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Physical activity intervention for chronic stroke rehabilitation in low-income settings

Effectiveness of mixed, community and collective physical activity intervention

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LIST OF ABBREVIATIONS

10Mwt	10-meter Walking Test
6MWT	6 Minute Walk Test
ACTIVLIM-Stroke	Activity limitation for stroke
ADL	Activities of daily living
AF	Arial fibrillation
AHA	American Heart Association
ANOVA	Analyses of Variance
ASA	American Stroke Association
BBS	Berg Balance Scale
BMI	Body Mass Index
CBCS	Circuit walking, balance, cycling and strength
CIs	Confidence Intervals
CBR	Community-Based rehabilitation
CIMT	Constraint-Induced Movement Therapy
CNE	Comité National d'Ethique
CNS	Central Nervous System
CSI-D	Cognitive Screening Instrument for Dementia
CT	Computed tomography
CVD	Cerebrovascular Disease
DALYs	Disability-adjusted life-years
DG	Delayed Group

EMS	Emergency Medical Services
ESO	European stroke Organisation
GBD	Global Burden of Stroke
GNI	Gross National Income
HADs	Hospital Anxiety and Depression Scale
HICs	High Income Countries
HIV	Human Immuno Deficiency virus
ICF	International Classification of Functioning, Disability, and Health
ICH	Intracerebral haemorrhage
IG	Immediate Group
IQR	Interquartile ranges
LMICs	Low-Income Countries
LT	Locomotor training
MCID	Minimal Clinically Important Difference
MDC	Minimal Detectable Change
MDs	Mean differences
MI	Myocardial infarction
MRI	Magnetic Resonance Imaging
MRS	Modified Rankin Scale
NCDs	Noncommunicable diseases
PM scale:	Participation Measurement scale
QoL	Quality of life
RCTs	Randomized Controlled Trials
SD	Standard deviation

SIAS	Stroke Impairments Assessment Set
SMDs	Standardized mean differences
SSA	Sub-Saharan Africa
TIA	Transient Ischemic Attack
TUG	Timed-Up and Go test
WHO	World Health Organization

Publications

➢ *Related to this thesis*

1. **Nindorera F**, Nduwimana I, Thonnard JL, Kossi O. Effectiveness of walking trainings on balance, motor functions, activity, participation and quality of life in people with chronic stroke: A systematic review with meta-analysis and meta-regression of recent randomized controlled trials. Disabil Rehabil. 2021:1-12. PMID: 33715555 DOI: 10.1080/09638288.2021.1894247

2. **Nindorera, F**., Nduwimana, I., Sinzakaraye, A., Bleyenheuft, Y., Thonnard, J. L., & Kossi, O. (2022). Relationships between walking speed, activities and participation in people with chronic stroke in Burundi. S Afr J Physiother, 78(1), 1800. https://doi.org/10.4102/sajp.v78i1.1800

3. **Nindorera, F**., Nduwimana, I., Sinzakaraye, A., Havyarimana, E., Bleyenheuft, Y., Thonnard, J. L., & Kossi, O. (2022). Effect of mixed and collective physical activity in chronic stroke rehabilitation: A randomized cross-over trial in low-income settings. Ann Phys Rehabil Med, 66(4), 101704. https://doi.org/10.1016/j.rehab.2022.101704

➢ *Other publications*

1. Nduwimana, I., **Nindorera, F**., Sinzakaraye, A., Bleyenheuft, Y., Thonnard, J. L., & Kossi, O. (2022). Biopsychosocial factors associated with chronic low back pain-related activity limitations in Burundi. S Afr J Physiother, 78(1), 1783. https://doi.org/10.4102/sajp.v78i1.1783

2. Nduwimana I, **Nindorera F**, Thonnard JL, Kossi O. Effectiveness of walking versus mind-body therapies in chronic

low back pain: A systematic review and meta-analysis of recent randomized controlled trials. Medicine (Baltimore). 2020 Aug 28;99(35):e21969. doi:10.1097/MD.0000000000021969. PMID: 32871946; PMCID: PMC7458239.

3. Kossi, O., **Nindorera, F**., Adoukonou, T., Penta, M., & Thonnard, J. L. (2019). Determinants of Social Participation at 1, 3, and 6 Months Poststroke in Benin. Arch Phys Med Rehabil, 100(11), 2071-2078. doi: 10.1016/j.apmr.2019.03.020

4. Kossi, O., **Nindorera, F**., Batcho, C. S., Adoukonou, T., Penta, M., & Thonnard, J. L. (2018). Measuring Participation After Stroke in Africa: Development of the Participation Measurement Scale. Arch Phys Med Rehabil, 99(4), 652-659. doi: 10.1016/j.apmr.2017.10.004

GENERAL INTRODUCTION

Mahoro is a 42-year-old public employee and father of three children who hoped to have a successful career, grow his family and most importantly support his children's education. As the only one who has attended school in his family, Mahoro also hoped to change the lives of his parents and siblings. But his dream came to an end when one morning while showering he stumbled and noticed that half his body was paralyzed. He consulted marabouts who took all his savings, participated in healing prayers and ended up in a hospital. He hoped to be able to walk properly and carry out his daily and professional activities but unfortunately, his hope remained hazy. Mahoro's life is problematic because, after suffering from high blood pressure, he had a stroke in a low-income country where this disease is not well known and where beliefs and economic status strongly influence its management. Like Mahoro, thousands of people in Africa every year, see their dreams come to an end in an eyeblink because of a stroke.

Stroke is the second leading cause of death and the first cause of disability in adults (GBD, 2021). The World Health Organization (WHO) recognized stroke as the greatest challenge to face for health systems globally in the twenty-first century (Who, 2003). The burden of stroke is dramatically high in low and middle-income countries, specifically in sub-Saharan Africa (SSA) (Adoukonou et al., 2021). In addition, stroke tends to affect more young African people (under the age of 60) relative to incidences in higher-income countries (Adoukonou et al., 2021; Owolabi et al., 2015; Sarfo et al., 2018). These

high numbers, combined with high mortality require urgent actions to reduce the burden of stroke in Africa (Adoukonou et al., 2021).

The WHO Rehabilitation 2030 agenda (Bernhardt et al., 2020) recognizes the importance of rehabilitation for stroke patients and highlights that developing and delivering cost-effective, equitable-access rehabilitation services to people is a challenge that needs to be addressed. This thesis aimed to particularly respond to this urgent call by characterizing stroke people in SSA, investigating and applying evidence-based low-cost treatments.

1.1 Stroke: Definition, etiology, risk factors, diagnosis and epidemiology

Definition of stroke

The term ‘stroke’ was introduced to medicine by William Cole in the late 17th century (Cole & Kimberley, 1689), and has remained a generic definition since then. Physiologically, stroke is an acute, focal injury of the central nervous system (CNS) of a vascular origin, contributing to local or systemic neurological damage (Adams et al., 2007). Technological advances have also provided the ability to define stroke by its cause and location and determine whether it is a cerebral infarct, subarachnoid hemorrhage or intracerebral bleed (Adams et al., 2007). According to the WHO, stroke is defined as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin” (Aho et al., 1980).

Because this definition is no longer accurate, as it does not consider the imaging and diagnostics aspects, the American Heart Association

(AHA) and the American Stroke Association (ASA) provided consensus definitions in an attempt to accurately describe the different types of stroke (Sacco et al., 2013). These types of stroke include *ischaemic stroke, Silent Central Nervous System (CNS) infarction, intracerebral hemorrhage, stroke from an intracerebral hemorrhage, silent cerebral hemorrhage, subarachnoid hemorrhage, stroke from subarachnoid hemorrhage, stroke from cerebral venous thrombosis, and Unspecified stroke* (Sacco et al., 2013). More details about consensus definitions are provided in supplementary material 1, table1).

Etiology of stroke

As described earlier, stroke is a sudden neurological outburst caused by impaired perfusion through the blood vessels to the brain. It can generally be classified as ischemic or hemorrhagic, based on the underlying mechanism of injury (Musuka et al., 2015).

Ischemic occlusions contribute to around 85% of stroke patients and cause deficient blood and oxygen supply to the brain (Kuriakose & Xiao, 2020). Ischemic occlusion generates thrombotic and embolic conditions in the brain. In thrombosis, the blood flow is affected by the narrowing of vessels due to atherosclerosis. Plaque build-up will eventually constrict the vascular chamber and form clots, causing a thrombotic stroke (Musuka et al., 2015). In an embolic stroke, decreased blood flow to the brain region causes an embolism; the blood flow to the brain reduces, causing severe stress and untimely cell death (necrosis).

Hemorrhagic stroke accounts for approximately 10–15% of all strokes and has a high mortality rate. Bleeding or leaky blood vessels cause hemorrhagic stroke. In this condition, the stress in the brain tissue and internal injury cause blood vessels to rupture. It produces toxic effects in the vascular system, resulting in an infarction (Aronowski & Zhao, 2011). Hemorrhagic stroke is classified into intracerebral (ICH) and subarachnoid hemorrhage. In ICH, blood vessels rupture and cause abnormal accumulation of blood within the brain. In subarachnoid hemorrhage, blood accumulates in the subarachnoid space of the brain due to a head injury or cerebral aneurysm (Kuriakose & Xiao, 2020).

Other key events contributing to stroke pathology are inflammation, energy failure, loss of homeostasis, acidosis, increased intracellular calcium levels, excitotoxicity, free radical-mediated toxicity, cytokine-mediated cytotoxicity, complement activation, impairment of the blood-brain barrier, activation of glial cells, oxidative stress and infiltration of leukocytes (Woodruff et al., 2011).

