a code and will not contain your name or address, or any information that directly identifies you. The research team and the other people listed above will keep the information they see or receive about you confidential, to the extent permitted by

applicable laws. Even though the risk of identifying you from the study data is very small, it can never be completely eliminated.

The research team will keep any personal health information about you in a secure and confidential location for 7 years and then destroy it according to NSHA policy. Your personal health information will not be shared with others without your permission.

After your part in the study ends, we may continue to review your health records for safety and data accuracy until the study is finished or you withdraw your consent.

You have the right to be informed of the results of this study once the entire study is complete.

The REB and people working for or with the REB may also contact you personally for quality assurance purposes.

Your access to records
You have the right to access, review, and request changes to your study data.

14. Declaration Of Financial Interest

This study is unfunded. The PI has no vested financial interest in conducting this study.

15. What About Questions Or Problems?

For further information about the study you may call the principal investigator, who is the person in charge of this study or the research coordinator.

The principal investigator is Dr. Marilyn MacKay-Lyons
Telephone: 902-494-2632
Your research coordinator is Tanya Chopra.
Telephone: 438-873-0567
In case of an emergency please contact Tanya Chopra at 438-873-0567.

16. What Are My Rights?

You have the right to all information that could help you make a decision about participating in this study. You also have the right to ask questions about this study and your rights as a research participant, and to have them answered to your satisfaction before you make any decision. You also have the right to ask questions and to receive answers throughout this study.

If you have any questions about your rights as a research participant, contact Patient Relations at (902) 473-2133 or healthcareexperience@nshealth.ca

In the next part you will be asked if you agree (consent) to join this study. If the answer is "yes", please sign the form.

17. Consent Form Signature Page

I have reviewed all of the information in this consent form related to the study called:

"Physical and affective characteristics associated with walking in the community: A cross sectional study of chronic stroke survivors."

I have been given the opportunity to discuss this study. All of my questions have been answered to my satisfaction.

I authorize access to my personal health information, and research study data as explained in this form.

This signature on this consent form means that I agree to take part in this study. I understand that I am free to withdraw at any time without affecting my future care.

_____	_____	_____ / _____ / ____
Signature of Participant	Name (Printed)	Year Month Day*
_____	_____	_____ / _____ / ____
Signature of Person Conducting Discussion	Name (Printed)	Year Month Day*
_____	_____	_____ / _____ / ____
Signature of Participant's Substitute Decision Maker	Name (Printed)	Year Month Day*
_____	_____	_____ / _____ / ____
Signature of Principal Investigator	Name (Printed)	Year Month Day*

Note: Please fill in the dates personally

I will be given a signed copy of this consent form.

APPENDIX D: DATA COLLECTION FORM

ASSESSMENT FORM						
Physical and affective characteristics associated with walking in the community: A cross-sectional study of chronic stroke survivors						
PARTICIPANT BACKGROUND DATA						
1. Participant Code **Participant's Name** _____ . **Email address_____.**				Date:_____. Assessor: .		
Address				**2. Postal code**		
Tel #(s)				Email		
Next-of kin				Relationship	Tel #	
Family doctor		Address			Tel #	
3. DOB (month/day/year) / / /			**4. Sex** ☐ Female ☐ Male			
5. Marital status	☐ Never married	☐Married	☐Divorced	☐ Separated	☐ Common law	☐ Widowed

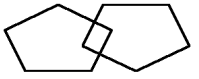
6. What is your employment status?		☐ Full-time	☐ Part-time	☐ On disability leave
☐Unemployed	☐ Homemaker	☐ Retired	Occupation (when employed) _____	
7. Prescription Medications				

ASSESSMENT CHECKLIST	√	Comments
Mini Mental State Examination		
Functional Ambulatory Category		
NIHSS scale		
Six-Minute Walk Test		
Ten-Meter Walk Test (2 trials)		
Berg Balance Scale		
Knee extensor strength testing		
Fatigue Severity Scale		
Patient Health Questionnaire-9		
Step Watch Activity Monitor		

Mini-Mental State Examination (MMSE)

Patient's Name: _____ Date: _____

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

FUNCTIONAL AMBULATORY CATEGORY		
FAC	**Ambulation**	**Definition**
0	**Nonfunctional ambulation**	Subject cannot ambulate, ambulates in parallel bars only, or requires supervision or physical assistance from more than one person to ambulate safely outside parallel bars.
1	**Ambulator-Dependent for Physical Assistance Level II**	Subject requires manual contacts of no more than one person during ambulation on level surfaces to prevent falling. Manual contacts are continuous and necessary to support body weight as well as maintain balance and/or assist coordination.
2	**Ambulator-Dependent for Physical Assistance Level I**	Subject requires manual contact of no more than one person during ambulation on level surfaces to prevent falling. Manual contact consists of continuous or intermittent light touch to assist balance or coordination
3	**Ambulator-Dependent for Supervision**	Subject can physically ambulate on level surfaces without manual contact of another person but for safety requires standby guarding on no more than one person because of poor judgement, questionable cardiac status, or the need for verbal cueing to complete the task
4	**Ambulator-Independent Level Surfaces only**	Subject can ambulate independently on level surfaces but requires supervision or physical assistance to negotiate any of the following: stairs, inclines or non-level surfaces.
5	**Ambulator-Independent**	Subject can ambulate independently on nonlevel and level surfaces, stairs and inclines.
Participant Category		

NIH STROKE SCALE (NIHSS)		
Instructions To be administered by neurologist/resident. Administer scale in order listed. Except where indicated the participant should not be coached. Score initial response. Do not go back & change scores. Scores should reflect what the participant does, not what the clinician thinks the participant can do.		
Domain	**Scale**	**Score**
1a. Level of Consciousness	**0** = Alert (keenly responsive) **1** = Not alert but arousable by minor stimulation **2** = Not alert; requires repeated stimulation to attend, or is obtunded & require strong or painful stimulation to make movements **3** = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid and flexic	**1.a**
1b. Level of Consciousness Questions *Ask the patient "What month is it? How old are you?*	**0** = Answers both questions correctly **1** = Answers one correctly **2** = Answers neither correctly	**1.b**
1c. Level of Consciousness Commands *Command patient to: "Open & close your eyes. Grip & release your hand."*	**0** = Performs both questions correctly **1** = Performs one correctly **2** = Performs neither correctly	**1c.**
2. Best Gaze *Establish eye contact & ask patient to "Follow my finger."*	**0** = Normal **1** = Partial gaze palsy **2** = Forced deviation or total gaze paresis	**2.**
3. Visual fields *Use confrontation, finger counting, or visual threat. Confront upper/lower quadrants of visual field.*	**0** = No visual loss **1** = Partial hemianopsia **2** = Complete hemianopsia **3** = Bilateral hemianopsia	**3.**
4. Facial Palsy *By words or pantomime, encourage patient to "Show me your teeth. Raise your eyebrows. Close your eyes."*	**0** = Normal symmetrical movement **1** = Minor paralysis (flattened nasolabial fold, asymmetry on smiling) **2** = Partial paralysis (lower face) **3** = Complete paralysis	**4.**
5. Arm motor *Alternately position patient's arms – extend each arm with palms down (90° if sitting, 45° if supine). Test nonparetic arm first.*	**0** = No drift **1** = Drift (meaning that arm falls before 10 seconds) **2** = Some effort vs gravity **3** = No effort vs gravity **4** = No movement **UN** = Amputation or joint fusion	**5.a** Left: **5.b** Right:

6. Leg motor *Alternately position patient's legs – extend each leg with palms down (30°always supine). Test nonparetic leg first.*	**0** = No drift **1** = Drift (meaning that arm falls before 5 seconds) **2** = Some effort vs gravity **3** = No effort vs gravity **4** = No movement **UN** = Amputation or joint fusion	**6.a** Left: **6.b** Right:
7. Limb Ataxia *Ask patient with eyes open to "Touch your finger to your nose. Touch your heel to your shin."*	**0** = Absent **1** = Present in one limb **2** = Present in two or more limbs	**7.**
8. Sensory *Test as many body parts as possible hands, arms, legs, trunk, face) for sensation using pinprick or noxious stimulus (in obtunded or aphasic patients)*	**0** = Normal **1** = Mild-to-moderate sensory loss **2** = Severe-to-total sensory loss	**8.**
9. Best Language *Using pictures & the sentence list provided, ask patient to "Describe what you see in this picture. Name the items in this picture. Read these sentences.*	**0** = No aphasia **1** = Mild-to-moderate aphasia **2** = Severe aphasia **3** = Mute, global aphasia	**9.**
10. Dysarthria *Using the simple word list provided, ask the patient to "Read these words" or "Repeat these words."*	**0** = Normal articulation **1** = Mild-to-moderate dysarthria **2** = Severe dysarthria **UN** = Intubated or other physical barrier	**10.**
11. Extinction & Inattention *Sufficient information to determine these scores may have been obtained prior to testing.*	**0** = No abnormality **1** = Visual, tactile, auditory, spatial or personal inattention **2** = Profound hemi-inattention or extinction to more than one modality	**11.**
	TOTAL SCORE	**/42**

MAMA

TIP – TOP

FIFTY – FIFTY

THANKS

HUCKLEBERRY

BASEBALL PLAYER

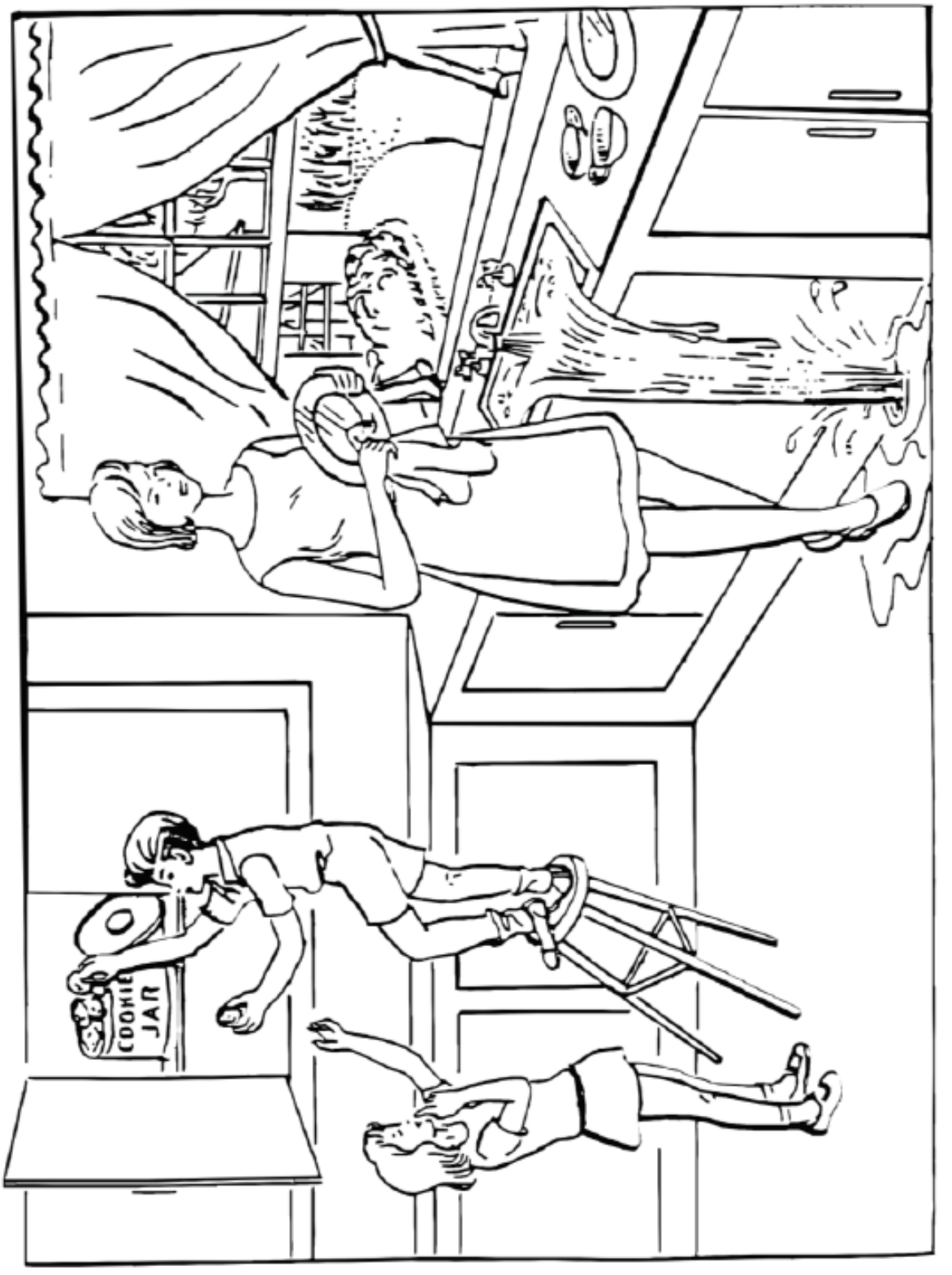
You know how.

Down to earth.

I got home from work.

Near the table in the dining room.

They heard him speak on the radio last night.