Stroke risk factors

The risk of stroke increases with age in both men and women (Kuriakose & Xiao, 2020). Existing medical condition like hypertension, coronary artery disease or hyperlipidemia increases the risk of stroke as nearly 60% of strokes are patients with a history of transient ischemic attack (Kuriakose & Xiao, 2020). Risk factors can be modifiable or non-modifiable. Non-modifiable risks include age, sex, ethnicity, transient ischemic attack (TIA) and hereditary characteristics (Mozaffarian et al., 2016). Known modifiable risks are

hypertension contributing to 55·5% of total strokes (Collins et al., 1990; GBD, 2021), high body mass Index (GBD, 2021), diabetes mellitus (GBD, 2021; Vermeer et al., 2006), ambient particulate matter pollution, sedentary lifestyle and diet (Li et al., 2012), atrial fibrillation (AF) (Wolf et al., 1991), alcohol and drug abuse (Gill et al., 1986), hyperlipidemia (Denti et al., 2003) and smoking (Bhat et al., 2008). Human immunodeficiency virus (HIV) infection has also been described as a risk factor for stroke mainly due to vascular effects associated with combination antiretroviral therapy (cART) treatment (Benjamin et al., 2012). It is crucial to note that the leading risk factors in low-income countries, particularly in sub-Saharan Africa, are hypertension, diabetes, hyperlipidemia and HIV infections. HIV infection is highly predominant in LMICs (Pandey & Galvani, 2019). These factors alone contribute to around 60% of strokes in this region (Owolabi et al., 2015).

Diagnosis and semiology of stroke

According to AHA/ASA expert consensus document (Sacco et al., 2013), current stroke diagnosis is based on clinical diagnosis, imaging diagnosis, serum biomarkers and the neuropathological evaluation of the brain. Depending on the specific symptomatology, clinical examination allows the physician to make assumptions about the vascular process, blood vessels involved and the disease mechanism (e.g., ischemia or hemorrhage). Depending on the vascular territory affected in the brain, the symptomatology will be different. For instance, symptomatology following the middle cerebral artery

infarction will include isolated frontal syndrome, transcortical motor aphasia/Broca's aphasia/conduction aphasia, ideomotor apraxia, motor alexia or hemineglect (Moulin & Decavel, 2004). The overall stroke semiology is described in supplementary material 1, tables 2 and 3.

Imaging studies: computed tomography (CT) scanning or magnetic resonance imaging (MRI) and other laboratory tests confirms the CNS lesion, its location, size, shape, and extent … Serum biomarkers and neuropathological evaluation of the brain are also diagnostic tools but are rarely used due to the accuracy (precision) of MRI.

Among these tools, solely the clinical diagnosis is accessible to most people in low-income countries, but its accuracy is still a challenge because there are few well-trained professionals.

Epidemiology of stroke

Stroke is a long, constantly increasing burden worldwide. Updated data (GBD, 2021) shows that, globally, stroke remained the second-leading cause of death (11·6% of total deaths) and the third-leading cause of death and disability combined. From 1990 to 2019, the absolute number of stroke incidence increased by 70·0% (Figure 1), prevalence increased by 85·0%, and deaths from stroke increased by 43·0%.

The epidemiology of stroke is related to economic status. Figure 2 illustrates the world bank distribution of countries according to their income levels. For instance, the age-standardized stroke-related mortality rate was 3·6 times higher in the World Bank low-income

countries than in the high-income countries, and the age-standardized stroke-related DALY rate was 3·7 times higher in the low-income group than the high-income group (GBD, 2021). There is a strong inverse relationship between stroke and socioeconomic status, attributable to inadequate hospital facilities and post-stroke care among low-income populations (Addo et al., 2012). Congruently, 86% of all stroke deaths around the world are observed in LMICs, prevalence and incidence are 3 to 6 times higher in Africa, especially Sub-Saharan countries (Owolabi et al., 2015, Adoukonou et al., 2021).

Recent trends show that sub-Saharan Africa (SSA) currently has the highest burden of stroke worldwide because the guidelines helping to decrease the burden are not yet met. Compared to the world, age-standardized stroke incidence rates in SSA are up to 316 per 100,000 (Cossi et al., 2012), prevalence rates up to 14 per 1,000 population and one-month mortality rates of up to 40% (Ezejimofor et al., 2017; Walker et al., 2010). Approximately 25% of this West African cohort strokes occurred among young adults <50 years old (Sarfo et al., 2018). Studies in this sub-Saharan African region (Benin and Tanzania) have shown a high prevalence in urban areas (Hertz et al., 2019). This disparity is probably due to a difference in the exposure to risk factors, such as high rates of uncontrolled hypertension, diabetes, smoking, excessive alcohol use, insufficient fruit and vegetable consumption, obesity, lack of exercise, professional and socio-economic stress, and HIV infection (Cossi et al., 2012; Walker et al., 2010).

In summary, low-income countries, especially those in sub-Saharan Africa, experience the highest prevalence, incidence, disability and case fatality rates of stroke compared to developed countries. In

addition, stroke affects the working-age population in these countries and represents a substantial economic burden for families and countries in general.

This difference in the incidence, prevalence and mortality rates of stroke between High-income countries (HICs) vs. Low-income countries (LMICs) can be explained by several factors. First, many African countries are undergoing an epidemiological transition driven by sociodemographic and lifestyle changes related to industrialization and a rise in many modifiable vascular disease risk factors. Second, health systems in many African countries are characterized by geographical and financial inaccessibility, rapid turnover of people in critical positions, lack of continuity in policy, lack of resources, poor management of available resources, and poor implementation (WHO, 2013). There is a strong need for appropriate systems of stroke care in Sub-Saharan Africa (SSA) and other LMICs regions to control the increasing death and disability associated with stroke (Langhorne et al., 2012). Third, the influence of cultural beliefs and religions is also a barrier to accessing early stroke management. Indeed, less than 20% of patients are admitted within three (3) hours of stroke onset (Adoukonou et al., 2012). Late presentation to the hospital has been reported to be associated with poor awareness of stroke signs and symptoms, a late referral from private hospitals, transportation problems, visits to traditional healers or prayers before coming to the hospital, and treatment at home (Urimubenshi et al., 2018).

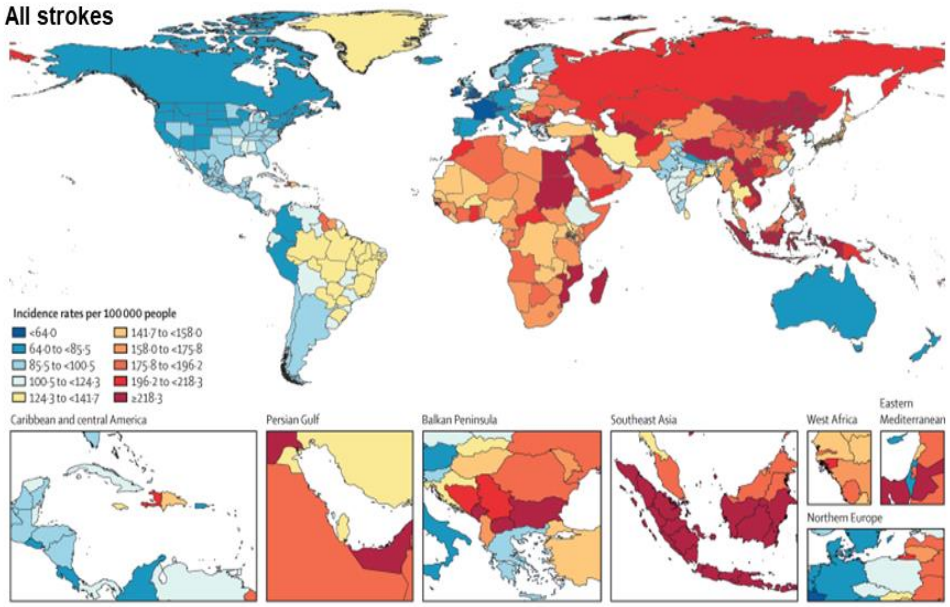


***Figure 1** (Adapted from GBD (2021): Age-standardized stroke incidence rates for all strokes*.

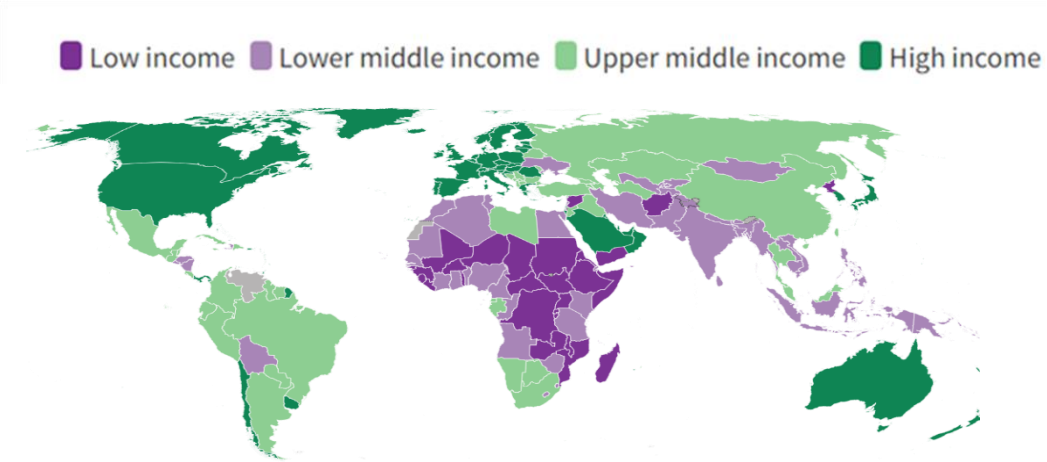


***Figure 2**: Map displaying the World by Income and Region (Worldbank, 2021)*

1.2 Consequences of stroke

Death

As stated in the epidemiology section, stroke remains the second leading cause of death worldwide and low-to-middle income countries show high rates compared to developed countries. Stroke survivors encounter different levels of disability.