COOKIE
JAR

SIX-MINUTE WALK TEST		
Supplemental oxygen during the test	Yes _____ No _____	Flow _____ L/min Type _____
Baseline Time: ___: ____ Heart Rate: _____bpm RPE: _____ Blood Pressure: ____/____ mmHg	End of the test Time: ___: ____ Heart Rate: _____bpm: _____ RPE: _____ Blood Pressure: ____/____ mmHg	
Stopped or paused before 6 minutes?	No: _____ Yes: _____	Reason:
Other symptoms at the end of the test Angina: _____ Dizziness: _____ Hip pain: _____ Calf pain: _____		
Number of laps: ____ (60 meters) + final partial lap: ____ meters = _____		
Total distance walked in 6 minutes: meters		
TEN-METER WALK TEST		
Seconds to ambulate 10 meters Trial 1: _____sec Trial 2: _____sec Average Time: _____sec		
Average Self-Selected Velocity: m/s		

Scale for Rate of Perceived Exertion

.0	Nothing at All
.05	Very, Very Light
1	Very Light
2	Light
3	Moderate
4	Somewhat Hard
5	Hard
6	
7	Very Hard
8	
9	
10	Very, Very Hard

BERG BALANCE SCALE	
1. Sit to Stand Instructions: "Please stand up. Try not to use your hands for support"	( ) 0: Needs moderate or maximal assistance to stand ( ) 1: Needs minimal assistance to stand or to stabilize ( ) 2: Able to stand using hands after several tries ( ) 3: Able to stand independently using hands ( ) 4: Able to stand with no hands and stabilize independently
2. Standing unsupported Instructions: "Please stand for 2 minutes without holding onto anything"	( ) 0: Unable to stand 30 seconds unassisted ( ) 1: Needs several tries to stand 30 seconds unsupported ( ) 2: Able to stand 30 seconds unsupported ( ) 3: Able to stand 2 minutes without supervision ( ) 4: Able to stand safely for 2 minutes If person is able to stand 2 minutes safely, score full points for sitting unsupported (item 3). Proceed to item 4.
3. Sitting with back unsupported with feet on floor or on a stool Instructions: "Sit with arms folded for 2 minutes	( ) 0: Unable to sit without support for 10 seconds ( ) 1: Able to sit for 10 seconds ( ) 2: Able to sit for 30 seconds ( ) 3: Able to sit for 2 minutes under supervision ( ) 4: Able to sit safely and securely for 2 minutes
4. Stand to sit Instructions: "Please sit down"	( ) 0: Needs no assistance ( ) 1: Sits independently but had uncontrolled descent ( ) 2: Uses back of legs against chair to control descent ( ) 3: Controls descent by using hands ( ) 4: Sits safely with minimal use of hands
5. Transfers Instructions: "Please move from chair to chair and back again" (Person moves one way toward a seat with armrests and one way toward a seat without armrests) Arrange chairs for pivot transfer	( ) 0: Needs two people to assist or supervise to be safe ( ) 1: Needs one person to assist ( ) 2: Able to transfer with verbal cueing and/or supervision ( ) 3: Able to transfer safely with definite use of hands ( ) 4: Able to transfer safely with monir use of hands
6. Standing unsupported with eyes closed Instructions: "Close your eyes and stand still for 10 seconds"	( ) 0: Needs help to keep from falling ( ) 1: Unable to keep eyes closed for 3 seconds but remains steady ( ) 2: Able to stand for 3 seconds ( ) 3: Able to stand for 10 seconds without supervision ( ) 4: Able to stand for 10 seconds safely

7. Stand unsupported with feet together Instructions: "Place your feet together and stand without holding on to anything"	( ) 0: Needs help to attain position and unable to hold for 15 seconds

	( ) 1: Needs help to attain position but able to stand for 15 seconds with feet together ( ) 2: Able to place feet together independently but unable to hold for 30 seconds ( ) 3: Able to place feet together independently and stand for 1 minute without supervision ( ) 4: Able to place feet together independently and stand for 1 minute safely
8. Reaching forward with outstretched arm Instructions: "Lift your arm to 90. Stretch out your fingers and reach forward as far as you can" (Examiner places a ruler and end of fingertips when arm is at 90 Fingers should not touch the ruler while reaching forward. The recorded measure is the distance toward that the fingers reach while the person is in the most forward lean position.)	( ) 0: Needs help to keep from falling ( ) 1: Reaches forward but needs supervision ( ) 2: Can reach forward more than 2 inches safely ( ) 3: Can reach forward more than 5 inches safely ( ) 4: Can reach forward confidently more than 10 inches
9. Pick up object from the floor from a standing position Instructions: "Please pick up the shoe/slipper that is placed in front of your feet"	( ) 0: Unable to try/needs assistance to keep from losing balance and falling ( ) 1: Unable to pick up shoe and needs supervision while trying ( ) 2: Unable to pick up shoe but comes with in 1-2 inches and maintains balance independently ( ) 3: Able to pick up shoe but needs supervision ( ) 4: Able to pick up shoe safely and easily
10. Turn to look behind over left and right shoulders while standing Instructions: "Turn you upper body to look directly over your left shoulder. Now try turning to look over you right shoulder"	( ) 0: Needs assistance to keep from falling ( ) 1: Needs supervision when turning ( ) 2: Turns sideways only but maintains balance ( ) 3: Looks behind one side only; other side shows less weight shift ( ) 4: Looks behind from both sides and weight shifts well

11. Turn 360□ Instructions: "Turn completely in a full circle. Pause, then turn in a full circle in the other direction"	( ) 0: Needs assistance while turning ( ) 1: Needs close supervision or verbal cueing ( ) 2: Able to turn 360□ safely but slowly ( ) 3: Able to turn 360□ safely to one side only in less than 4 seconds ( ) 4: Able to turn 360□ in less than 4 seconds to each side
12. Place alternate foot on bench or stool while standing unsupported Instructions: "Place each foot alternately on the bench (or stool). Continue until each	( ) 0: Needs assistance to keep from falling/unable to try ( ) 1: Able to complete fewer than two steps; needs minimal assistance

foot has touched the bench (or stool) four times". (Recommended use of 6-inch-high-bench.)	( ) 2: Able to complete four steps without assistance but with supervision ( ) 3: Able to stand independently and complete eight steps in more than 20 seconds ( ) 4: Able to stand independently and safely and complete eight steps in less than 20 seconds
13. Stand unsupported with one foot in front Instructions: "Place one foot directly in front of the other. If you feel that you can't 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" (Demonstrate this test item)	( ) 0: Loses balance while stepping or standing ( ) 1: Needs help to step but can hold for 15 seconds ( ) 2: Able to take small step independently and hold for 30 seconds ( ) 3: Able to place one foot ahead of the other independently and hold for 30 seconds ( ) 4: Able to place feet in tandem position independently and hold for 30 seconds.
14. Standing on one leg Instructions: "Stand on one leg as long as you can without holding".	( ) 0: Unable to try or needs assistance to prevent fall ( ) 1: Tries to lift leg, unable to hold 3 seconds but remains standing independently ( ) 2: Able to lift leg independently and hold up to 3 seconds ( ) 3: Able to lift leg independently and holds for 5 to 10 seconds ( ) 4: Able to lift leg independently and hold more than 10 seconds
Total score: __/56	

KNEE EXTENSOR STRENGTH TESTING USING HAND-HELD DYNAMOMETER	
Trial	Newtons
1	
2	
Trial chosen:	

PATIENT HEALTH QUESTIONNAIRE-9				
Over the last 2 weeks, how often have you been bothered by any of the following problems? (Circle the number to indicate your answer)	**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 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
Total Score:	/27			
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	Somewhat difficult	Very Difficult	Extremely difficult	

FATIGUE SEVERITY SCALE							
Please circle the number between 1 and 7 which you feel best fits the following statements. This refers to your usual way of life within the last week. 1 indicates "strongly disagree" and 7 indicates "strongly agree."							
Read and circle a number.	**Strongly disagree**			→		**Strongly agree**	
1. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2. Exercise brings on my fatigue.	1	2	3	4	5	6	7
3. I am easily fatigued.	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is among my most disabling symptoms	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family or social life.	1	2	3	4	5	6	7
Total Score	/63						

VISUAL ANALOGUE FATIGUE SCALE (VAFS)
Please mark an "X" on the number which describes your global fatigue with 0 being worst and 10 being normal.

0 1 2 3 4 5 6 7 8 9 10

APPENDIX E: REPORT CARD GIVEN TO THE PARTICIPANTS

Report Card

Name: _____ Date:

Thank you for participating in the study. Below is a summary of your performance.

Balance: We tested your balance using the Berg Balance Scale. Your score on the scale is
_____ /56. Your score indicates:

- 41-56: You are at a low risk of falling.
- 21-40: You are at a medium risk of falling.
- 0-20: You are a high risk of falling.

Fatigue: We measured fatigue using the Fatigue Severity Scale. Your score on the scale is
_____/63. Your score indicates:

- Less than 36: Suggests no signs of fatigue.
- 36 or more: Suggests a level of fatigue which should be mentioned when you see your family doctor.

Depression: We used the Patient Health Questionnaire-9 for measuring the severity of depression. Your score is _____/27. Your score indicates:

- 0-9: Mild depression
- 10 or more: Suggests a level of depression that should be bought to the attention of your family doctor.

Walking Endurance: You walked _____ meters in 6 minutes. A healthy person of your age can walk ___ meter. The following table will give you information about community distances which you can travel:

Location	Distance	Location	Distance
Crosswalk: Residential	10 m	Crosswalk: Commercial	30 m
Gas station	40 m	Restaurant	60 m
Post office	80 m	Physician's office	90 m
Bank	100 m	Religious Centre	110 m
Shopping mall	160 m	Drugstore	330 m
Department store	360 m	Supermarket	380 m
Bus stop	400 m	Superstore	610 m
Club warehouse	680 m	Rail station	800 m

Walking Speed: Your walking speed is _____ m/s. You fall under the following category:

- Less than 0.4 metres/second: Suggests the ability to walk within your home with or without assistance.
- 0.4-0.8 m/s: Suggests the ability to walk outside in your community with assistance or supervision.
- Greater than 0.8 m/s: Suggests the ability to walk outside in your community without assistance and without supervision.

Normative values of walking speed in each age group for men and women are mentioned in the following table:

Age	Men	Women
20-29	1.36 m/s	1.34 m/s
30-39	1.43 m/s	1.34 m/s
40-49	1.43 m/s	1.39 m/s
50-59	1.43 m/s	1.31 m/s
60-69	1.34 m/s	1.24 m/s
70-79	1.26 m/s	1.13 m/s
80-89	0.97 m/s	0.94 m/s

Muscle strength: We measured the strength of quadriceps muscle which runs in the front of your thigh. Your muscle strength is _____ newtons.

APPENDIX F

		Age	Sex	Time since stroke	FAC	NIHSS	6MWT	10MWT	BBS	Knee extensor strength	FSS	PHQ-9	Steps
Age	r	1	-0.24	0.08	-0.18	-0.19	-0.17	-0.10	--0.23	-0.04	-0.10	-0.11	-0.22
	p		0.141	0.647	0.300	0.287	0.336	0.558	0.185	0.824	0.558	0.540	0.218
Sex	r	-0.25	1	-0.01	-0.02	-0.03	-0.18	-0.14	-0.06	-0.05	0.01	0.02	0.10
	p	0.141		0.963	0.891	0.877	0.308	0.413	0.716	0.760	0.954	0.907	0.584
Time since	r	0.08	-0.01	1	-0.05	0.40*	-0.25	-0.23	-0.28	-0.29	-0.21	-0.02	-0.19
Stroke	p	0.647	0.963		0.77	0.018	0.143	0.191	0.110	0.089	0.236	0.910	0.288
FAC	r	-0.18	-0.02	-0.05	1	-0.25	0.25	0.33	0.37	0.11	-0.21	-0.22	0.17
	p	0.300	0.891	0.770		0.157	0.154	0.06	0.030	0.531	0.241	0.214	0.351
NIHSS	r	-0.19	-0.03	0.40*	-0.25	1	-0.45*	-0.43**	-0.42*	-0.44	0.16	0.32	-0.29
	p	0.287	0.877	0.018	0.157		0.007	0.009	0.011	0.009	0.349	0.060	0.091
6MWT	r	-0.17	-0.18	-0.25	0.25	-0.45**	1	0.88**	0.86**	0.49**	-0.24	-0.26	0.59**
	p	0.336	0.308	0.143	0.154	0.007		0.000	0.000	0.003	0.116	0.133	0.000
10MWT	r	-0.10	-0.14	-0.23	0.33	-0.43**	0.88**	1	0.75**	0.31	-0.21	-0.30	0.60**
	p	0.558	0.413	0.191	0.055	0.009	0.000		0.000	0.069	0.238	0.083	0.000
BBS	r	-0.23	-0.06	-0.28	0.37*	-0.42	0.86**	0.75**	1	0.52**	-0.27	-0.29	0.56**
	p	0.185	0.716	0.110	0.030	0.11	0.000	0.000		0.001	0.116	0.087	0.001
Knee extensor strength	r	-0.04	-0.05	-0.29	0.11	-0.44**	0.48**	0.31	0.52**	1	-0.08	-0.26	0.03
	p	0.824	0.760	0.089	0.531	0.009	0.003	0.069	0.001		0.659	0.140	0.857
FSS	r	-0.10	0.01	-0.21	-0.20	0.16	-0.24	-0.21	-0.27	-0.08	1	0.52**	-0.08
	p	0.558	0.954	0.236	0.241	0.349	0.166	0.238	0.116	0.659		0.001	0.661
PHQ-9	r	-0.11	0.02	-0.02	-0.22	0.32	-0.26	-0.30	-0.29	-0.26	0.52**	1	0.140
	p	0.540	0.907	0.910	0.214	0.060	0.133	0.083	0.087	0.140	0.001		0.430
Steps	r	-0.22	0.10	-0.19	0.17	-0.29	0.59**	0.60**	0.56**	0.03	-0.08	0.140	1
	p	0.218	0.584	0.288	0.351	0.091	0.000	0.000	0.001	0.857	0.661	0.430	

APPENDIX G: MANUSCRIPT OF THE NARRATIVE REVIEW

Post-Stroke Fatigue - An overlooked concern that negatively impacts stroke recovery and function: A Narrative Review

Tanya Chopra[a], Robin Parker[b], Marilyn MacKay Lyons[a]

[a] School of Physiotherapy, Dalhousie University, Halifax, Canada

[b] W.K. Kellogg Health Sciences Library, Dalhousie University, Halifax, Canada

Corresponding Author: Tanya Chopra

Address: School of Physiotherapy, Office 421 Forrest Building, Dalhousie University, 5869 University Avenue, PO Box 15000, Halifax, NS, B3H 4R2, Canada

Telephone number: +1-438-873-0567

E-mail: tanyachopra94@gmail.com

Abstract

BACKGROUND: "More is better" is rapidly becoming the mantra for the dose of neurorehabilitation needed to optimize recovery of people post-stroke. Emphasis is on intensity, repetition, and frequency of training. By embracing this philosophy, a pervasive clinical feature – post-stroke fatigue (PSF) – is being overshadowed.

OBJECTIVES: To 1) review the literature on PSF, 2) discuss main themes of the review to inform clinical practice, and 3) identify knowledge gaps to inform future research.

METHODS: A literature search was performed using CINAHL, PubMed, and Cochrane databases.

RESULTS: Of 2,201 citations, 131 abstracts were selected for full text screening, and 124 publications were included. PSF is prevalent in 29-68% of the stroke population and its management is a foremost, unmet need of stroke survivors. PSF is associated with multiple factors: depression, pain, sleep disturbances, functional dependence, and compromised quality of life, all of which compromise rehabilitation and recovery.

CONCLUSION: PSF needs to be addressed early and consistently to achieve a personalized rather than formulaic approach to rehabilitation. Among the important questions need of answers are: To what extent does PSF mediate the dose-response relationship of rehabilitation interventions? How should PSF be factored into defining the patient's optimal intervention plan and dose?

Keywords: Fatigue, Stroke, Rehabilitation, Intervention

1. INTRODUCTION

Fatigue after stroke, often referred to as post-stroke fatigue (PSF), is a prevalent concern of many people in the acute, subacute, and chronic stages of stroke. This type of fatigue is distinct from both exertional[143] and mental fatigue[144] and is characterized by disproportionate weariness or exhaustion triggered by simple activities that often is not resolved with ordinary rest[145].Stroke survivors have described PSF as their "most common invisible impairment"[146,147]. It is associated with functional dependence in activities of daily living and instrumental activities of daily living [148-152],[153-156], as well as strained spousal relationships and sexual dysfunction[157-159]. Moreover, PSF is a significant predictor not only of poor health-related quality of life at 3 months post-stroke [150,160] and long-term follow up,[65,161,162],[163] but also of long-term mortality[164].

Despite the far-reaching impact of PSF on life after stroke, stroke survivors have claimed to be unaware that PSF could form part of their illness trajectory[165]. They also have noted that signs of fatigue and potential coping strategies were seldom discussed during hospitalization[166]. Lack of awareness of PSF among employers, work colleagues, clinicians, and survivors themselves has been shown to be a significant barrier to employment after stroke[146,147]. PSF also has an adverse impact on stroke rehabilitation – the presence of PSF has been identified as a key factor limiting appropriate delivery of therapy[167] and participation in rehabilitation has been shown to be inversely related to the severity of PSF.[168,169] Further, neglecting PSF during rehabilitation could have unintended consequences in terms of patient-centered care and stroke recovery. For example, the current emphasis on increased intensity of therapeutic interventions to

exploit neuroplastic mechanisms of recovery [170] may actually be a disservice to people with significant PSF.

We were motivated to undertake this narrative review of PSF in response to a perceived need to increase the awareness of stroke rehabilitation clinicians about PSF. The review begins with a brief overview of the prevalence of PSF and assessment of PSF. Attention then turns to possible mechanisms of PSF and clinical correlates of PSF. Finally, pharmacological and non-pharmacological interventions PSF are discussed.

2. METHODS

A comprehensive literature search was performed by a reference librarian (RP) using PubMed, CINAHL and Cochrane CENTRAL (inception to April 15, 2019). Search terms included words related to stroke, cerebrovascular accident, fatigue, lassitude, tiredness, weariness, brain vascular accident. Figure 1 outlines the search strategy used for PubMed. The search was supplemented by hand-searching reference lists of review articles. The authors (TC and MML) reviewed all full texts for eligibility; disagreements were resolved through discussion.

The following inclusion criteria were used:

1. Qualitative and quantitative human studies with sample size of more than 5, published in English which quantitatively measured PSF using valid and reliable tools.
2. Studies with a primary or secondary purpose of addressing PSF in terms of prevalence, mechanisms, associated factors, pharmacological and non-pharmacological interventions.
3. Grey literature including reports, conference proceedings, doctoral thesis and dissertations, single case series and abstracts.

In addition, one exclusion criterion was applied - studies that focused specifically on muscle fatigue or mental fatigue after stroke were excluded.

As shown in Figure 2, the search yielded 2201 studies, 124 of which met the selection criteria.

3. PREVALENCE OF PSF

Frequency of symptoms of fatigue post-stroke has been reported to be as much as three times that of age-matched controls[171]. The reported prevalence of PSF ranges from 23-77%,[172-176] the variability of which can be attributed largely to methodological differences (e.g., heterogeneity in patient selection, time since stroke, assessment tools, and diagnostic cut-off values) [177,178]. In a systematic review and meta-analyses the pooled estimate of PSF prevalence was 50%, irrespective of whether data on people with psychiatric history or depression were included.[177]

There is some, albeit inconsistent, evidence that PSF tends to be more frequent in female patients and older patients but is not influenced by stroke severity or side of stroke[179]. Typically, fatigue sets in within the first two weeks after stroke onset.[166,180,181] A history of pre-stroke fatigue appears to be predictive of both a higher probability of experiencing PSF in the acute phase of stroke[182] although PSF has been described by patients as a "different type of fatigue" than they had ever experienced before[183]. Early fatigue is a strong predictor of fatigue in the chronic stage of stroke[184]. Although several longitudinal studies have reported a decline in PSF over time, [166,180,181] other studies noted a significantly higher prevalence at 1 year post-onset compared to either admission[185] or 3

months post-stroke[186]. These inconsistencies in prevalence data underline the need for longitudinal studies using a common data set and assessment schedule.

4. ASSESSMENT OF PSF

The complexity of PSF impedes its assessment. Nevertheless, a number of tools have been developed to assess the presence and severity of PSF. The majority of the PSF literature have used one or more of 5 assessment tools: Fatigue Severity Scale (FSS), Fatigue Impact Scale (FIS), Fatigue Assessment Scale (FAS), Fatigue Subscale of the Profile of Mood States (POMS), and Vitality Subscale of the Short Form Health Survey. Characteristics and psychometric properties of each tool are summarized in Table 1 .

5. MECHANISMS OF PSF

Fatigue during the acute stage of stroke tends to be interpreted as a non-specific, adaptive reaction to a major disruptive event (stroke), hospitalization and/or demands of adjusting to life after stroke, but if the fatigue persists several weeks after stroke, it is regarded as more of a health concern[187]. Recent investigations have provided evidence that long-term PSF has a physiological basis with distinctive behavioural patterns, refuting the notion that chronic PSF is influenced largely by psychosocial factors [188]. In fact, multiple mechanisms may underlie PSF. To develop evidence-based interventions for PSF a better understanding of possible mechanisms underlying this condition is needed[189]. Here we consider a number of possibilities - location of the stroke, biochemical imbalances, sensorimotor disturbances, undernourishment and physical inactivity.

5.1 Lesion location

The relationship between PSF and lesion location is unclear, partly due to the variability in the tools used to measure PSF and the time post-stroke of assessments. Two studies examining the relationship reported that PSF was associated largely with subcortical lesions (particularly subcortical white matter infarcts, and basal ganglia infarcts, caudate infarcts and deep cerebral micro bleeds)[190-192], whereas findings from another study using MRI data was inconclusive[193]. The striato-thalmo-cortical loop connects the striatum (part of the basal ganglia) to pre-frontal cortex with the thalamus being the final common pathway of the cortical projections from the basal ganglia. An increase in net thalamic inhibition modifies the cortical response to basal ganglia. Thus damage to this circuitry, which can occur in stroke, leads to poverty and slowness in the initiation and execution of willed and associated movements,[194] as well as loss of motivation in self-initiated tasks[190] - common features of fatigue.

5.2 Inflammation and biochemical imbalances

Inflammation in the brain is mediated by the production and release of proinflammatory cytokines, such as interleukin-1β, by the immune system.[195] This process of immune dysregulation is thought to contribute to excessive fatigue characteristic of chronic fatigue syndrome, Parkinson disease, multiple sclerosis, fibromyalgia,[196] and possibly stroke [195]. Serum levels of interleukin-1 measured within 72 hours post-stroke correlate positively with 6-month FSS scores whereas interleukin-ra and interleukin-9, antagonists of interleukin-1β, correlate negatively with 12-month FSS scores.[196] By 18 months these relationships had dissipated.

Inflammation after stroke also upregulates indoleamine-pyrrole 2,3-dioxygenase, the enzyme that catalyzes the rate-limiting step in the synthesis of kynurenine from

tryptophan (TRP) in central and peripheral cells [197]. The high serum levels of kynurenic acid detected in patients with PSF[198] reduce the bioavailability of TRP needed for 5-hydroxy tryptamine synthesis which promotes wakefulness [199]. These biochemical disturbances provide another possible explanation for the PSF-related symptoms of abnormal tiredness and need for excessive sleep [200]. As further evidence of this possibility, Ormstad and colleagues reported that patients with FSS scores of >4 had significantly lower TRP index values at 12 months and higher serum level of kynurenic acid at 18 months compared with patients with FSS scores of <4[198]. A limitation of these findings is that plasma markers used in this study are not as accurate as cerebrospinal fluid markers in assessing the biochemical environment in the brain. [187]

5.3 Depressed corticomotor excitability and sensorimotor deficits

Inflammation early post-stroke can also depress cortical excitability. [188] Proinflammatory cytokines inhibit voltage-gated sodium currents, resulting in higher motor cortex thresholds as demonstrated in brain stimulation studies.[188] In a study of 70 non-depressed, chronic stroke survivors, those with high levels of PSF exhibited lower motor cortex activation and greater perceived effort to move. [201] Another study reported that stroke survivors with severe PSF but without explicit muscle weakness demonstrated slower movement times during ballistic movements of the hemiparetic limbs, which were attributed to depressed corticomotor excitability[201,202].

Impaired sensory processing has also been implicated in the link between corticomotor system impairment and PSF[201]. Sensory prediction errors are generated when descending commands from the brain that specify sensory predictions are compared with incoming sensory signals, [188]. The decision of whether to attend to these errors is dependent on the

precision of the sensory inputs Although seemingly counterintuitive, when sensory precision is increased by altered central processing of reafferent activity from the peripheral musculature, greater perceived effort and limb heaviness are experienced [188]. In a study (n=69), 31individuals reported limb heaviness and had a FSS-7 score of 4.8±1.53 where as 38 individuals did not report limb heaviness and had a FSS-7 score of 2.68±1.53. There was a statistically significant difference between the fatigue scores of the 2 groups($p < 0.001$) .[203].

5.4 Undernourishment

A potential but under-investigated mechanism of PSF is undernourishment. Evidence indicates that the risk of malnutrition ranges from 24%, at 4 months post-stroke to 26% at 16 months post-stroke[204]. Although lack of proper nutrition could theoretically precipitate PSF, the notion of reversed causality also warrants attention. Westergren[205] postulated that a bidirectional relationship might exist between fatigue and lack of nourishment: PSF may adversely affect motivation to eat and meal preparation, leading to undernourishment; conversely, termination of eating after stroke prior to reaching satiety may result in undernourishment and PSF[205].

5.5 Physical inactivity

PSF may be triggered by the deconditioned state commonly seen post-stroke[206]. However, cause and effect has not been established and, again, the association between PSF and physical inactivity may reflect reversed causality. Many people after stroke enter a vicious cycle of increased sedentary behaviors, leading to further activity avoidance, decreased strength, depleted energy reserves, and persistent fatigue[65]. A longitudinal study found that lower levels of physical activity at one month post-stroke

independently predicted higher levels of fatigue at 6 and 12-month follow-ups,[65] whereas another small study found no association between PSF and measures of physical fitness[71]. A recent meta-analysis reported a negative correlation (r = -22, P = 0.01) between post-stroke physical activity and fatigue, measured using the FSS[207].

The multifaceted processes that may contribute to the high prevalence of PSF are illustrated in Figure 3. Future research is warranted, not only to verify the underlying mechanism(s) but also to identify those that are at play in a given patient so as to facilitate personalized approaches to PSF management.

6. CLINICAL COORELATES RELATED TO PSF

Multiple factors are related to the presentation of PSF in the acute and chronic phase of stroke recovery. In this section we discuss the psychological and physical correlates of PSF in stroke survivors.

6.1. Psychological factors

Fatigue is a common symptom of depression.[178] Many studies have found a significant relationship between PSF and post-stroke depression (PSD) [65,150,151,178,180,182,208-210] but interpretation of this relationship remains unclear [182]. In a meta-analysis, a positive association between fatigue after stroke and depressive symptoms has been reported (odds ratio = 4.14, 95% CI = 2.73-6.27)[175]. Temporal associations between PSF and PSD have been established in longitudinal studies, demonstrating that both early PSD and long term PSD predict long-term PSF[178,211]. Douven et al. noted a bi-directional relationship between PSF and PSD at 3 months post-stroke that was sustained at 1-year follow-up - patients with PSF had higher depression scores and patients with PSD had

higher fatigue scores[208]. However, because some people experience PSF in the absence of PSD, PSF and PSD should be regarded as distinct sequelae of stroke [185].

Neuroticism, characterized by anxiety, irritability, emotional instability and impulsiveness, has been shown to be predictive of PSF independent of depressive symptoms[212]. Suicidal tendencies have been reported in people with PSF who also have alterations in the brainstem nuclei[145,213]. Further, stroke- specific anxiety [65,149,151,209], low internal locus of control[185] and high external locus of control directed to physicians[185] are known correlates of PSF. Fortunately, there is some evidence of effectiveness of interventions that target depression and anxiety in people with PSF, [214-216] as discussed in the last section.

People with PSF may also have a higher probability of presenting with concomitant cognitive impairments[217-219]. Although several studies have reported greater incidence of deficits in a variety of cognitive domains - working memory, attention, visuospatial function, executive function and processing speed,[144,210,220-222] others have not[223]. It is likely that inconsistencies in the assessment of both PSF and cognition and the time post-stroke onset of the studies contributes to conflicting findings.