Disability

Disability is a complex and multidimensional aspect covering the interaction between a person's health condition and contextual factors, including environmental and personal factors (Dahl, 2002). Stroke is the first cause of disability and the third-leading cause of death and disability combined worldwide (GBD, 2021). Stroke among young adults has devastating consequences because of the long-lasting impact of stroke-related disability on quality of life and productivity (Sarfo et al., 2018).

Disability in the ICF conceptual framework

The International Classification of Functioning, Disability and Health advanced the understanding and measurement of disability (Vargus-Adams & Majnemer, 2014). The ICF emphasizes environmental factors in creating disability, and problems with human functioning are categorized into three interconnected areas:

- impairments are problems in body function or alterations in body structure – for example, paralysis or muscle weakness; cardiorespiratory fitness, fatigue,

- activity limitations are difficulties in managing activities – for example, walking or eating;
- Participation restrictions are problems with involvement in any area of life – for example, facing discrimination in employment or transportation.

Disability refers to difficulties encountered in any or all three areas of functioning. The ICF can also be used to understand and measure the positive aspects of functioning, such as body functions, activities, participation and environmental facilitation. The ICF adopts the neutral language and does not distinguish between the type and cause of disability – for instance, between "physical" and "mental" health. Stroke-related disability arises from the interaction of health conditions with contextual factors – environmental and personal factors as shown in figure 3.

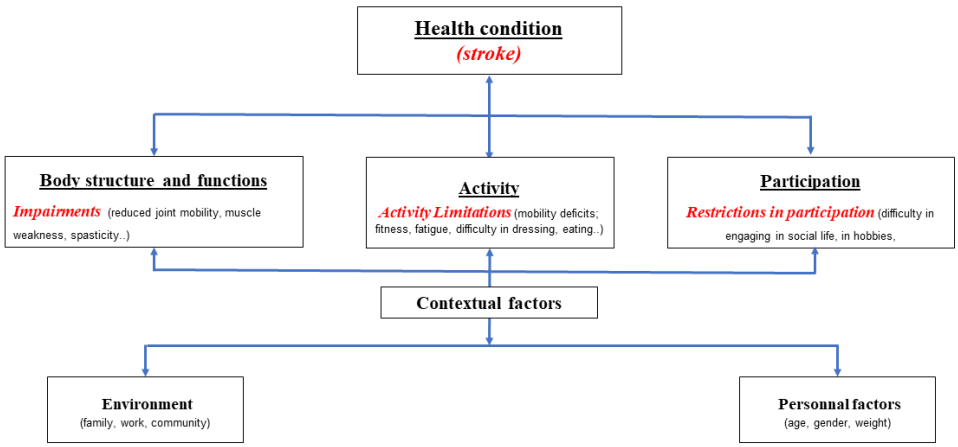


***Figure 3*: Illustration of the consequences of stroke according to the ICF framework. The dimensions of functioning are in black bold and underlined, while the negative aspect of the disease with respect to each functioning dimension are in red bold (adapted from WHO, 2007).**

The most common deficit after stroke is hemiparesis, with more than 80% of stroke patients experiencing this condition acutely and more than 40% chronically (Cramer et al., 1997). Common manifestations of motor impairment include muscle weakness or contracture, changes in muscle tone, joint laxity, and impaired motor control. Motor function deficits due to stroke affect the patients' mobility, their limitation in daily life activities, their participation in society and their odds of returning to professional activities. These factors contribute to overall low quality of life and sedentary lifestyle behavior (Hatem et al., 2016). While the ability to be independent in the community is considered as important by 75% of stroke survivors (Lord et al., 2004), activity limitation and participation restriction remain highly prevalent up to 4 years after stroke (Gadidi et al., 2011; Kossi et al., 2019). During stroke rehabilitation, interventions should therefore target mainly activity limitations and participation restrictions to improve the functioning and potentially the quality of life in the affected individuals. Thus, measurement tools are needed, especially for activity and participation, with good psychometric properties and culturally suitable to assess and quantify changes after patient-centered interventions.

Assessment of disability

The use of the ICF framework when assessing people with stroke enables clinical reasoning and improves a holistic approach to identifying the patient's problems (Moradi et al., 2018). Historically, the assessment was mainly focused on impairments, and several

assessment tools have been developed. More recently, with the ICF framework's popularisation, much research in developed countries has begun to focus on assessing activity limitations and participation restrictions (Gadidi et al., 2011; Penta et al., 2001). Currently, there is a wide range of measures for activity limitations, participation restrictions and quality of life.

Unlike other variables such as "height," "weight," or "distance," "activity limitations and participation restrictions" are latent variables whose measurement can only be inferred from their manifestations by observing or interviewing the individual (Penta et al., 2005). Nevertheless, a measure is objective when it is linear and unidimensional (Penta et al., 2005) and these latent variables need to be objective. In addition to linearity and unidimensionality, these tools must be cross-cultural and valid to be used anywhere. Recent work has led to the development of two questionnaires, the ACTIVLIM-Stroke scale (Batcho et al., 2014; Batcho et al., 2012) and PM-scale (Kossi et al., 2018; Kossi & Thonnard, 2018). These tools are built with the Rasch model, ensuring their linearity and unidimensionality, and have been calibrated with African populations. Today, sub-Saharan Africa has good measurement tools to assess the disability components of stroke patients.

In this thesis, we considered essential to assess the three levels of ICF. Therefore, we chose Stroke Impairment Assessment Set (SIAS) to evaluate the global impairment domain. SIAS is a valid and reliable measure of global stroke impairments (Liu et al., 2002; Tsuji et al.,

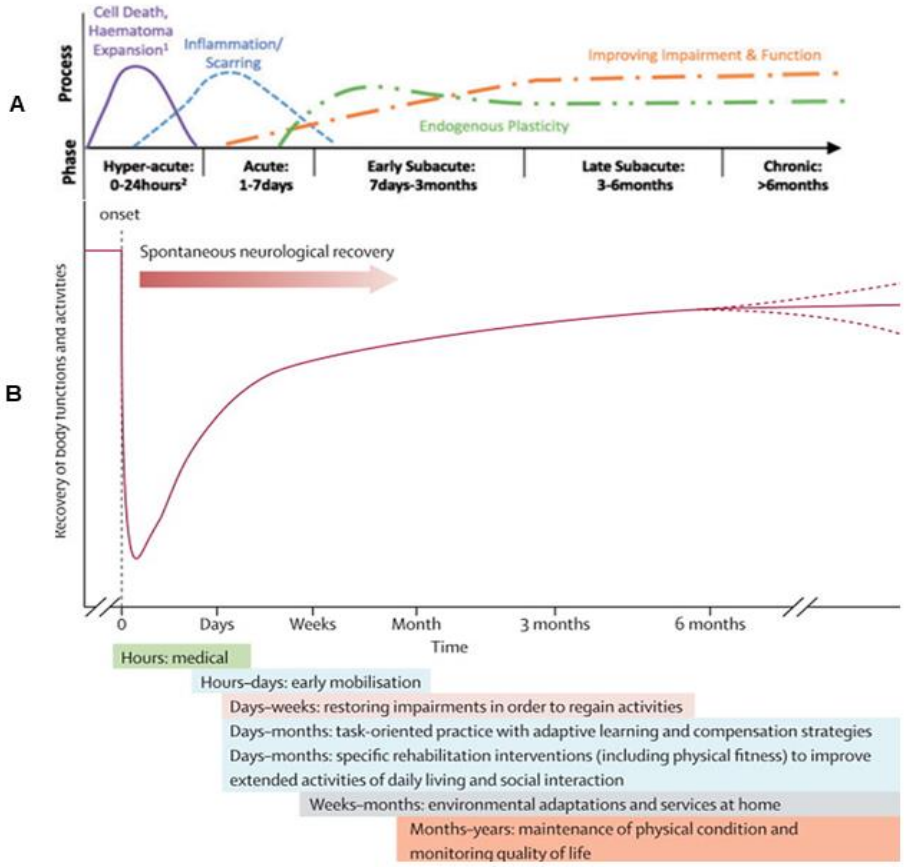
2000) widely used in the African clinical field. In addition, we assessed cognitive and psychosocial health functions with the Community Screening Interview for Dementia (CSI-D) and the Hospital Anxiety and Depression Scale (HADS). These tools are easy to use and understandable for the illiterate. The Berg Balance Scale (BBS) was also chosen to assess balance impairments.

We assessed independence in daily life activities and mobility at the activity level. Functional independence in ADL was measured by the ACTIVLIM-Stroke scale, a 20-item self-reported questionnaire instrument, culturally suitable for the African context. The 6 min walk test (6MWT) and the 10 m walk test (10mWT) are widely used community and clinical mobility tests (Bohannon & Williams, 2011; Steffen et al., 2002). The 6MWT measures walking endurance based on the distance while the 10mWT measures the walking speed.

Finally, participation was measured with the Participation Measurement Scale (PM-Scale), a 22-item Rasch-built stroke-specific scale that refers to daily situations encountered by stroke survivors in Africa and has good psychometric qualities (Kossi et al., 2018; Kossi & Thonnard, 2018). Overall these tools were chosen to detect improvements after rehabilitation interventions in the 3 ICF domains.