6.2 Physical factors

Although physical deconditioning has been postulated as a potential mechanism underlying PSF, as discussed above, there is conflicting evidence regarding the impact of PSF on physical activity. In a longitudinal study, fatigue measured by FSS was negatively correlated with steps counts at 1 month ($r=0.39$, $p<0.001$) and 6 months ($r=0.31$, $p=0.01$) but the relationship was lost at 12 months[65]. In another longitudinal study, fatigue measured at discharge from hospital was negatively related to walking

activity at 1 month post stroke ($r=0.39$, $p<0.05$) but the relationship was not significant at 3 months and 6 months[224]. In contrast, a cross-sectional study reported no significant relationships between step counts, peak oxygen consumption, and FSS scores at 6 months post-stroke[23]. Variability in step count protocols, time since stroke, and assessment of PSF may have contributed to these discrepant findings.

Positive correlations have been found between constant or intermittent pain or paraesthesia in a hemiparetic body part and PSF at 6 months[211,225] and 12 months[226] after stroke onset. Other sequelae common after stroke - insomnia, excessive daytime sleepiness, and poor sleep quality - have also been shown to have a significant relationship with PSF[65,152,182,227,228]. As well, preliminary findings suggest that sleep apnea, a complication of stroke, may be related to PSF[229,230]. In a small qualitative study involving 15 people averaging 3 month after stroke onset, 40% of participants identified disturbed and inadequate sleep as the main reason for PSF, and 93% reported that sleep was beneficial in reducing their fatigue [228].

In summary, preliminary evidence exists of psychological and physical factors commonly presenting after stroke that appear to be associated with PSF. It is important that PSF be differentiated from symptoms such as depression[231]. Further research is needed to ascertain the complex interactions of these factors.

7. INTERVENTIONS FOR PSF

Although PSF is regarded as a modifiable clinical entity post-stroke[207], testimonials by stroke survivors suggest that health professionals tend to minimize the importance of PSF.[232] Such lack of acknowledgement has negatively impacted the extent of research

conducted on PSF.[189] In this section, the limited knowledge available regarding both pharmacological and non-pharmacological management of PSF is summarized.

7.1. Pharmacological interventions

Effective drug therapies to treat PSF are very limited, as reflected in the conclusion of the 2015 Canadian Stroke Best Practices Recommendations that evidence was not sufficient to recommend a specific pharmacological treatment for PSF[233.] Although PSF is strongly associated with depression, anti-depressants have not been effective in reducing PSF [234]. The finding that selective serotonin reuptake inhibitors (e.g., fluoxetine, duloxetine, citalopram) do not relieve PSF[235,236] suggests that the serotonergic system may not be closely related to PSF, which is consistent with the view that depression and anxiety are phenomena distinct from PSF.

A small scale study without placebo control (40 patients with brainstem and diencephalic stroke) demonstrated that a wakefulness-promoting drug, modafinil, relieved PSF.[237] However, a subsequent randomized controlled trial (RCT) involving 41 people post-stroke reported that a 90-day trial modafinil did not result a significant difference in fatigue scores between experimental and control groups at 6 months[233]. Liu and colleagues conducted an RCT (N= 61 people post-stroke) to investigate a 28-day course of *Astragalus membranaceus,* a Chinese herb with anti-inflammatory properties, on PSF[238]. The results were encouraging – a significant decrease in fatigue scores was found between the treatment and placebo group at 3-month follow-up (P=0.05) [238].

7.2 Non-pharmacological interventions

Non-pharmacological interventions should be given due consideration in the management of PSF, not only because PFS appears refractory to pharmacological agents

but the possibility exists that certain medications can have unintended negative effects on neurological recovery[239,240]. Evidence exists of positive associations between PSF and the use of sedative drugs[241], antidepressants[150,242]and antihypertensive drugs[243]**.** In terms of non-pharmacological approaches, the 2015 Canadian Stroke Best Practice Recommendations endorsed implementation of energy conservation strategies, planned exercise programs, education, and good sleep hygiene[244]

Regardless of the intervention strategy used, acknowledging PSF as a clinical entity and establishing a balance between rest and activity are fundamental..[245] "Managing Fatigue" is a course designed for implementation by occupational therapists that consists of six one-hour modules on PSF management issues (e.g., rest, communication, body mechanics, activity modification, and priority setting) [245]. In a pilot RCT with 19 participants, 3-18 months post-stroke, those participants randomized to the Managing Fatigue course demonstrated a non-significant trend in greater reductions in PSF at the 3-month follow up compared to the control (general education) group[245].

Treatment interventions targeting psychological factors such as depressive symptoms, anxiety, poor coping, loss of control, emotional and behavioural symptoms have been developed for treating PSF[175]. In a feasibility study, 12 patients who were on average16 months post-stroke attended six one-hour treatment sessions of cognitive behavioural therapy, each separated by a two-week interval, plus a follow-up booster session[214]. The aim was to break the vicious cycle that perpetuates fatigue by challenging the cognitive presentation of fatigue and encouraging increased daily activities[214]. The intervention was acceptable to the majority of participants and feasible to conduct in the local health service[214]. Improvements were noted in fatigue severity, self-reported general recovery,

memory, thinking, emotion, mobility and social activity at the 3-month follow-up assessment[214]. Importantly, statistical power was limited and the study lacked a control group. Another small-scale study randomized 15 people, 1.5-3 years post-stroke to either cognitive behavioural therapy (CBT) or usual care rehabilitation group[216]. In the CBT group only, therapeutic gains in fatigue, sleep quality, and depression were seen at post-intervention and maintained at the 4-month follow-up, and insomnia attenuated over time[216].

In animal models of focal ischemia, exercise reduces cerebral infarct volume and improves neurobehavioral scores which might promote brain recovery and improve fatigue[65]. Exercise training has been shown to moderate fatigue in chronic conditions other than stroke (e.g. cancer[108,] and multiple sclerosis,[246,247]), possibly through anti-inflammatory mechanisms. [110] However, surprisingly little is known about the effect of exercise specifically on PSF. An RCT involving 83 people who had PSF and were 3-4 years post-stroke compared cognitive and graded activity training (COGRAT) to cognitive training (CO) alone[215]. The cognitive therapy consisted of CBT and teaching pacing and relaxation compensatory strategies and the graded activity training consisted of strength training, treadmill walking, flexibility exercises and physical fitness homework of walking at home starting with 20 minutes twice week[215]. The findings that the COGRAT group showed clinically relevant improvement in fatigue at the 6 month follow up (χ^2= 9.63, p=0.002) provided support for the benefits of general exercise. [215].

Despite lack of evidence to support exercise and physical activity to reduce PSF during stroke rehabilitation, compelling arguments exist to support exercise as a strategy for

PSF management. First, exercise can play a role in reversing physical deconditioning and sedentary behavior that may be contributing to PSF. Second, exercise reduces systemic markers of inflammation (e.g., pro-inflammatory cytokines)[248,249], thus conferring a preventive or remedial effect on inflammatory processes postulated to underlie some presentations of PSF. The 2016 American Heart Association/American Stroke Association Guidelines for Adult Stroke Rehabilitation and Recovery recommend aerobic exercise as a way to reduce PSF[250]. At the same time, however, Sterr and Furlan cautioned against applying the "the more the better" ideology with people experiencing PSF[170]. Rather, they advised that the individual patient's fatigue threshold be considered when establishing the dose of exercise (i.e., duration and intensity) to avoid triggering either exercise-induced fatigue (an objective decline in motor performance) or perceived fatigue (a subjective sense of exhaustion)[170].

8. CONCLUSIONS

Research is limited on every aspect of PSF addressed in this review - an unexpected finding given that people post-stroke and health professionals ranked management and prevention of PSF in the top 10 research priorities for life after stroke[251]. Several mechanisms have been postulated to explain PSF but further study is needed to identify which actually precipitate this burdensome clinical condition. Positive associations between PSF and psychological factors (depression and anxiety) and physical factors (physical inactivity, pain, sleep disturbances) have been documented but causality has not been established. Finally, lack of definitive research has impeded development of effective pharmacological and non-pharmacological interventions to tackle this common, yet elusive sequela of stroke.

REFERENCES

1 Kharb, A., Saini, V., Jain, Y. & Dhiman, S. A review of gait cycle and its parameters. *IJCEM International Journal of Computational Engineering & Management* **13**, 78-83 (2011).

2 Walter Johnson , O. O., Mayowa Owolabi , Sonal Sachdev. *Stroke: a global response is needed*, <http://www.who.int/bulletin/volumes/94/9/16-181636.pdf> (2016).

3 Warlow, C., Sudlow, C., Dennis, M., Wardlaw, J. & Sandercock, P. Stroke. *Lancet* **362**, 1211-1224, doi:10.1016/S0140-6736(03)14544-8 (2003).

4 Oh, D. Community ambulation: clinical criteria for therapists' reasoning and decision-making in stroke rehabilitation. *Int J Phys Med Rehabil* **1**, 2 (2013).

5 Eng, J. J. & Tang, P.-F. Gait training strategies to optimize walking ability in people with stroke: a synthesis of the evidence. *Expert review of neurotherapeutics* **7**, 1417-1436 (2007).

6 Elsworth, C. *et al.* A study of perceived facilitators to physical activity in neurological conditions. *International Journal of Therapy and Rehabilitation* **16**, 17-24 (2009).

7 Tudor-Locke, C. & Bassett, D. How many steps are enough? Pedometer-determined physical activity indices. *Sports Med* **34**, 1-8 (2004).

8 Roos, M. A., Rudolph, K. S. & Reisman, D. S. The structure of walking activity in people after stroke compared with older adults without disability: a cross-sectional study. *Physical therapy* **92**, 1141-1147 (2012).

9 Kunkel, D., Fitton, C., Burnett, M. & Ashburn, A. Physical inactivity post-stroke: a 3-year longitudinal study. *Disability and rehabilitation* **37**, 304-310 (2015).

10 Balasubramanian, C. K., Clark, D. J. & Fox, E. J. Walking adaptability after a stroke and its assessment in clinical settings. *Stroke research and treatment* **2014** (2014).

11 Gillen, G. *Stroke rehabilitation: a function-based approach*. (Elsevier Health Sciences, 2015).

12 Shumway-Cook, A. & Woollacott, M. H. *Motor control: translating research into clinical practice*. (Lippincott Williams & Wilkins, 2007).

13 Lord, S. E. & Rochester, L. Measurement of community ambulation after stroke: current status and future developments. *Stroke* **36**, 1457-1461 (2005).

14 Fulk, G. D., Reynolds, C., Mondal, S. & Deutsch, J. E. Predicting home and community walking activity in people with stroke. *Archives of physical medicine and rehabilitation* **91**, 1582-1586 (2010).

15 Mudge, S. & Stott, N. S. Timed walking tests correlate with daily step activity in persons with stroke. *Archives of physical medicine and rehabilitation* **90**, 296-301 (2009).

16 Zalewski, K. R. & Dvorak, L. Barriers to physical activity between adults with stroke and their care partners. *Topics in Stroke Rehabilitation* **18**, 666-675 (2011).

17 Watanabe, M. *et al.* The relationship between bilateral knee muscle strength and gait performance after stroke: the predictive value for gait performance. *Journal of physical therapy science* **27**, 3227-3232 (2015).
18 Hsu, A.-L., Tang, P.-F. & Jan, M.-H. Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke1. *Archives of physical medicine and rehabilitation* **84**, 1185-1193 (2003).
19 Barbeau, H. Locomotor training in neurorehabilitation: emerging rehabilitation concepts. *Neurorehabilitation and Neural Repair* **17**, 3-11 (2003).
20 Alzahrani, M. A., Dean, C. M., Ada, L., Dorsch, S. & Canning, C. G. Mood and balance are associated with free-living physical activity of people after stroke residing in the community. *Stroke research and treatment* **2012** (2012).
21 Chemerinski, E., Robinson, R. G. & Kosier, J. T. Improved recovery in activities of daily living associated with remission of poststroke depression. *Stroke* **32**, 113-117 (2001).
22 Patten, S. B., Williams, J. V., Lavorato, D. H. & Eliasziw, M. A longitudinal community study of major depression and physical activity. *General hospital psychiatry* **31**, 571-575 (2009).
23 Michael, K. M., Allen, J. K. & Macko, R. F. Fatigue after stroke: relationship to mobility, fitness, ambulatory activity, social support, and falls efficacy. *Rehabil Nurs* **31**, 210-217 (2006).
24 Garber, C. E. & Friedman, J. H. Effects of fatigue on physical activity and function in patients with Parkinson's disease. *Neurology* **60**, 1119-1124 (2003).
25 Feigin, V. L. *et al.* Update on the Global Burden of Ischemic and Hemorrhagic Stroke in 1990-2013: The GBD 2013 Study. *Neuroepidemiology* **45**, 161-176, doi:10.1159/000441085 (2015).
26 Meschia, J. F. & Brott, T. Ischaemic stroke. *Eur J Neurol* **25**, 35-40, doi:10.1111/ene.13409 (2018).
27 Haast, R. A., Gustafson, D. R. & Kiliaan, A. J. Sex differences in stroke. *J Cereb Blood Flow Metab* **32**, 2100-2107, doi:10.1038/jcbfm.2012.141 (2012).
28 Appelros, P., Stegmayr, B. & Terent, A. Sex differences in stroke epidemiology: a systematic review. *Stroke* **40**, 1082-1090, doi:10.1161/STROKEAHA.108.540781 (2009).
29 Smajlovic, D. Strokes in young adults: epidemiology and prevention. *Vasc Health Risk Manag* **11**, 157-164, doi:10.2147/VHRM.S53203 (2015).
30 Katsnelson, M. J., Della-Morte, D. & Rundek, T. Stroke in young. *Periodicum biologorum* **114**, 347-353 (2012).
31 Lozano, R. *et al.* Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet* **380**, 2095-2128 (2012).
32 Deresse, B. & Shaweno, D. Epidemiology and in-hospital outcome of stroke in South Ethiopia. *J Neurol Sci* **355**, 138-142, doi:10.1016/j.jns.2015.06.001 (2015).
33 Mukherjee, D. & Patil, C. G. Epidemiology and the global burden of stroke. *World Neurosurg* **76**, S85-90, doi:10.1016/j.wneu.2011.07.023 (2011).