1.3 Stroke management (medical and physical management)

According to current international recommendations (Rudd et al., 2017), stroke management depends on the stage of the disease (Fig. 4A). Usually, four phases are described: the hyper-acute phase is the first 24 hours after the stroke; the acute phase lasts for a week after the hyper-acute phase; the sub-acute phase begins on the 7th day and lasts until the 6th month; the chronic phase begins six (6) months after stroke (Bernhardt et al., 2017). Stroke care aims to minimize brain injury and maximize patient recovery. According to Kwakkel and colleagues (2004), recovery is a "complex process that occurs through a combination of spontaneous and learning-dependent processes", including restitution, substitution and compensation (Kwakkel et al., 2004). With this understanding, Langhorne et al (2011) drew up a hypothetical pattern of recovery after a stroke with the timing of intervention strategies (Langhorne et al., 2011). This pattern is presented in figure 4B.



<u>Figure 4</u>: Hypothetical pattern of recovery after stroke with the timing of intervention strategies; adapted from (Bernhardt et al., 2017; Langhorne et al., 2011).

With reference to this pattern, stroke management is strictly medical in the hyper-acute phase, followed by early rehabilitation in the acute phase. The main objective during the acute and sub-acute phase is to recover as much as possible from the impairments. In the chronic phase of stroke, maintaining an optimal physical condition and quality of life as well as adaptation to the community, are the main focus of rehabilitation.

Stroke management strategy

To develop a response to stroke, the American Heart Association (AHA) developed the Stroke Chain of Survival (Powers et al., 2019), a key pathway in early diagnosis and management to minimize death and sequelae following stroke. This chain involves five steps to be taken by patients, family members, and prehospital and emergency room personnel in caring for stroke patients (Contactcare, 2022; Rudd et al., 2017): (1) Rapid recognition and reaction to stroke warning signs; (2) rapid emergency medical services (EMS) dispatch; (3) rapid EMS system transport and hospital pre-notification; (4) guideline-based stroke care (rapid diagnosis and treatment in the hospital, early rehabilitation), and (5) quality post-stroke care (Rehabilitation; secondary prevention). Unfortunately, this strategy is not implemented in most low- and middle-income African countries. Medical treatment (short-term or long-term) and rehabilitation are the only interventions available in most low-income African countries (though not always readily available).

1.4 Rehabilitation

Rehabilitation is “a dynamic process that helps a disabled person to acquire knowledge and skills to maximize physical, psychological, and social function” (Turner-Stokes, 2000). The WHO estimates that 75% of the years spent with disability worldwide are linked to health conditions for which rehabilitation is beneficial (WHO, 2019). Rehabilitation is a holistic process that should begin early after the stroke (>24 hours) to improve functional ability and reduce stroke

consequences (Cumming et al., 2011; Ding & Zhang, 2021; Mariana de Aquino Miranda et al., 2021). In other words, rehabilitation after a stroke aims at reducing disability by facilitating recovery of impairments, activity limitations, or restrictions in participation (Clark et al., 2021). Stroke rehabilitations guidelines (Winstein et al., 2016) highlight that rehabilitation should be integrated into services to meet three requirements:

- Ongoing inpatient rehabilitation: to ensure all stroke patients receive early, active rehabilitation by a dedicated stroke team, health systems should have comprehensive services which include and link the fundamentals of acute and rehabilitation care.
- Care after hospital discharge: rehabilitation delivered in the home or community settings should be offered to all stroke survivors as needed.
- Long-term rehabilitation: stroke survivors with residual impairments should continue rehabilitation to set new goals and improve task-oriented activity.

Historically, stroke rehabilitation has mainly focused on fixing motor impairments based on neurodevelopmental therapies such as Bobath, Kabat, Perfetti concepts (Brunnstrom, 1956; Brunnstrom, 1961; Hafsteinsdóttir et al., 2005; Pathak et al., 2021; Rood, 1954). These therapies use mainly handling, passive techniques (passive mobilization and stretching) intending to inhibit abnormal muscle tone, facilitate normal movement patterns , and prevent muscles contractures (Pathak et al., 2021). However, recent studies have not confirmed the

effectiveness of these neurodevelopmental approaches (Scrivener et al., 2020; Hatem et al., 2016). Consequently, multiple interventions have emerged to improve motor function, mobility and/or cognitive deficits. Their efficiency was demonstrated as more significant that of neurodevelopmental approaches (Hatem et al., 2016; Rensink et al., 2009). These interventions, mainly those targeting the upper extremity, are based on the principles of motor learning.

a. Motor skill learning-based interventions: Upper extremity training

Theories of brain plasticity and motor learning have been developed to understand the mechanisms of recovery from impairments after stroke. Brain plasticity, also known as neuroplasticity or neural plasticity can be defined as "the ability of the nervous system to change its activity in response to intrinsic or extrinsic stimuli by reorganizing its structure, functions, or connections" (Mateos-Aparicio & Rodríguez-Moreno, 2019). Motor learning reflects a relatively permanent change in a person's capability to perform a motor skill (Schmidt et al., 2019). Instead of teaching compensatory strategies that do not reduce impairment but allow the patient to return home as soon as possible, interventions based on the principles of motor learning and neuroplasticity have started to emerge. The motor learning principles documented in the literature that make an intervention effective are "massed/spaced practice, dosage, task-specific practice, goal-oriented practice, variable practice, increasing difficulty, multisensory stimulation, rhythmic cueing, explicit feedback/knowledge of results,

implicit feedback/knowledge of performance, modulate effector selection, action observation/embodied practice, motor imagery, and social interaction" (Maier et al., 2019).

Effective evidence-based interventions on upper-limb motor function include task-oriented training (Rensink et al., 2009), constraint-induced movement therapy (CIMT) (Hatem et al., 2016), bimanual therapy (BT), all based on motor skill learning. In addition, effectiveness has been shown for muscle strengthening exercise (Hatem et al., 2016), virtual reality training (Laver et al., 2017), robot-assisted trainings (Baronchelli et al., 2021), brain stimulation (Kesikburun, 2022) and/or electrical stimulation (Loh et al., 2022).

In summary, effective rehabilitation interventions on upper extremities are based on motor learning and neuroplasticity principles (Maier et al., 2019; Schmidt et al., 2019): (1) they promote an active task-oriented movement; (2) intensity; a high-intensity is associated with improvement (Anjos et al., 2022); (3) functional and structured exercise with progressive difficulty are used to increase motor engagement and motivation, and this allows progress learning of new complex skills (Schmidt et al., 2019). Although these interventions are promising, they require supervision by many well-trained professionals and/or require expensive equipment.

b. Walking training and mobility-based interventions: Lower extremity training

Effective evidence-based interventions on lower-extremity motor function and mobility include walking training (treadmill, overground gait training and circuit class therapy) (English et al., 2017), repetitive task training (RTT) (French et al., 2016), active physical rehabilitation (Pollock et al., 2014), cycling (Da Rosa Pinheiro et al., 2021; Kim et al., 2015) and balance training (Moreno-Segura et al., 2022). Despite the scarce of high-quality studies examining the effectiveness of rehabilitation interventions on activity and participation, moderate evidence have shown that circuit class trainings and repetitive task interventions are effective on mobility, physical fitness, activities of daily living and participation (Barclay et al., 2015; English et al., 2017; French et al., 2016; Saunders et al., 2020). These evidence-based therapies come from HICs, are mostly performed in laboratory settings and often require expensive equipment. Some interventions targeting global motor function/ walking are likely to be adapted with few material and less well-trained professionals. In addition to interventions targeting the lower or upper extremities, special attention is also given to secondary prevention.

Prevention

It is estimated that 11% of stroke patients will have a recurrence within a year of their first stroke and 26% within five (5) years (Mohan et al., 2011). The overwhelming majority of strokes can be prevented through blood pressure control, a healthy diet, regular physical activity, and smoking cessation (Kleindorfer et al., 2021). Globally, secondary stroke prevention is based on the following recommendations: lifestyle modifications (regular physical exercise, stopping smoking and improving diet); medical treatment (blood pressure lowering therapy, antiplatelet therapy, anticoagulant, cholesterol lowering therapy) (Kleindorfer et al., 2021). This thesis focuses specifically on physical activity.

- Physical activity as a rehabilitative and preventive tool

In response to the increasing burden of chronic diseases, efforts are focused on prevention and management. To this end, the WHO has recently released new guidelines on physical activity (WHO, 2020), and these guidelines contain for the first time, specific recommendations for adults and older adults living with chronic conditions and/or with disabilities. With these recommendations, people with chronic conditions and/or disability should do at least 150–300 minutes per week of moderate-intensity aerobic physical activity; or at least 75–150 minutes of vigorous-intensity aerobic physical activity. They should also do muscle-strengthening exercises at a moderate or greater intensity that involve all major muscle groups on two (2) or more days a week. Unfortunately, very few stroke survivors follow these

recommendations. Indeed, factors such as physical impairments, lack of motivation, cost, and environmental factors have been reported as the main barriers to physical activity adherence (Damush et al., 2007).

Physical activity is “any bodily movement produced by the skeletal muscles, responsible for an increase in energy expenditure.” Exercise is “a type of physical activity that is planned, structured and repetitive with the objective to improve or maintain physical fitness” (Thompson, 2022). Physical activity can be either aerobic (or endurance training), anaerobic (resistance training), or mixed (endurance and resistance). The type of training depends on one's goals and the available resources. However, although few studies have shown the effects of mixed exercise, the combination of endurance and resistance training could add positive effects. Training can also be delivered in individual or a group format. Group activities may be preferred for their motivational, interactive, encouraging and cost-effective effects (Zumeta et al., 2016).