34 Mittmann, N. *et al.* Impact of disability status on ischemic stroke costs in Canada in the first year. *Can J Neurol Sci* **39**, 793-800 (2012).
35 Miller, E. L. *et al.* Comprehensive overview of nursing and interdisciplinary rehabilitation care of the stroke patient: a scientific statement from the American Heart Association. *Stroke* **41**, 2402-2448, doi:10.1161/STR.0b013e3181e7512b (2010).
36 Tennant, A., Geddes, J. M., Fear, J., Hillman, M. & Chamberlain, M. A. Outcome following stroke. *Disabil Rehabil* **19**, 278-284 (1997).
37 Sinanović, O., Mrkonjić, Z., Zukić, S., Vidović, M. & Imamović, K. Post-stroke language disorders. *Acta Clin Croat* **50**, 79-94 (2011).
38 Tipping, B. Issues in the long-term management of stroke: main article. *CME: Your SA Journal of CPD* **26**, 70-74 (2008).
39 Cawood, J., Visagie, S. & Mji, G. Impact of post-stroke impairments on activities and participation as experienced by stroke survivors in a Western Cape setting. *South African Journal of Occupational Therapy* **46**, 10-15 (2016).
40 Maleka, M., Stewart, A. & Hale, L. The experience of living with stroke in low urban and rural socioeconomic areas of South Africa. *South African Journal of Physiotherapy* **68**, 25-29 (2012).
41 Rhoda, A. Limitations in activity and participation experienced by stroke patients: A qualitative inquiry. *South African Journal of Physiotherapy* **68**, 20-24 (2012).
42 Mudzi, W., Stewart, A. & Musenge, E. Community participation of patients 12 months post-stroke in Johannesburg, South Africa. *African journal of primary health care & family medicine* **5** (2013).
43 Viscogliosi, C. *et al.* Differences in participation according to specific cognitive deficits following a stroke. *Applied Neuropsychology* **18**, 117-126 (2011).
44 Spitzer, J., Tse, T., Baum, C. M. & Carey, L. M. Mild impairment of cognition impacts on activity participation after stroke in a community-dwelling Australian cohort. *OTJR: occupation, participation and health* **31**, S8-S15 (2011).
45 Beaudoin, A. J. *et al.* Visuoperceptual deficits and participation in older adults after stroke. *Australian occupational therapy journal* **60**, 260-266 (2013).
46 Duncan, P. W. *et al.* Management of adult stroke rehabilitation care: a clinical practice guideline. *stroke* **36**, e100-e143 (2005).
47 Hendricks, H. T., Van Limbeek, J., Geurts, A. C. & Zwarts, M. J. Motor recovery after stroke: a systematic review of the literature. *Archives of physical medicine and rehabilitation* **83**, 1629-1637 (2002).
48 Li, S., Francisco, G. E. & Zhou, P. Post-stroke hemiplegic gait: new perspective and insights. *Frontiers in physiology* **9**, 1021 (2018).
49 Middleton, A., Fulk, G. D., Beets, M. W., Herter, T. M. & Fritz, S. L. Self-selected walking speed is predictive of daily ambulatory activity in older adults. *Journal of aging and physical activity* **24**, 214-222 (2016).
50 Alzahrani, M. A., Dean, C. M. & Ada, L. Ability to negotiate stairs predicts free-living physical activity in community-dwelling people with stroke: an observational study. *Australian Journal of Physiotherapy* **55**, 277-281 (2009).

51 Nichols, D. S. Balance retraining after stroke using force platform biofeedback. *Physical therapy* **77**, 553-558 (1997).
52 van Meulen, F. B. *et al.* Analysis of balance during functional walking in stroke survivors. *PloS one* **11**, e0166789 (2016).
53 Mudge, S. & Stott, N. S. Test—retest reliability of the StepWatch Activity Monitor outputs in individuals with chronic stroke. *Clinical Rehabilitation* **22**, 871-877 (2008).
54 Michael, K. M., Allen, J. K. & Macko, R. F. Reduced ambulatory activity after stroke: the role of balance, gait, and cardiovascular fitness. *Archives of physical medicine and rehabilitation* **86**, 1552-1556 (2005).
55 Yang, D. J. *et al.* The correlation between muscle activity of the quadriceps and balance and gait in stroke patients. *Journal of physical therapy science* **28**, 2289-2292 (2016).
56 Hyun, C. W. *et al.* Hemiparetic knee extensor strength and balance function are predictors of ambulatory function in subacute stroke patients. *Annals of rehabilitation medicine* **39**, 577-585 (2015).
57 Patterson, S. L. *et al.* Determinants of walking function after stroke: differences by deficit severity. *Archives of physical medicine and rehabilitation* **88**, 115-119 (2007).
58 Pradon, D., Roche, N., Enette, L. & Zory, R. Relationship between lower limb muscle strength and 6-minute walk test performance in stroke patients. *Journal of Rehabilitation Medicine* **45**, 105-108 (2013).
59 Staub, F. & Bogousslavsky, J. Fatigue after stroke: a major but neglected issue. *Cerebrovascular Diseases* **12**, 75-81 (2001).
60 Billinger, S. A. *et al.* 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, doi:10.1161/STR.0000000000000022 (2014).
61 Krupp, L. B., LaRocca, N. G., Muir-Nash, J. & Steinberg, A. D. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of neurology* **46**, 1121-1123 (1989).
62 Michael, K. M., Allen, J. K. & Macko, R. F. Fatigue after stroke: relationship to mobility, fitness, ambulatory activity, social support, and falls efficacy. *Rehabilitation Nursing* **31**, 210-217 (2006).
63 Robinson, C. A., Shumway-Cook, A., Ciol, M. A. & Kartin, D. Participation in community walking following stroke: subjective versus objective measures and the impact of personal factors. *Physical therapy* **91**, 1865-1876 (2011).
64 Bijleveld-Uitman, M., van de Port, I. & Kwakkel, G. Is gait speed or walking distance a better predictor for community walking after stroke? *Journal of rehabilitation medicine* **45**, 535-540 (2013).
65 Duncan, F. *et al.* Exploratory longitudinal cohort study of associations of fatigue after stroke. *Stroke* **46**, 1052-1058, doi:10.1161/STROKEAHA.114.008079 (2015).

66 Michael, K. & Macko, R. F. Ambulatory activity intensity profiles, fitness, and fatigue in chronic stroke. *Top Stroke Rehabil* **14**, 5-12, doi:10.1310/tsr1402-5 (2007).
67 Diagnostic, D. (American Psychiatric Publishing, 2013).
68 Gbiri, C. A., Akinpelu, A. O. & Odole, A. C. Prevalence, pattern and impact of depression on quality of life of stroke survivors. *International Journal of Psychiatry in Clinical Practice* **14**, 198-203 (2010).
69 Goodwin, R. D. & Devanand, D. P. Stroke, depression, and functional health outcomes among adults in the community. *Journal of geriatric psychiatry and neurology* **21**, 41-46 (2008).
70 Feibel, J. H. & Springer, C. J. Depression and failure to resume social activities after stroke. *Archives of physical medicine and rehabilitation* **63**, 276-277 (1982).
71 Baert, I., Feys, H., Daly, D., Troosters, T. & Vanlandewijck, Y. Are patients 1 year post-stroke active enough to improve their physical health? *Disability and rehabilitation* **34**, 574-580 (2012).
72 Bassett, D. R., Toth, L. P., LaMunion, S. R. & Crouter, S. E. Step counting: a review of measurement considerations and health-related applications. *Sports Medicine* **47**, 1303-1315 (2017).
73 Klassen, T. D. *et al.* "Stepping Up" activity poststroke: ankle-positioned accelerometer can accurately record steps during slow walking. *Physical therapy* **96**, 355-360 (2016).
74 Gronley, J. K. & Mulroy, S. J. Classification of walking handicap in the stroke population. *Stroke* (1995).
75 Giggins, O. M., Clay, I. & Walsh, L. Physical activity monitoring in patients with neurological disorders: a review of novel body-worn devices. *Digital Biomarkers* **1**, 14-42 (2017).
76 Chen, M.-D., Kuo, C.-C., Pellegrini, C. A. & Hsu, M.-J. Accuracy of Wristband Activity Monitors during Ambulation and Activities. *Medicine and science in sports and exercise* **48**, 1942-1949 (2016).
77 Crouter, S. E., Schneider, P. L. & Bassett, J. D. Spring-levered versus piezo-electric pedometer accuracy in overweight and obese adults. *Medicine and science in sports and exercise* **37**, 1673-1679 (2005).
78 Grant, P. M., Dall, P. M., Mitchell, S. L. & Granat, M. H. Activity-monitor accuracy in measuring step number and cadence in community-dwelling older adults. *Journal of aging and physical activity* **16**, 201-214 (2008).
79 Foster, R. C. *et al.* Precision and accuracy of an ankle-worn accelerometer-based pedometer in step counting and energy expenditure. *Preventive medicine* **41**, 778-783 (2005).
80 Mudge, S., Stott, N. S. & Walt, S. E. Criterion validity of the StepWatch Activity Monitor as a measure of walking activity in patients after stroke. *Archives of physical medicine and rehabilitation* **88**, 1710-1715 (2007).
81 Hickey, A., John, D., Sasaki, J. E., Mavilia, M. & Freedson, P. Validity of activity monitor step detection is related to movement patterns. *Journal of Physical Activity and Health* **13**, 145-153 (2016).

82 Karabulut, M., Crouter, S. E. & Bassett, D. R. Comparison of two waist-mounted and two ankle-mounted electronic pedometers. *European journal of applied physiology* **95**, 335-343 (2005).
83 Zhu, S. & Huang, S. S. (Google Patents, 2015).
84 Blum, L. & Korner-Bitensky, N. Usefulness of the Berg Balance Scale in stroke rehabilitation: a systematic review. *Physical therapy* **88**, 559-566 (2008).
85 Berg, K., Wood-Dauphinee, S. & Williams, J. The Balance Scale: reliability assessment with elderly residents and patients with an acute stroke. *Scandinavian journal of rehabilitation medicine* **27**, 27-36 (1995).
86 Flansbjer, U.-B., Blom, J. & Brogårdh, C. The reproducibility of Berg Balance Scale and the Single-leg Stance in chronic stroke and the relationship between the two tests. *PM&R* **4**, 165-170 (2012).
87 Mao, H.-F., Hsueh, I.-P., Tang, P.-F., Sheu, C.-F. & Hsieh, C.-L. Analysis and comparison of the psychometric properties of three balance measures for stroke patients. *Stroke* **33**, 1022-1027 (2002).
88 Tyson, S. & Connell, L. How to measure balance in clinical practice. A systematic review of the psychometrics and clinical utility of measures of balance activity for neurological conditions. *Clinical rehabilitation* **23**, 824-840 (2009).
89 Butland, R., Pang, J., Gross, E., Woodcock, A. & Geddes, D. Two-, six-, and 12-minute walking tests in respiratory disease. *British medical journal (Clinical research ed.)* **284**, 1607 (1982).
90 McGavin, C., Gupta, S. & McHardy, G. Twelve-minute walking test for assessing disability in chronic bronchitis. *Br Med J* **1**, 822-823 (1976).
91 Laboratories, A. C. o. P. S. f. C. P. F. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* **166**, 111-117 (2002).
92 Kubo, H. *et al.* Safety and Feasibility of the 6-Minute Walk Test in Patients with Acute Stroke. *Journal of Stroke and Cerebrovascular Diseases* **27**, 1632-1638 (2018).
93 Eng, J. J., Dawson, A. S. & Chu, K. S. Submaximal exercise in persons with stroke: test-retest reliability and concurrent validity with maximal oxygen consumption. *Archives of physical medicine and rehabilitation* **85**, 113-118 (2004).
94 Dunn, A. *et al.* Protocol variations and six-minute walk test performance in stroke survivors: a systematic review with meta-analysis. *Stroke research and treatment* **2015** (2015).
95 Ng, S. S. *et al.* Walkway length, but not turning direction, determines the six-minute walk test distance in individuals with stroke. *Archives of physical medicine and rehabilitation* **92**, 806-811 (2011).
96 Tyson, S. & Connell, L. The psychometric properties and clinical utility of measures of walking and mobility in neurological conditions: a systematic review. *Clinical rehabilitation* **23**, 1018-1033 (2009).
97 Flansbjer, U.-B., Holmbäck, A. M., Downham, D., Patten, C. & Lexell, J. Reliability of gait performance tests in men and women with hemiparesis after stroke. *Journal of rehabilitation medicine* **37**, 75-82 (2005).

98 Collen, F. M., Wade, D. T. & Bradshaw, C. M. Mobility after stroke: reliability of measures of impairment and disability. *International disability studies* **12**, 6-9 (1990).
99 Daniel, C. R. & Battistella, L. R. Using the six minute walk test to evaluate walking capacity in patients with stroke. *Acta Fisiátrica* **21**, 195-200 (2016).
100 Dalgas, U., Severinsen, K. & Overgaard, K. Relations between 6 minute walking distance and 10 meter walking speed in patients with multiple sclerosis and stroke. *Archives of physical medicine and rehabilitation* **93**, 1167-1172 (2012).
101 Teasell, R. EBRSR: Evidence-Based Review of Stroke Rehabilitation. 2011. *URL: http://www. ebrsr. com/[accessed 2011-11-07][WebCite Cache]* (2011).
102 Kang, H.-J. *et al.* Comparative validity of depression assessment scales for screening poststroke depression. *Journal of affective disorders* **147**, 186-191 (2013).
103 Smarr, K. L. & Keefer, A. L. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). *Arthritis care & research* **63**, S454-S466 (2011).
104 Aben, I., Verhey, F., Lousberg, R., Lodder, J. & Honig, A. Validity of the beck depression inventory, hospital anxiety and depression scale, SCL-90, and hamilton depression rating scale as screening instruments for depression in stroke patients. *Psychosomatics* **43**, 386-393 (2002).
105 Williams, L. S. *et al.* Performance of the PHQ-9 as a screening tool for depression after stroke. *stroke* **36**, 635-638 (2005).
106 Leeds, L., Meara, R. & Hobson, J. The utility of the Stroke Aphasia Depression Questionnaire (SADQ) in a stroke rehabilitation unit. *Clinical rehabilitation* **18**, 228-231 (2004).
107 Mead, G. *et al.* Evaluation of fatigue scales in stroke patients. *Stroke* **38**, 2090-2095 (2007).
108 Hinkle, J. L. *et al.* Poststroke fatigue: emerging evidence and approaches to management: a scientific statement for healthcare professionals from the American Heart Association. *Stroke*, STR. 0000000000000132 (2017).
109 Zedlitz, A., Van, M. M., Van, E. M., Geurts, A. & Fasotti, L. Psychometric properties of FSS and CIS-20r for measuring post-stroke fatigue. *International Journal of Psychology* **2**, 27 (2016).
110 Cumming, T. B. & Mead, G. Classifying post-stroke fatigue: Optimal cut-off on the Fatigue Assessment Scale. *Journal of psychosomatic research* **103**, 147-149 (2017).
111 Shahid, A., Wilkinson, K., Marcu, S. & Shapiro, C. M. in *STOP, THAT and One Hundred Other Sleep Scales* (eds Azmeh Shahid, Kate Wilkinson, Shai Marcu, & Colin M. Shapiro) 163-165 (Springer New York, 2012).
112 Brråndal, A., Eriksson, M., Wester, P. & Lundin-Olsson, L. Reliability and validity of the Swedish Fatigue Assessment Scale when self-administrered by persons with mild to moderate stroke. *Topics in stroke rehabilitation* **23**, 90-97 (2016).

113 Fink, A. M. *et al.* Psychometric properties of three instruments to measure fatigue with myocardial infarction. *Western journal of nursing research* **32**, 967-983 (2010).
114 Fisk, J. D. *et al.* Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. *Clinical Infectious Diseases* **18**, S79-S83 (1994).
115 Neuberger, G. B. Measures of fatigue: the fatigue questionnaire, fatigue severity scale, multidimensional assessment of fatigue scale, and short form-36 vitality (energy/fatigue) subscale of the short form health survey. *Arthritis Care & Research: Official Journal of the American College of Rheumatology* **49**, S175-S183 (2003).
116 Nadarajah, M., Mazlan, M., Abdul-Latif, L. & Goh, H.-T. Test-retest reliability, internal consistency and concurrent validity of Fatigue Severity Scale in measuring post-stroke fatigue. *European journal of physical and rehabilitation medicine* **53**, 703-709 (2017).
117 Howard, V. J. & McDonnell, M. N. Physical activity in primary stroke prevention: just do it! *Stroke* **46**, 1735-1739 (2015).
118 Durcan, S. An Investigation Of The Factors Associated With Community Ambulation In Chronic Stroke. (2014).
119 van de Port, I. G., Kwakkel, G. & Lindeman, E. Community ambulation in patients with chronic stroke: how is it related to gait speed? *Journal of Rehabilitation Medicine* **40**, 23-27 (2008).
120 Field, A. *Discovering statistics using SPSS*. (Sage publications, 2009).
121 Gouelle, A. Use of functional ambulation performance score as measurement of gait ability. *Journal of Rehabilitation Research & Development* **51**, 665 (2014).
122 Bohannon, R. W., Andrews, A. W. & Thomas, M. W. Walking speed: reference values and correlates for older adults. *Journal of Orthopaedic & Sports Physical Therapy* **24**, 86-90 (1996).
123 Wiles, C. & Karni, Y. The measurement of muscle strength in patients with peripheral neuromuscular disorders. *Journal of Neurology, Neurosurgery & Psychiatry* **46**, 1006-1013 (1983).
124 Domholdt, E. Physical therapy research. *Principles and applications* (1993).
125 Field, A. *Discovering statistics using IBM SPSS statistics*. (sage, 2013).
126 Tudor-Locke, C. E. & Myers, A. M. Methodological considerations for researchers and practitioners using pedometers to measure physical (ambulatory) activity. *Research quarterly for exercise and sport* **72**, 1-12 (2001).
127 Iwane, M. *et al.* Walking 10, 000 steps/day or more reduces blood pressure and sympathetic nerve activity in mild essential hypertension. *Hypertension Research* **23**, 573-580 (2000).
128 English, C., Manns, P. J., Tucak, C. & Bernhardt, J. Physical activity and sedentary behaviors in people with stroke living in the community: a systematic review. *Physical therapy* **94**, 185-196 (2014).
129 Mudge, S., Barber, P. A. & Stott, N. S. Circuit-based rehabilitation improves gait endurance but not usual walking activity in chronic stroke: a randomized

controlled trial. *Archives of physical medicine and rehabilitation* **90**, 1989-1996 (2009).

130 Fini, N. A., Holland, A. E., Keating, J., Simek, J. & Bernhardt, J. How physically active are people following stroke? Systematic review and quantitative synthesis. *Physical therapy* **97**, 707-717 (2017).

131 Tudor-Locke, C. *et al.* How fast is fast enough? Walking cadence (steps/min) as a practical estimate of intensity in adults: a narrative review. *Br J Sports Med* **52**, 776-788 (2018).

132 Members, W. g. *et al.* Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* **119**, 480-486 (2009).

133 Bowden, M. G., Balasubramanian, C. K., Behrman, A. L. & Kautz, S. A. Validation of a speed-based classification system using quantitative measures of walking performance poststroke. *Neurorehabilitation and neural repair* **22**, 672-675 (2008).

134 Berg, K. O., Wood-Dauphinee, S. L., Williams, J. I. & Maki, B. Measuring balance in the elderly: validation of an instrument. *Canadian journal of public health= Revue canadienne de sante publique* **83**, S7-11 (1992).

135 Kwong, P., Ng, S., Chung, R. & Ng, G. A structural equation model of the relationship between muscle strength, balance performance, walking endurance and community integration in stroke survivors. *PloS one* **12**, e0185807 (2017).

136 Hessam, M. *et al.* Relationship between functional balance and walking ability in individuals with chronic stroke. *Journal of physical therapy science* **30**, 993-996 (2018).

137 Cole, S. R. *et al.* Illustrating bias due to conditioning on a collider. *International journal of epidemiology* **39**, 417-420 (2009).

138 Gerrits, K. H. *et al.* Isometric muscle function of knee extensors and the relation with functional performance in patients with stroke. *Archives of physical medicine and rehabilitation* **90**, 480-487 (2009).

139 Kobayashi, T., Leung, A. K. & Hutchins, S. W. Correlations between knee extensor strength measured by a hand-held dynamometer and functional performance in patients with chronic stroke. *Isokinetics and exercise science* **19**, 33-37 (2011).

140 Ivey, F. M. *et al.* Strength training for skeletal muscle endurance after stroke. *Journal of Stroke and Cerebrovascular Diseases* **26**, 787-794 (2017).

141 Robertson, R., Robertson, A., Jepson, R. & Maxwell, M. Walking for depression or depressive symptoms: a systematic review and meta-analysis. *Mental health and physical activity* **5**, 66-75 (2012).

142 Danks, K. A., Pohlig, R. T., Roos, M., Wright, T. R. & Reisman, D. S. The relationship between walking capacity, biopsychosocial factors, self-efficacy and walking activity in individuals post stroke. *Journal of neurologic physical therapy: JNPT* **40**, 232 (2016).

143 Tseng, B. Y., Billinger, S. A., Gajewski, B. J. & Kluding, P. M. Exertion fatigue and chronic fatigue are two distinct constructs in people post-stroke. *Stroke* **41**, 2908-2912, doi:10.1161/STROKEAHA.110.596064 (2010).
144 Johansson, B. & Ronnback, L. Mental fatigue and cognitive impairment after an almost neurological recovered stroke. *ISRN Psychiatry* **2012**, 686425, doi:10.5402/2012/686425 (2012).
145 Staub, F. & Bogousslavsky, J. Fatigue after stroke: a major but neglected issue. *Cerebrovasc Dis* **12**, 75-81, doi:10.1159/000047685 (2001).
146 Balasooriya-Smeekens, C., Bateman, A., Mant, J. & De Simoni, A. Barriers and facilitators to staying in work after stroke: insight from an online forum. *BMJ Open* **6**, e009974, doi:10.1136/bmjopen-2015-009974 (2016).
147 Palstam, A., Törnbom, M. & Sunnerhagen, K. S. Experiences of returning to work and maintaining work 7 to 8 years after a stroke: a qualitative interview study in Sweden. *BMJ open* **8**, e021182 (2018).
148 Wondergem, R. *et al.* The Course of Activities in Daily Living: Who Is at Risk for Decline after First Ever Stroke? *Cerebrovasc Dis* **43**, 1-8, doi:10.1159/000451034 (2017).
149 Drummond, A. *et al.* The Nottingham Fatigue after Stroke (NotFAST) study: factors associated with severity of fatigue in stroke patients without depression. *Clin Rehabil* **31**, 1406-1415, doi:10.1177/0269215517695857 (2017).
150 Chen, Y. K. *et al.* Poststroke fatigue: risk factors and its effect on functional status and health-related quality of life. *Int J Stroke* **10**, 506-512, doi:10.1111/ijs.12409 (2015).
151 Elf, M., Eriksson, G., Johansson, S., von Koch, L. & Ytterberg, C. Self-Reported Fatigue and Associated Factors Six Years after Stroke. *PLoS One* **11**, e0161942, doi:10.1371/journal.pone.0161942 (2016).
152 Park, J. Y. *et al.* Functional outcome in poststroke patients with or without fatigue. *Am J Phys Med Rehabil* **88**, 554-558, doi:10.1097/PHM.0b013e3181a0dae0 (2009).
153 van de Port, I. G., Kwakkel, G., Schepers, V. P., Heinemans, C. T. & Lindeman, E. Is fatigue an independent factor associated with activities of daily living, instrumental activities of daily living and health-related quality of life in chronic stroke? *Cerebrovasc Dis* **23**, 40-45, doi:10.1159/000095757 (2007).
154 Badaru, U. M., Ogwumike, O. O., Adeniyi, A. F. & Olowe, O. O. Variation in Functional Independence among Stroke Survivors Having Fatigue and Depression. *Neurol Res Int* **2013**, 842980, doi:10.1155/2013/842980 (2013).
155 Donnellan, C. *et al.* Mapping patients' experiences after stroke onto a patient-focused intervention framework. *Disability and rehabilitation* **35**, 483-491 (2013).
156 Ezeugwu, V. E., Garga, N. & Manns, P. J. Reducing sedentary behaviour after stroke: perspectives of ambulatory individuals with stroke. *Disability and rehabilitation* **39**, 2551-2558 (2017).
157 Kautz, D. D. & Van Horn, E. R. Sex and Intimacy after Stroke. *Rehabil Nurs* **42**, 333-340, doi:10.1002/rnj.296 (2017).

158 Nilsson, M. I., Fugl-Meyer, K., von Koch, L. & Ytterberg, C. Experiences of Sexuality Six Years After Stroke: A Qualitative Study. *J Sex Med* **14**, 797-803, doi:10.1016/j.jsxm.2017.04.061 (2017).
159 Thompson, H. S. & Ryan, A. The impact of stroke consequences on spousal relationships from the perspective of the person with stroke. *J Clin Nurs* **18**, 1803-1811, doi:10.1111/j.1365-2702.2008.02694.x (2009).
160 Tang, W. K. *et al.* Is fatigue associated with short-term health-related quality of life in stroke? *Arch Phys Med Rehabil* **91**, 1511-1515, doi:10.1016/j.apmr.2010.06.026 (2010).
161 Naess, H., Waje-Andreassen, U., Thomassen, L., Nyland, H. & Myhr, K. M. Health-related quality of life among young adults with ischemic stroke on long-term follow-up. *Stroke* **37**, 1232-1236, doi:10.1161/01.STR.0000217652.42273.02 (2006).
162 Mead, G. E. *et al.* Fatigue after stroke: baseline predictors and influence on survival. Analysis of data from UK patients recruited in the International Stroke Trial. *PLoS One* **6**, e16988, doi:10.1371/journal.pone.0016988 (2011).
163 Goh, H.-T., Tan, M.-P., Mazlan, M., Abdul-Latif, L. & Subramaniam, P. Social Participation Determines Quality of Life Among Urban-Dwelling Older Adults With Stroke in a Developing Country. *Journal of geriatric physical therapy (2001)* (2018).
164 Glader, E. L., Stegmayr, B. & Asplund, K. Poststroke Fatigue: A 2-Year Follow-Up Study of Stroke Patients in Sweden. *Stroke* **33**, 1327-1333, doi:10.1161/01.str.0000014248.28711.d6 (2002).
165 White, J. H. *et al.* Exploring the experience of post-stroke fatigue in community dwelling stroke survivors: a prospective qualitative study. *Disabil Rehabil* **34**, 1376-1384, doi:10.3109/09638288.2011.645111 (2012).
166 Kirkevold, M., Christensen, D., Andersen, G., Johansen, S. P. & Harder, I. Fatigue after stroke: manifestations and strategies. *Disabil Rehabil* **34**, 665-670, doi:10.3109/09638288.2011.615373 (2012).
167 Clarke, D. J. *et al.* Why do stroke survivors not receive recommended amounts of active therapy? Findings from the ReAcT study, a mixed-methods case-study evaluation in eight stroke units. *Clinical rehabilitation* **32**, 1119-1132 (2018).
168 Yang, S.-Y. & Kong, K. H. Level and predictors of participation in patients with stroke undergoing inpatient rehabilitation. *Singapore Med J* **54**, 564-568 (2013).
169 Beaudry, L., Fortin, S. & Rochette, A. Adapted dance used in subacute rehabilitation post-stroke: impacts perceived by patients, relatives and rehabilitation therapists: Qualitative study. *Disability and rehabilitation*, 1-10 (2019).
170 Sterr, A. & Furlan, L. A case to be made: theoretical and empirical arguments for the need to consider fatigue in post-stroke motor rehabilitation. *Neural regeneration research* **10**, 1195 (2015).
171 van der Werf, S. P., van den Broek, H. L., Anten, H. W. & Bleijenberg, G. Experience of severe fatigue long after stroke and its relation to depressive