As a sedentary lifestyle is one of the main consequences of disability (Hornnes et al., 2010), the American Heart/Stroke Association (AHA/ASA) have also issued guidelines specifically for physical activity in stroke management and secondary prevention (Billinger et al., 2014). Hence, stroke survivors should perform aerobic exercise 3-5 times per week, 20-60 min/session at 55%-80% of maximum heart rate and resistance training 2-3 times per week at 50%-80% of maximum resistance (1RM). However, only a small number of stroke survivors can reach these recommendations, whether in HICs or

LMICs, but participation could be increased by dealing with facilitators such as motivation, social support and training content “interest and enjoyment” (Withall et al., 2011).

Numerous studies available in high-income countries (HICs) have contributed to developing of physical activity programs in stroke management. In these HICs, there is currently considerable evidence that physical exercise improves mobility, muscle strength, functional capacity, the ability to perform activities of daily living, and quality of life, and it reduces the risk for subsequent cardiovascular events (Billinger et al., 2014; Saunders et al., 2020; Veldema & Jansen, 2020). In addition to these functional effects, physical activity has beneficial impacts on neuroplasticity (Penna et al., 2021), memory and learning (Firth et al., 2018) , and risk factors for recurrent stroke (Brouwer et al., 2021). It should be remembered that the equipment and materials used in physical exercise training protocols in these high-income countries are somehow expensive and, consequently not readily accessible in low-income settings. These equipment include mainly walking robots, treadmills, cycloergometers, semi-recumbent bicycles, press legs, virtual reality devices (Laver et al., 2020; Laver et al., 2017; Mehrholz et al., 2017; Saunders et al., 2020). Hence, there is an important unmet need for cost-effective community-based physical activity for stroke rehabilitation in low-income African settings.

❖ Rehabilitation of stroke survivors in Sub-Saharan Africa

The World Stroke Organization recommends that after a stroke, patients should have access to rehabilitation specialists, including physiotherapists, occupational therapists, and speech and language therapists (Lindsay et al., 2014). Low-income African countries have so far been unable to implement stroke recommendations (from early management to long-term rehabilitation and secondary prevention). According to a recent systematic review (Yaria et al., 2021), stroke guidelines from low-income countries fell short in terms of quality, coverage and content.

Despite the high prevalence of stroke in these countries, rehabilitation is characterized by several limiting factors that make it less accessible. Firstly, the few existing rehabilitation services are located mainly in urban areas. Patients and family members must travel long distances to reach these services (Urimubenshi et al., 2018). Secondly, qualified human resources in this field are scarce and are mostly not hired by the government. This leads to a geographical maldistribution and a failure of the stability of medical professionals. Thirdly, the few existing services are critically lacking in equipment and infrastructures. For instance, CT/MRI brain imaging, stroke unit services were reported to be rare and too expensive in Africa (Wasserman et al., 2009). Globally, essential challenges are shortage or high cost of medical care and transportation, brain imaging infrastructure, stroke units, outpatient services and healthcare personnel (Adoukonou et al., 2012).

To improve access to rehabilitation care, community-based rehabilitation (CBR) program was developed in most African settings. The CBR principle is to train caregivers or family members as rehabilitative care-providers (WHO, 2011). Although this CBR program increased the accessibility to rehabilitation in low and middle-income countries, their efficacy was never really investigated. It can be hypothesized as limited since care is delivered by non-professionals (community members) and mainly based on non-evidence passive techniques (mobilization, stretching, verticalization, manual guidance etc.) as routinely practiced in conventional rehabilitation services (WHO, 2011, Pathak et al., 2021).

However, there is now an increasing number of studies testing the efficacy of home-based interventions to improve access to rehabilitation. Among these, self-rehabilitation (Everard et al., 2021; Niama Natta et al., 2021) and telerehabilitation (Laver et al., 2020; Sarfo et al., 2017) have shown low to moderate evidence. Currently, it is hard to draw conclusions about their effectiveness because interventions and comparators varied considerably across studies and middle to HICs countries.

Thus, there is a strong need to improve the quality of rehabilitation care in stroke people in Africa, which would necessarily use rigorous scientific studies. Considering the high prevalence of stroke, the subsequent disability in our clinical settings, and the difficulties related to the accessibility of care, a community, mixed and collective physical activity program with low-cost material using

intensive and functional-based approaches seems critically interesting to investigate. This has the potential to offer a cost-effective and goal-oriented intervention to stroke individuals, with little demand for qualified human resources. Such an intervention would also be a way to implement the prevention of stroke recurrence. We hypothesize that the community modality requires little or no travel costs, and the group modality requires fewer physiotherapists and provides motivation and social interaction.

1.5 Purposes

By contributing to the growth of research and evidence-based rehabilitation, this thesis investigates the effectiveness of community, group-based and mixed physical activity in chronic stroke rehabilitation in low-income settings. We assume that a group and community-based physical activity intervention would be beneficial and affordable as it will avoid travel costs and dependence on several human resources. To reach this aim, we (1) investigated the characteristics of the stroke patients in Burundi so that the future intervention could take into account their level of balance impairments, activity limitations, and participation restrictions, (2) reviewed and quantified the effects of the existing walking training protocols for the improvement of various aspects of physical function of people with chronic stroke to define the best training parameters for this population, and (3) finally we designed a new intervention: the Circuit walking, Balance, Cycling and Strength training (CBCS) and investigated its feasibility and efficiency to improve activities of daily living (ADL), motor performance, and social participation in stroke survivors.

CHAPTER I (Study 1)[1]

Relationships between walking speed, activities and participation in people with chronic stroke in Burundi

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[1] As this chapter is already published, responses to the jury members were added to manuscript as footnotes.

1.1. Abstract

Background: Reduced walking speed following a stroke may limit activities of daily living (ADLs) and restrict social participation.

Objectives: To describe the level of balance impairment, activity limitations, and participation restrictions and to investigate their relationships with walking speed in Burundians with stroke

Methods: This was a cross-sectional study involving stroke survivors. Walking speed, balance, ADLs and social participation were assessed with the 10-meter walk test (10 mWT), the Berg balance scale (BBS), the activity limitation stroke scale and the participation measurement scale, respectively. In order to determine ambulatory independence status, participants were stratified into three walking speed groups (household, limited and full community ambulation), based on the Perry's classification.

Results: Fifty-eight adults (52.1 ± 11.4 years) with chronic stroke were recruited. Most participants had severe balance impairments (median BBS score, 27). Their mean (±SD) walking speeds, ADL levels and social participation levels were 0.68 ± 0.34 m/s, 50.8% ± 9.3% and 52.8% ± 8.6%, respectively. Walking speed correlated moderately with balance (rho = 0.5, $p < 0.001$) and strongly with ADL ($r = 0.7$, $p < 0.001$) but not with participation ($r = 0.2$, $p = 0.25$).

Conclusion[2]: Using socio-culturally suitable tools, the present study showed that walking speed correlates strongly with balance and ADL, but not with participation in people with chronic stroke in Burundi, a low-income country.

KEYWORDS: Activity limitations; low-income settings; social participation; stroke; walking speed.

Clinical implications: Exercises targeting walking speed would be very useful for people with chronic stroke living in low-resource countries, in order to promote their functional independence.

[2] Since correlation does not mean causality, this finding suggests that community walking speed is one of the factors that can influence ADL independence, and that should not be underestimated in rehabilitation.

1.2. Introduction

Stroke is the second leading cause of death and a major cause of disability worldwide (Katan & Luft, 2018). Disability due to stroke remains highly prevalent up to three years after the event (Kossi et al., 2021). In a 2016 meta-analysis, the pooled prevalence rate for stroke in Africa was estimated to be 3.5 cases per 1000 people, with an annual increasing trend of 12.0% (Ezejimofor et al., 2016). Relative to high income countries, stroke affects more young people in middle and low-income countries, and the affliction of younger aged people with stroke produces an economic burden in such countries (Katan & Luft, 2018). Furthermore, the highest incidence, prevalence, and case fatality rates of stroke in the world have been reported in Africa (Adoukonou et al., 2021).

The World Health Organization's International Classification of Functioning, Disability, and Health (ICF) recognizes functional disability as multidimensional and involving nonlinear concepts of the interaction between a person's health condition and contextual factors. Commonly, stroke survivors experience activity limitations and social participation difficulties, even following a relatively good recovery from impairments (van der Zee et al., 2013). Reported prevalence rates of social participation restrictions among stroke patients range from 12% to 64% (Adoukonou et al., 2018; Kossi et al., 2019). Improvement of ICF components depends on several factors, including the national economic situation, access to rehabilitation, and cultural beliefs (Lekander et al., 2017; Mbada et al., 2019; Mendis, 2013). In low-

income countries, like Burundi, understanding the challenges faced by people who have suffered a stroke would be useful for identifying the long-term issues that care-based services for stroke will need to address (Ch'ng et al., 2008).