symptoms and disease characteristics. *Eur Neurol* **45**, 28-33, doi:10.1159/000052085 (2001).
172 Moran, G. M. *et al.* Fatigue, psychological and cognitive impairment following transient ischaemic attack and minor stroke: a systematic review. *Eur J Neurol* **21**, 1258-1267, doi:10.1111/ene.12469 (2014).
173 Egerton, T., Hokstad, A., Askim, T., Bernhardt, J. & Indredavik, B. Prevalence of fatigue in patients 3 months after stroke and association with early motor activity: a prospective study comparing stroke patients with a matched general population cohort. *BMC Neurol* **15**, 181, doi:10.1186/s12883-015-0438-6 (2015).
174 Lerdal, A. *et al.* Poststroke fatigue--a review. *J Pain Symptom Manage* **38**, 928-949, doi:10.1016/j.jpainsymman.2009.04.028 (2009).
175 Wu, S., Barugh, A., Macleod, M. & Mead, G. Psychological associations of poststroke fatigue: a systematic review and meta-analysis. *Stroke* **45**, 1778-1783, doi:10.1161/STROKEAHA.113.004584 (2014).
176 Baylor, C., Yorkston, K. M., Jensen, M. P., Truitt, A. R. & Molton, I. R. Scoping review of common secondary conditions after stroke and their associations with age and time post stroke. *Top Stroke Rehabil* **21**, 371-382, doi:10.1310/tsr2105-371 (2014).
177 Cumming, T. B., Packer, M., Kramer, S. F. & English, C. The prevalence of fatigue after stroke: A systematic review and meta-analysis. *Int J Stroke* **11**, 968-977, doi:10.1177/1747493016669861 (2016).
178 Snaphaan, L., van der Werf, S. & de Leeuw, F. E. Time course and risk factors of post-stroke fatigue: a prospective cohort study. *Eur J Neurol* **18**, 611-617, doi:10.1111/j.1468-1331.2010.03217.x (2011).
179 Ponchel, A., Bombois, S., Bordet, R. & Hénon, H. Factors Associated with Poststroke Fatigue: A Systematic Review. *Stroke Research and Treatment* **2015**, 1-11, doi:10.1155/2015/347920 (2015).
180 Choi-Kwon, S., Han, S. W., Kwon, S. U. & Kim, J. S. Poststroke fatigue: characteristics and related factors. *Cerebrovasc Dis* **19**, 84-90, doi:10.1159/000082784 (2005).
181 Duncan, F., Wu, S. & Mead, G. E. Frequency and natural history of fatigue after stroke: a systematic review of longitudinal studies. *J Psychosom Res* **73**, 18-27, doi:10.1016/j.jpsychores.2012.04.001 (2012).
182 Lerdal, A. *et al.* Physical impairment, depressive symptoms and pre-stroke fatigue are related to fatigue in the acute phase after stroke. *Disabil Rehabil* **33**, 334-342, doi:10.3109/09638288.2010.490867 (2011).
183 Whitehead, L. C., Unahi, K., Burrell, B. & Crowe, M. T. The experience of fatigue across long-term conditions: A qualitative meta-synthesis. *Journal of pain and symptom management* **52**, 131-143. e131 (2016).
184 Sisson, R. A. Life after a stroke: coping with change. *Rehabilitation Nursing* **23**, 198-203 (1998).
185 Schepers, V. P., Visser-Meily, A. M., Ketelaar, M. & Lindeman, E. Poststroke fatigue: course and its relation to personal and stroke-related factors. *Arch Phys Med Rehabil* **87**, 184-188, doi:10.1016/j.apmr.2005.10.005 (2006).

186 Skaner, Y., Nilsson, G. H., Sundquist, K., Hassler, E. & Krakau, I. Self-rated health, symptoms of depression and general symptoms at 3 and 12 months after a first-ever stroke: a municipality-based study in Sweden. *BMC Fam Pract* **8**, 61, doi:10.1186/1471-2296-8-61 (2007).
187 De Doncker, W., Dantzer, R., Ormstad, H. & Kuppuswamy, A. Mechanisms of poststroke fatigue. *J Neurol Neurosurg Psychiatry* **89**, 287-293, doi:10.1136/jnnp-2017-316007 (2018).
188 Kuppuswamy, A., Rothwell, J. & Ward, N. A model of poststroke fatigue based on sensorimotor deficits. *Curr Opin Neurol* **28**, 582-586, doi:10.1097/WCO.0000000000000260 (2015).
189 Ormstad, H. & Eilertsen, G. A biopsychosocial model of fatigue and depression following stroke. *Med Hypotheses* **85**, 835-841, doi:10.1016/j.mehy.2015.10.001 (2015).
190 Tang, W. K. *et al.* Acute basal ganglia infarcts in poststroke fatigue: an MRI study. *J Neurol* **257**, 178-182, doi:10.1007/s00415-009-5284-2 (2010).
191 Tang, W. K. *et al.* Poststroke fatigue is associated with caudate infarcts. *J Neurol Sci* **324**, 131-135, doi:10.1016/j.jns.2012.10.022 (2013).
192 Tang, W. K. *et al.* Cerebral microbleeds and fatigue in stroke. *Eur Neurol* **71**, 213-216, doi:10.1159/000354845 (2014).
193 Kutlubaev, M. A., Duncan, F. H. & Mead, G. E. Biological correlates of post-stroke fatigue: a systematic review. *Acta Neurol Scand* **125**, 219-227, doi:10.1111/j.1600-0404.2011.01618.x (2012).
194 Chaudhari A, B. P. Fatigue and basal ganglia. *Neurol Sci* **179**, S34-S42 (2000).
195 Barrington, J., Lemarchand, E. & Allan, S. M. A brain in flame; do inflammasomes and pyroptosis influence stroke pathology? *Brain Pathol* **27**, 205-212, doi:10.1111/bpa.12476 (2017).
196 Ormstad, H., Aass, H. C., Amthor, K. F., Lund-Sorensen, N. & Sandvik, L. Serum cytokine and glucose levels as predictors of poststroke fatigue in acute ischemic stroke patients. *J Neurol* **258**, 670-676, doi:10.1007/s00415-011-5962-8 (2011).
197 Ormstad, H., Verkerk, R., Aass, H. C., Amthor, K. F. & Sandvik, L. Inflammation-induced catabolism of tryptophan and tyrosine in acute ischemic stroke. *J Mol Neurosci* **51**, 893-902, doi:10.1007/s12031-013-0097-2 (2013).
198 Ormstad, H., Verkerk, R., Amthor, K. F. & Sandvik, L. Activation of the kynurenine pathway in the acute phase of stroke and its role in fatigue and depression following stroke. *J Mol Neurosci* **54**, 181-187, doi:10.1007/s12031-014-0272-0 (2014).
199 Monti, J. M. Serotonin control of sleep-wake behavior. *Sleep Med Rev* **15**, 269-281, doi:10.1016/j.smrv.2010.11.003 (2011).
200 Eilertsen, G., Ormstad, H. & Kirkevold, M. Experiences of poststroke fatigue: qualitative meta-synthesis. *J Adv Nurs* **69**, 514-525, doi:10.1111/jan.12002 (2013).
201 Kuppuswamy, A., Clark, E. V., Turner, I. F., Rothwell, J. C. & Ward, N. S. Post-stroke fatigue: a deficit in corticomotor excitability? *Brain* **138**, 136-148, doi:10.1093/brain/awu306 (2015).

202 Kuppuswamy, A., Clark, E. V., Sandhu, K. S., Rothwell, J. C. & Ward, N. S. Post-stroke fatigue: a problem of altered corticomotor control? *J Neurol Neurosurg Psychiatry* **86**, 902-904, doi:10.1136/jnnp-2015-310431 (2015).
203 Kuppuswamy, A., Clark, E., Rothwell, J. & Ward, N. S. Limb Heaviness: A Perceptual Phenomenon Associated With Poststroke Fatigue? *Neurorehabil Neural Repair* **30**, 360-362, doi:10.1177/1545968315597071 (2016).
204 Jönsson, A.-C., Lindgren, I., Norrving, B. & Lindgren, A. Weight loss after stroke: a population-based study from the Lund Stroke Register. *Stroke* **39**, 918-923 (2008).
205 Westergren, A. Nutrition and its relation to mealtime preparation, eating, fatigue and mood among stroke survivors after discharge from hospital - a pilot study. *Open Nurs J* **2**, 15-20, doi:10.2174/1874434600802010015 (2008).
206 MacKay-Lyons, M. J. & Makrides, L. Longitudinal changes in exercise capacity after stroke1. *Archives of physical medicine and rehabilitation* **85**, 1608-1612 (2004).
207 Thilarajah, S. *et al.* Factors Associated With Post-Stroke Physical Activity: A Systematic Review and Meta-Analysis. *Arch Phys Med Rehabil*, doi:10.1016/j.apmr.2017.09.117 (2017).
208 Douven, E. *et al.* Temporal Associations between Fatigue, Depression, and Apathy after Stroke: Results of the Cognition and Affect after Stroke, a Prospective Evaluation of Risks Study. *Cerebrovasc Dis* **44**, 330-337, doi:10.1159/000481577 (2017).
209 Galligan, N. G., Hevey, D., Coen, R. F. & Harbison, J. A. Clarifying the associations between anxiety, depression and fatigue following stroke. *J Health Psychol* **21**, 2863-2871, doi:10.1177/1359105315587140 (2016).
210 Pihlaja, R., Uimonen, J., Mustanoja, S., Tatlisumak, T. & Poutiainen, E. Post-stroke fatigue is associated with impaired processing speed and memory functions in first-ever stroke patients. *J Psychosom Res* **77**, 380-384, doi:10.1016/j.jpsychores.2014.08.011 (2014).
211 Naess, H., Lunde, L., Brogger, J. & Waje-Andreassen, U. Fatigue among stroke patients on long-term follow-up. The Bergen Stroke Study. *J Neurol Sci* **312**, 138-141, doi:10.1016/j.jns.2011.08.002 (2012).
212 Lau, C. G. *et al.* Neuroticism and Fatigue 3 Months After Ischemic Stroke: A Cross-Sectional Study. *Arch Phys Med Rehabil* **98**, 716-721, doi:10.1016/j.apmr.2016.08.480 (2017).
213 Tang, W. K., Lu, J. Y., Mok, V., Ungvari, G. S. & Wong, K. S. Is fatigue associated with suicidality in stroke? *Arch Phys Med Rehabil* **92**, 1336-1338, doi:10.1016/j.apmr.2011.02.018 (2011).
214 Wu, S. *et al.* Development of a psychological intervention for fatigue after stroke. *PLoS One* **12**, e0183286, doi:10.1371/journal.pone.0183286 (2017).
215 Zedlitz, A. M., Rietveld, T. C., Geurts, A. C. & Fasotti, L. Cognitive and graded activity training can alleviate persistent fatigue after stroke: a randomized, controlled trial. *Stroke* **43**, 1046-1051, doi:10.1161/STROKEAHA.111.632117 (2012).

216 Nguyen, S. *et al.* Cognitive behavioural therapy for post-stroke fatigue and sleep disturbance: a pilot randomised controlled trial with blind assessment. *Neuropsychol Rehabil*, 1-16, doi:10.1080/09602011.2017.1326945 (2017).
217 Lagogianni, C., Thomas, S. & Lincoln, N. Examining the relationship between fatigue and cognition after stroke: A systematic review. *Neuropsychol Rehabil* **28**, 57-116, doi:10.1080/09602011.2015.1127820 (2018).
218 van Eijsden, H. M., van de Port, I. G. L., Visser-Meily, J. M. A. & Kwakkel, G. Poststroke fatigue: who is at risk for an increase in fatigue? *Stroke research and treatment* **2012** (2012).
219 Winkens, I., Van Heugten, C. M., Fasotti, L., Duits, A. A. & Wade, D. T. Manifestations of mental slowness in the daily life of patients with stroke: a qualitative study. *Clinical rehabilitation* **20**, 827-834 (2006).
220 Radman, N. *et al.* Poststroke fatigue following minor infarcts: a prospective study. *Neurology* **79**, 1422-1427, doi:10.1212/WNL.0b013e31826d5f3a (2012).
221 Elgh, E. & Hu, X. Dynamic Trajectory of Long-term Cognitive Improvement up to Ten Years in Young Community-Dwelling Stroke Survivors: A Cohort Study. *Frontiers in Neurology* **10**, 97 (2019).
222 van Rijsbergen, M. W., Mark, R. E., Kop, W. J., de Kort, P. L. & Sitskoorn, M. M. Psychological factors and subjective cognitive complaints after stroke: Beyond depression and anxiety. *Neuropsychological rehabilitation*, 1-14 (2018).
223 Kutlubaev, M. A. *et al.* CT and Clinical Predictors of Fatigue at One Month after Stroke. *Cerebrovasc Dis Extra* **3**, 26-34, doi:10.1159/000347113 (2013).
224 Mahendran, N., Kuys, S. S. & Brauer, S. G. Which impairments, activity limitations and personal factors at hospital discharge predict walking activity across the first 6 months poststroke? *Disability and rehabilitation*, 1-7 (2018).
225 Miller, K. K. *et al.* Fatigue and pain: relationships with physical performance and patient beliefs after stroke. *Top Stroke Rehabil* **20**, 347-355, doi:10.1310/tsr2004-347 (2013).
226 Choi-Kwon, S. *et al.* Musculoskeletal and central pain at 1 year post-stroke: associated factors and impact on quality of life. *Acta Neurol Scand* **135**, 419-425, doi:10.1111/ane.12617 (2017).
227 Appelros, P. Prevalence and predictors of pain and fatigue after stroke: a population-based study. *Int J Rehabil Res* **29**, 329-333, doi:10.1097/MRR.0b013e328010c7b8 (2006).
228 Barbour, V. L. & Mead, G. E. Fatigue after Stroke: The Patient's Perspective. *Stroke Res Treat* **2012**, 863031, doi:10.1155/2012/863031 (2012).
229 Sandberg, O., Franklin, K. A., Bucht, G. & Gustafson, Y. Sleep apnea, delirium, depressed mood, cognition, and ADL ability after stroke. *J Am Geriatr Soc* **49**, 391-397 (2001).
230 Hermann, D. M. & Bassetti, C. L. Sleep-related breathing and sleep-wake disturbances in ischemic stroke. *Neurology* **73**, 1313-1322, doi:10.1212/WNL.0b013e3181bd137c (2009).
231 Mead, G., Bernhardt, J. & Kwakkel, G. Stroke: physical fitness, exercise, and fatigue. *Stroke research and treatment* **2012** (2012).