Walking is often severely affected after stroke and the high prevalence of balance impairments remains a problem (Kossi et al., 2021; Pinto et al., 2014). People tend to reduce their walking speed to prevent the risk of falling, and a slow walking speed may limit one's ability to perform activities of daily living (ADLs) and limit one's participation in family and community experiences (Faria-Fortini et al., 2019; Wang et al., 2020). On a sample of 147 patients, Perry and colleagues (Perry et al., 1995) defined functional walking status according to three community walking speed categories: household ambulation (speed < 0.4 m/s, indicating severe walking limitations), limited-community ambulation (speed in the range of 0.4–0.8 m/s, indicating moderate walking limitations), and full-community ambulation (speed > 0.8 m/s, reflecting slight or mild walking limitations). Although this classification comes from high-income context, it can provide information on the functional status of walking in low-income countries. Factors shown to influence ADL abilities and social participation include age, gender, medication use, duration after stroke, number of physical therapy sessions, walking speed, balance, and motor function (Faria-Fortini et al., 2018; Kossi et al., 2019). However, consistently, walking speed has been shown to be the best indicator of walking performance (Faria-Fortini et al., 2019). Thus, physical outcomes such as walking speed should not be assessed in isolation

when considering community ambulation post-stroke (Durcan et al., 2016). To date, relationship between walking speed and stroke outcomes has been studied in developing and high-income countries but to the best of our knowledge, none have been done in Burundi (Faria-Fortini et al., 2019; Wang et al., 2020). Therefore, the present study aimed (a) to describe balance impairments, ADL levels, and social participation levels of chronic stroke patients in Burundi, and (b) to investigate their relationships with walking speed.

1.3. Methods

Study design and setting

A cross-sectional study was conducted at the National Center of Reference in Physical Therapy and Medical Rehabilitation, University Hospital Roi-Khaled, Bujumbura between September 2019 and February 2020.

Study population

Burundians people who suffered a stroke made up our population. Potential participants were identified by consulting admission records in hospitals and rehabilitation centers. Data for all potential participants were screened to ensure that they met our inclusion criteria: clinical diagnosis (imaging or neurologist's diagnosis) of a primary or recurring unilateral stroke; chronic stroke stage (time since stroke ≥ six months); age ≥ 18 years old; and ability to walk 10 m with or without an assistive device. Participants with a major cognitive impairment (Community Screening Interview for Dementia score ≥ 7) (Hall et al., 2000) and those who had other

neurological impairments with permanent degenerative damage (e.g. Parkinson's disease, Alzheimer disease, etc.) were excluded.

Ethical consideration

Potential participants were informed about the objectives of the study and then were invited to provide consent. This study was conducted in accordance with the Declaration of Helsinki and approved by the Burundi national Ethics Committee under the number CNE/25/2019.

Sampling strategy

A purpose sampling technique was used to recruit participants. The minimum sample size was determined by considering 5% margin of error, 95% confidence level and around 0.4% stroke prevalence (A. S. Kim et al., 2015). The total sample size was proportionated to the five public and private hospitals in Bujumbura city based on their total number of beds. The minimum sample size required at the University Hospital Roi-Khaled of Bujumbura was then estimated at 53 participants.

Procedure and outcome measures

Questionnaires were administered in face-to-face interviews and clinical tests were conducted in rehabilitation settings. A trained physiotherapist with four years of clinical experience collected the data.

Walking speed

Walking speed was measured with the 10-meter walk test (10mWT). The 10mWT measures comfortable or maximal walking speed. Participants were asked to walk comfortably on a 14-m marked pathway; they were timed over the middle 10-m distance to record their comfortable walking speeds (Bohannon, 1997). The average speed over 3 trials was recorded. Based upon their walking speeds, the participants were stratified into three walking status groups according to Perry's classification (Perry et al., 1995), as follows: household ambulation (< 0.4 m/s), limited-community ambulation (0.4–0.8 m/s), and full-community ambulation (>0.8 m/s).

Balance

The Berg Balance Scale (BBS) was used to assess balance impairment and fall risk. The BBS was developed to measure balance in elderly individuals (Berg et al., 1992). It consists of 14 items that are each scored on a scale of 0 (unable to do the task) to 4 (able to complete the task fully). The maximum total score on the test is 56 (higher score means better balance). The items include simple mobility tasks (e.g., transfers, standing unsupported, sit-to-stand) and more difficult tasks (e.g., tandem standing, turning 360°, single-leg stance). The BBS is valid, reliable, responsive and a BBS score ≤42 has been identified previously as a predictor of risk of falling (Tilson et al., 2012).

Activity limitations

ADL limitations were evaluated with the ACTIVLIM-stroke scale, a 20-item Rasch-built stroke-specific scale designed to measure

functional independence (Batcho et al., 2012). This scale has been validated cross-cultural between African and European contexts. Participants were asked to rate each task on a three-level scale: impossible (0), difficult (1), easy (2). Total ACTIVLIM-stroke raw scores (ranging from 0 "more limited" to 40 "normal") were subjected to logit and centile metric transformation allowing parametric statistics. Higher scores indicate less difficulty with ADLs.

Participation restrictions

Social participation restrictions were assessed with the Participation Measurement Scale (PM-Scale), a 22-item Rasch-built stroke-specific scale for measuring social participation (Kossi et al., 2018; Kossi & Thonnard, 2018). The PM-Scale is a self-reported questionnaire scale that addresses one's overall involvement in daily situations and presents good psychometrics qualities in stroke survivors in Africa. Participants were asked to provide their perceived participation or implications on a three-level scale: not at all (0), weakly (1), or strongly (2). Total raw scores on the PM-Scale range from 0 (more restricted) to 44 (normal), while the linear measure logits ranging from –6.56 to 6.51, corresponding to 0–100 centiles. Higher values indicate higher participation.

In the present study, we converted raw scores from these two questionnaires (ACTIVLIM-Stroke and PM-Scale) into centiles with an online tool at www.rehab-scales.org.

Statistical analysis

Descriptive statistics were used to summarize the study sample's characteristics. Continuous quantitative variables with a normal distribution are reported as means with standard deviations (SDs), while ordinal or non-normal distributed data are reported as medians with interquartile ranges (IQRs). Scores were compared across groups with analyses of variance (ANOVAs) and Bonferroni post hoc tests as indicated. Spearman correlation (rho) analysis was used for dichotomous and ordinal variables whereas Pearson correlation (r) analysis was used for continuous variables. The magnitude of each relationship was interpreted based on the Munro's correlation descriptors: very low (0–0.25), low (0.26–0.49), moderate (0.50–0.69), high (0.70–0.89), and very high (0.90–1.00) (Martin, 2004). SPSS for Windows (version 27, IBM) was used for all statistical analysis. The significance threshold was set at $p < 0.05$.

1.4. Results

Participant characteristics

The sociodemographic and clinical characteristics of the study participants, grouped according to walking speed status, are presented in Table 1. The participant enrollment process is shown in Figure 5. Briefly, of a total of 336 individuals with stroke who were identified in the hospital admission registries and rehabilitation centers, 58 with confirmed chronic stroke (46 men, mean age = 52.1 ± 11.4) met our inclusion criteria and were included in this study. Post-stroke intervals ranged from 6 to 120 months (median, 18.5 months). With respect to

walking speed status, 15 participants (26%) were classified as household ambulators (walking speed, 0.26 ± 0.09 m/s), 25 (43%) were limited-community ambulators (walking speed, 0.64 ± 0.11m), and 18 (31%) were full-community ambulators (walking speed, 1.11 ± 0.13 m/s).

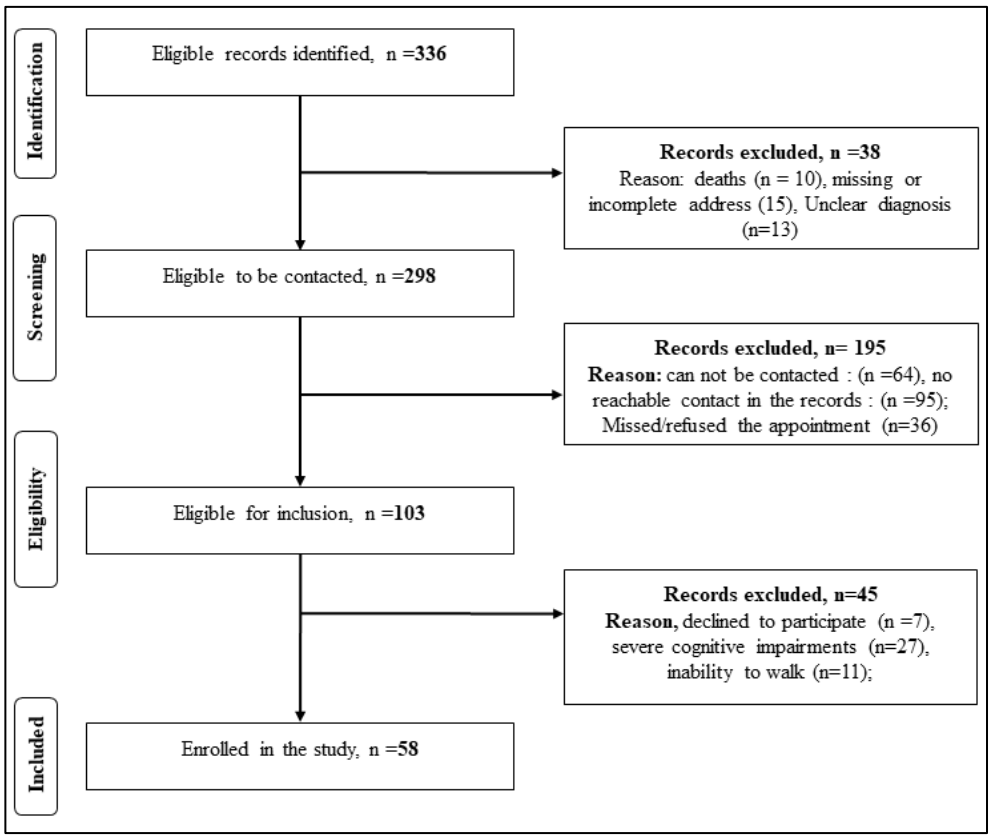

Figure 5. Flow chart of participant eligibility and inclusion

Table 1. Socio-demographic and clinical characteristics of the sample stratified by walking speed status

		Sub-groups according to the walking speed on 10mWT(m/s)			
Variables	**Total (N= 58)**	**<0.4 (n = 15)**	**0.4–0.8 (n =25)**	**>0.8 (n =18)**	**p-value**
Age, years, mean ± SD	**52.1±11.4**	53.2±9.4	54.5±10.2	47.9±13.7	0.16†
Distribution according to the median age, n (%)					0.33 b††
≤50 years/>50 years	**27/31**	6/9	10/15	11/7	
BMI, mean ± SD	**25.5±4.6**	26.5±6.4	25.6±3.9	24.4±3.6	0.41†
Gender, n					0.71b††
Male/Female	**46/12**	11/4	21/4	14/4	
Post-stroke duration, month, median [IQR]	**18.5[9-33]**	11[9-24]	25[8.5-36.5]	18[10-29]	0.70‡
Distribution according to post-stroke duration, n (%)					0.08††
6-12 months /12-24 months/ >24 months	**24/15/19**	8/4/3	10/3/12	6/8/4	
Affected side, n					0.24 ††
Right/ Left	**30/28**	5/10	14/11	11/7	
MRS, median [IQR]	**3[2-3]**				
Stroke type, n					0.83 ††
Ischemic/ Hemorrhagic/undetermined	**25/26/7**	8/6/1	9/12/4	8/8/2	
Walking speed ($m.s^{-1}$, mean ± SD)	**0.68 ±0.34**	0.26±0.09	0.64±0.11	1.11 ±0.13	<0.001†

Abbreviations: SD, standard deviation; IQR, interquartile ranges; MRS, Modified Rankin Scale; BMI, Body Mass Index; † One way-ANOVA. †† Chi-square tests. ‡ Kruskal–Wallis tests.

Impairments, activity limitations, and participation restrictions

Table 2 shows the description of the participant's overall outcomes as well as a distribution according to their walking speed level.

Table 2. Descriptive data of walking speed, balance, activity limitations and participation

Variables		Sub-groups according to the walking speed on 10mWT (m/s)		
	Total (n= 58)	**Household ambulation** <0.4 (n = 15)	**Limited ambulation** 0.4–0.8 (n = 25)	**Full-community ambulation** >0.8 (n = 18)
BBS scores, median [IQR]	**27[18-33]**	16[10-24]	28[21.5-32]	32.5[26-36]
ACTIVLIM-Stroke, %, mean±SD	**51±9%**	42.3±8.6	50.1±7.2	58.4±5.2
PM-Scale, %, mean±SD	**52±8%**	47.5±9.2	54.6±9.2	54.8±5.5

Abbreviations: SD, standard deviation; BBS, Berg Balance Scale; PM-scale, Participation Measurement scale; IQR, interquartile ranges

Balance

The median score (IQR) on the BBS for the whole sample was 27 (18–33). Fifty-five participants (95%) scored below 40 on the BBS. A moderate but significant correlation was found between walking speed and balance (rho = 0.5, $p < 0.05$; Figure 6). A Kruskal-Wallis test showed significant differences between the three walking speed groups on the BBS ($p = 0.001$).

Activity limitations

ADL limitations, according to ACTIVLIM-Stroke scale scores, which were associated with each walking speed status group, are presented in Figure 7, in a graph illustrating the threshold score ranges

for the groups for each item, as well as the relationship between ordinal raw scores and the corresponding linear measurements (in logits and in %, according to Batcho et al.'s calibration (2012). The overall mean ACTIVLIM-Stroke score percent value for the whole sample was 50.8 ± 9.3%, indicating that the participants were able to perform the first six easiest items easily (from "opening a door" to "using the toilet") and the eighth item ("getting out of bed"), but could not perform the four most difficult items (from sweeping or vacuuming to carrying heavy load).

Upon closer inspection, we found ADL differences between the walking speed status groups:

i. Household ambulators (speed < 0.4 m/s) had a mean score percent value of 42 ± 9%, indicating that they performed the four easiest items easily (from opening a door to ringing a doorbell). They were able to perform with difficulty several activities requiring some strength and motor coordination, including "getting out of bed", "taking off a t-shirt…". Overall, they were unable the perform 40% of the queried ADLs.
ii. Limited-community ambulators (04–0.8 m/s) had a mean score percent value of 50 ± 7%, meaning that they performed the eight easiest items, but had difficulty with activities such as getting out of a car, and standing for a long time.Overall, they were unable to perform 20% of the queried ADLs.
iii. Full community ambulators (>0.8 m/s) had a mean score percent value of 58 ± 5%, indicating that most patients could perform basic tasks ("brushing one's teeth", "taking off a tee-shirt", and "using the toilet") easily, while being unable to perform the three most difficult activities

requiring high locomotor endurance, high manual dexterity or high strength.

A one-way ANOVA showed a significant difference of ADL limitation scores (ACTIVILIM-Stroke scores, $p < 0.001$) according to walking speed level, with significant differences in all pair-wise inter-group comparisons (both Bonferroni post hoc; $p < 0.001$). Overall, walking speed strongly correlates with ADL ($R = 0.73$, $p < 0.001$; Figure 6)

Participation restrictions

Restrictions in social participation, as evidenced by PM-Scale scores, that were associated with each walking speed status group are presented in Figure 8 together a threshold map of expected score ranges for the groups for each item and an illustration of the relationship between the ordinal raw scores and the corresponding linear measure values (in logits and in %) (according to the calibration of Kossi et al. (Kossi et al., 2018). The sample's mean participation score percent value was 52 ± 8%, indicating that patients were strongly involved in the 9 lowest-demand items (from "understanding a goodbye gesture" to "choose my job based on my physical abilities") while they are not engaged in social activities involving leadership and inter-personal interactions (e.g.; "participate in religious feasts", "speak to an audience", and "occupy a position of responsibility in a regional organization").

Upon closer inspection, we found differences in social participation restrictions across the walking speed status groups:

i. Household ambulators had a mean score percent value of 47 ± 9%, indicating that they had regular involvement in only simple social activities related to general tasks and demands, communication, and learning and applying knowledge (e.g., "understanding a gesture of goodbye" and "make a simple mental arithmetic", etc.). They had limited involvement in intermediate activities such as "choose clothing" and showed weak results for "have confidence". They were not involved in many major activities of life involving interpersonal interactions and relationships nor in community, social, and civic activities.

ii. Limited-community ambulators (mean, 54 ± 9%) and full community ambulators (mean, 54 ± 5%), had similar social participation levels, including strong involvement in the 9 lowest-demand items, weak involvement in the following 8 items, and an inability to participate in tasks such as "participate in caring for children", "participate in religious feats", "speak to an audience", and "occupy a position of responsibility".

A one-way ANOVA test indicated significant differences in social participation (PM-Scale scores, $p \leq 0.05$, Figure 7) regarding the walking speed levels. Bonferroni post hoc tests showed that the limited and full-community ambulator groups, which were statistically similar to each other ($p > 0.05$), reported higher social participation levels than household ambulators (both $p < 0.05$). Overall, walking speed as a continuous variable did not correlate significantly with social participation ($R = 0.2$, $p > 0.05$; Figure 6).

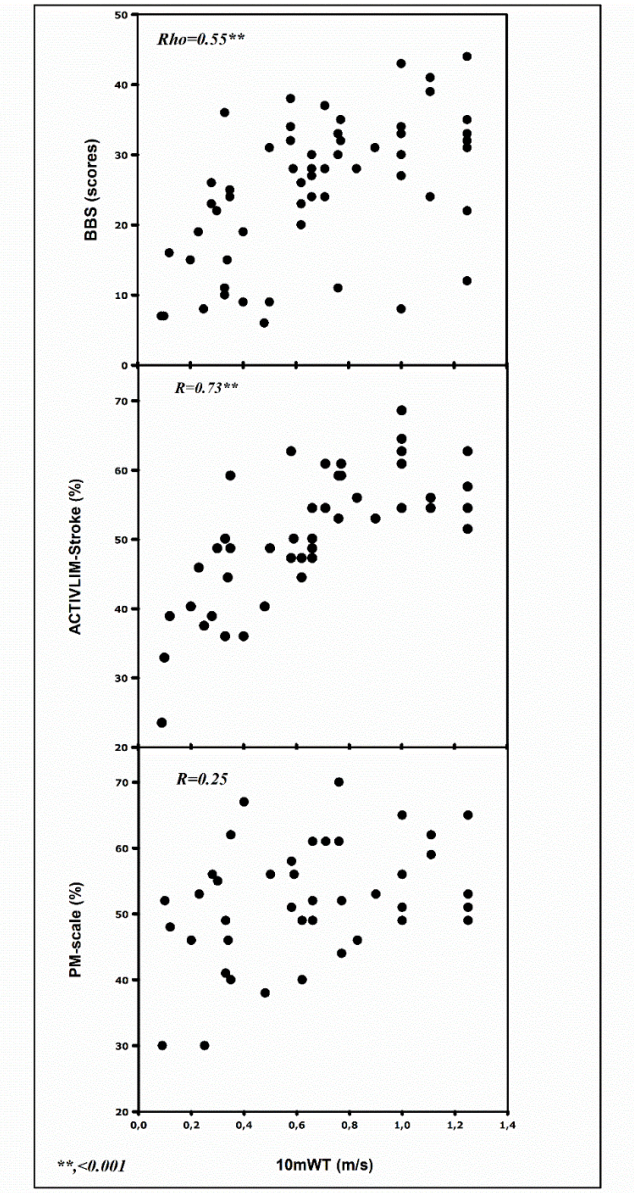

***Figure 6*: Association between walking speed and balance (BBS scores); activity limitation (ACTIVLIM stroke scale) and social participation (PM-scale[3])**