232 Flinn, N. A. & Stube, J. E. Post-stroke fatigue: qualitative study of three focus groups. *Occup Ther Int* **17**, 81-91, doi:10.1002/oti.286 (2010).
233 Poulsen, M. B., Damgaard, B., Zerahn, B., Overgaard, K. & Rasmussen, R. S. Modafinil May Alleviate Poststroke Fatigue: A Randomized, Placebo-Controlled, Double-Blinded Trial. *Stroke* **46**, 3470-3477, doi:10.1161/STROKEAHA.115.010860 (2015).
234 Wu, S. *et al.* Interventions for post-stroke fatigue. *Cochrane Database Syst Rev*, CD007030, doi:10.1002/14651858.CD007030.pub3 (2015).
235 Karaiskos, D., Tzavellas, E., Spengos, K., Vassilopoulou, S. & Paparrigopoulos, T. Duloxetine versus citalopram and sertraline in the treatment of poststroke depression, anxiety, and fatigue. *The Journal of neuropsychiatry and clinical neurosciences* **24**, 349-353 (2012).
236 Choi-Kwon, S., Choi, J., Kwon, S. U., Kang, D.-W. & Kim, J. S. Fluoxetine is not effective in the treatment of poststroke fatigue: a double-blind, placebo-controlled study. *Cerebrovascular Diseases* **23**, 103-108 (2007).
237 Brioschi, A. *et al.* Effect of modafinil on subjective fatigue in multiple sclerosis and stroke patients. *Eur Neurol* **62**, 243-249, doi:10.1159/000232927 (2009).
238 Liu, C. H. *et al.* Effects of the traditional Chinese herb Astragalus membranaceus in patients with poststroke fatigue: A double-blind, randomized, controlled preliminary study. *J Ethnopharmacol* **194**, 954-962, doi:10.1016/j.jep.2016.10.058 (2016).
239 Conroy, B. *et al.* An exploration of central nervous system medication use and outcomes in stroke rehabilitation. *Archives of physical medicine and rehabilitation* **86**, 73-81 (2005).
240 Goldstein, L. B. Potential effects of common drugs on stroke recovery. *Archives of Neurology* **55**, 454-456 (1998).
241 Wang, S.-S., Wang, J.-J., Wang, P.-X. & Chen, R. Determinants of fatigue after first-ever ischemic stroke during acute phase. *PloS one* **9**, e110037 (2014).
242 Naess, H., Lunde, L. & Brogger, J. The triad of pain, fatigue and depression in ischemic stroke patients: the Bergen Stroke Study. *Cerebrovascular Diseases* **33**, 461-465 (2012).
243 Harbison, J., Walsh, S. & Kenny, R. Hypertension and daytime hypotension found on ambulatory blood pressure is associated with fatigue following stroke and TIA. *QJM: An International Journal of Medicine* **102**, 109-115 (2008).
244 Eskes, G. A. *et al.* Canadian Stroke Best Practice Recommendations: Mood, Cognition and Fatigue Following Stroke practice guidelines, update 2015. *Int J Stroke* **10**, 1130-1140, doi:10.1111/ijs.12557 (2015).
245 Clarke, A., Barker-Collo, S. L. & Feigin, V. L. Poststroke fatigue: does group education make a difference? A randomized pilot trial. *Top Stroke Rehabil* **19**, 32-39, doi:10.1310/tsr1901-32 (2012).
246 Andreasen, A., Stenager, E. & Dalgas, U. The effect of exercise therapy on fatigue in multiple sclerosis. *Multiple Sclerosis Journal* **17**, 1041-1054 (2011).

247 Kessels, E., Husson, O. & Van der Feltz-Cornelis, C. M. The effect of exercise on cancer-related fatigue in cancer survivors: a systematic review and meta-analysis. *Neuropsychiatric disease and treatment* **14**, 479 (2018).
248 Lancaster, G. I. & Febbraio, M. A. The immunomodulating role of exercise in metabolic disease. *Trends in immunology* **35**, 262-269 (2014).
249 Nimmo, M., Leggate, M., Viana, J. & King, J. The effect of physical activity on mediators of inflammation. *Diabetes, Obesity and Metabolism* **15**, 51-60 (2013).
250 Winstein, C. J. *et al.* Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* **47**, e98-e169 (2016).
251 Pollock, A., St George, B., Fenton, M. & Firkins, L. Top 10 research priorities relating to life after stroke--consensus from stroke survivors, caregivers, and health professionals. *Int J Stroke* **9**, 313-320, doi:10.1111/j.1747-4949.2012.00942.x (2014).

Table 16: Summary of frequently used scales for assessment of PSF.

Scale	**Characteristics**	**Psychometric properties**
Fatigue Severity Scale (FSS)	•10-item instrument to self-rate fatigue in past week. [108 108 108 107 107 107 107 106 104 104 104 104] •7-point Likert scale ranging from 1(strongly disagree) to 7 (strongly agree). •Range of scores 0-63. •Well-accepted cut-off for classifying fatigue (≥4), facilitating prevalence comparisons across studies.	•Internal consistency: 0.88-0.95 •Intraclass correlation coefficient [R]: 0.76-0.80 •Limited face validity for PSF
Fatigue Impact Scale (FIS)	•40-item instrument to evaluate effect of fatigue on cognitive functioning, physical functioning and psychological functioning as perceived over past month. •5-point Likert scale ranging from 0 (no problem) to 4 (extreme problem) •Range of scores= 0-160, higher score indicating greater fatigue •21-item Modified Fatigue Impact Scale may be used if full Scale is too fatiguing[111111111110110110110109107107107107]	•Internal consistency: 0.93
Fatigue Assessment Scale (FAS)	•10 fatigue-related questions •5-point Likert scale from 1 (*never*) to 5 (*always*) •Range of scores = 10-50, higher score indicating greater fatigue •Cut-off of >24 proposed for classification of PSF	•Cronbach alpha: 0.58-0.62 •Construct validity: 0.71
Fatigue Subscale of the Profile of Mood States (POMS)	•7-item subscale of POMS to evaluate contribution of fatigue to changes in mood[113] • 5-point Likert scale ranging from 0(not at all) to 4(extremely)	•Cronbach's alpha: 0.88-0.89 •Construct validity: 0.75
Vitality Scale of SF-36	• Widely used to measure quality of life and physical and mental components of health •6-point Likert scale ranging from 1 (*all the time*) to 6 (*none of the time*) .	•Cronbach's alpha: 0.76-0.78 •Construct validity: 0.58

PubMed
(((((((("Fatigue"[Mesh: NoExp]) OR fatigue*[tiab])) OR lassitude[tiab]) OR tiredness[tiab]) OR ((weariness[tiab] OR weary[tiab] OR wearied[tiab]))) OR lethargy[tiab]))

AND

(((((acquired neurological patholog*[tiab]) OR (((((stroke[tiab] OR strokes[tiab] OR transient ischaemic attack* OR tia[tiab] OR tias[tiab] OR cva[tiab] OR cvas[tiab] OR cerebrovascular accident*[tiab] OR apoplex*[tiab] OR transient brainstem ischemia*[tiab] OR transient cerebral ischemia*[tiab] OR transient ischemic attack*[tiab] OR "Ischemic Attack, Transient"[Mesh] OR "Stroke"[Mesh] OR transient cerebral ischaemia*[tiab] OR transient brainstem ischaemia*[tiab] OR transient brain ischaemia*[tiab] OR transient brain ischemia*[tiab])))))))) OR brain vascular accident*[tiab])

Figure 1. Search strategy used in PubMed.

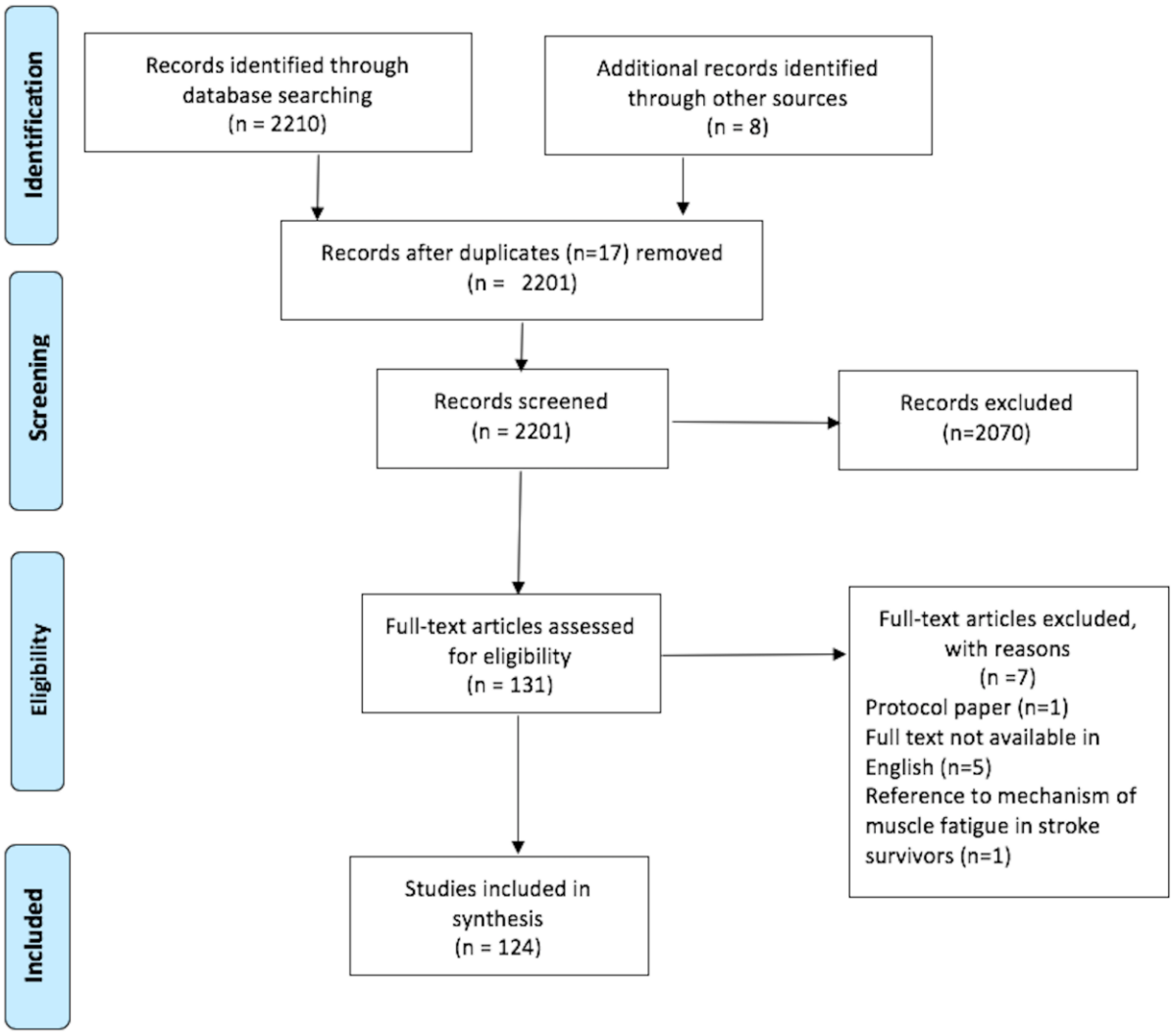


Figure 2. Flow chart for study selection.

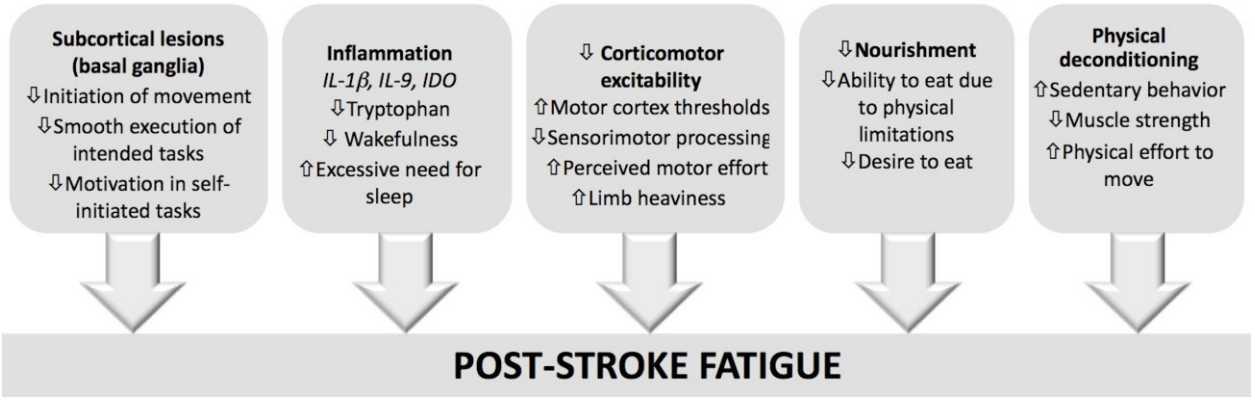


Figure 3. Potential mechanisms underlying post-stroke fatigue. IL-1□, interleukin-1 Beta; IL-9, interleukin-9; IDO, indoleamine-pyrrole 2,3-dioxygenase