[3] This figure has been modified to put the dependent variable on the x-axis

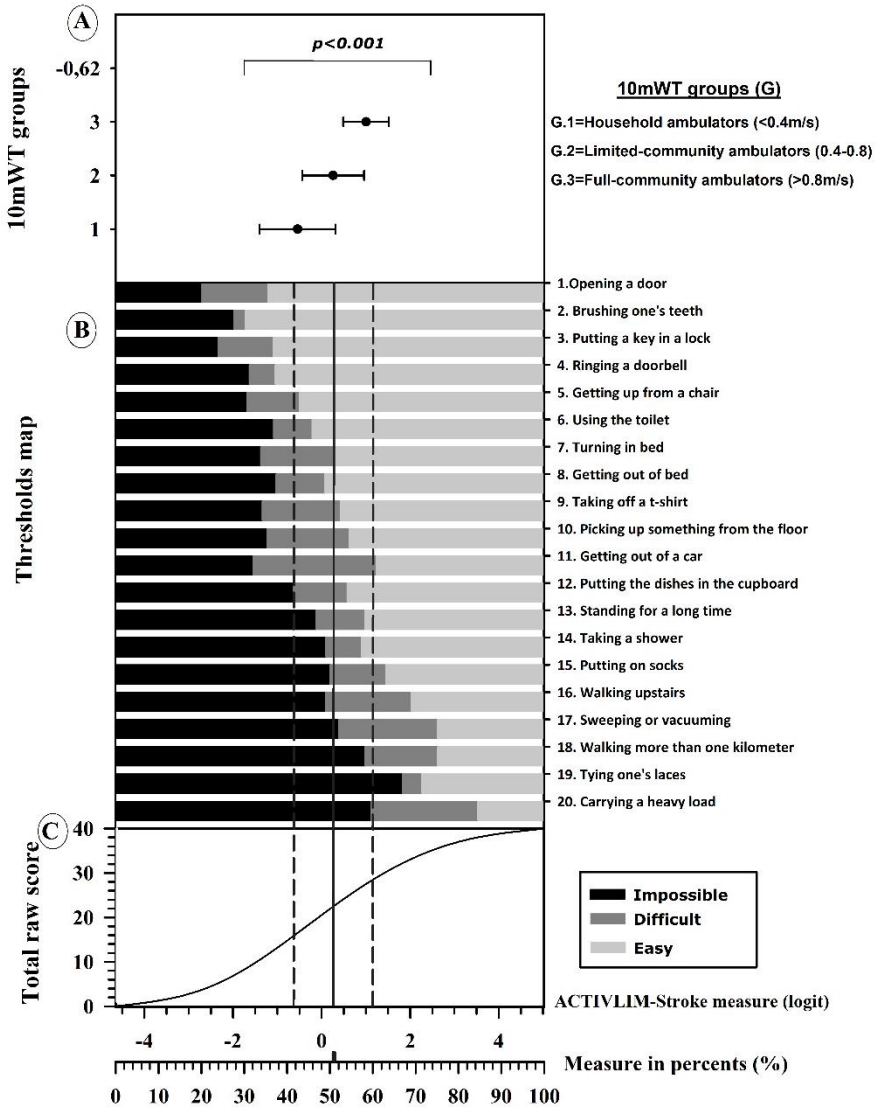

Figure 7. Description of the activity limitation outcome[4]

[4] This figure has been modified and interpreted to fit the partial credit model originally used to develop the scale.

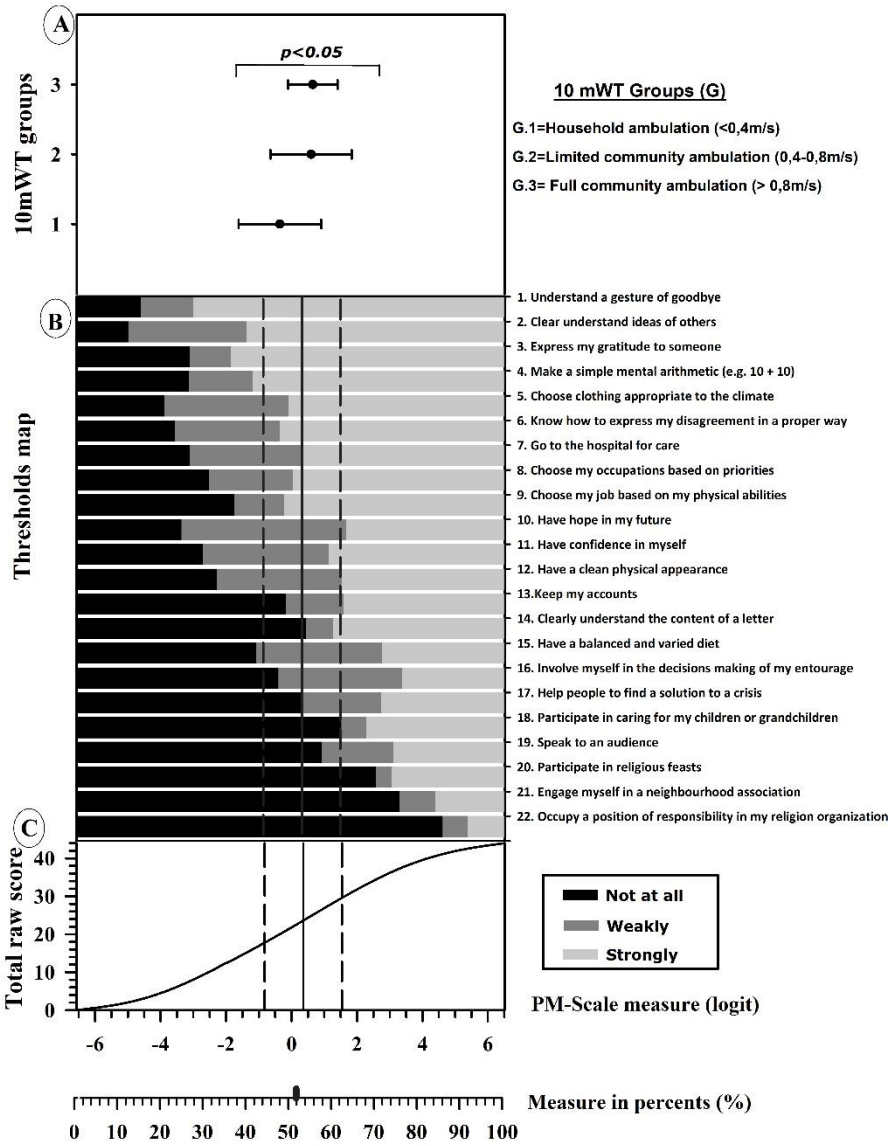

***Figure 8**. Description of the social participation outcome.*

1.5. Discussion

The present study described the level of balance impairments, the ability to perform ADLs and social participation and examined their relationships with walking speed, among people at the chronic stage of stroke in Burundi, a low-income country. Firstly, we found that most patients experienced poor balance indicative of a risk of falling, low walking speed, moderate ADL limitations and social participation restrictions. Additionally, household ambulators (low walking speed) showed high ADL limitations and moderate social participation restrictions, and there was a moderate and significant relationship between walking speed and balance. ADL limitation scores correlated strongly with walking speed, such that lower walking speeds were associated with more limitations. Walking speed did not correlate with social participation.

Impaired balance affects the ability of stroke patients to walk whether in developed or low-income settings. The low walking speed and poor balance in our sample may be linked to mainly limited early stroke management and access to rehabilitation in low-income settings as has been shown in previous studies (Bernhardt et al., 2020; Urimubenshi et al., 2018). According to his systematic review, Urimubenshi (2018) concluded that stroke care in Africa fell below the recommended standards and invited African policy makers and health care professionals to combine efforts to improve access to organized stroke care. Recently, there has been a call to action aimed at developing and delivering cost-effective and equitably accessible rehabilitation services in low and middle-income countries (Bernhardt

et al., 2020). Studies examining the frequency of balance impairments following a stroke (Chang et al., 2015; Kossi et al., 2021; Vincent-Onabajo et al., 2018) have reported prevalence rates ranging from 16.7% (Vincent-Onabajo et al., 2018) to as high as 83% (Chang et al., 2015; Kossi et al., 2021). The present finding of a higher walking speed being related to good balance is consistent with prior studies (Obembe et al., 2014; Ojagbemi & Owolabi, 2013). Balance disorders are characterized by a short support time and an asymmetrical left versus right step length, which leads to a slow walking speed (Khan & Chevidikunnan, 2021). Two major goals of rehabilitation are to enable or improve walking ability and to promote independence in ADLs, both of which are highly dependent upon standing balance (Kossi et al., 2019).

Overall, participants in this study showed limitations affecting about half of the assessed ADLs, confirming the persistence of substantial activity limitations in the chronic phase of stroke. These results are consistent with those of a 2019 study carried out in a comparable context of low-income countries (Kossi et al., 2019). In that study, Kossi et al. observed a mean activity level of 55% on the ACTIVLIM-Stroke scale in a sample of 64 stroke survivors 6 months poststroke. In 2020, Mwaka-Rutare et al. (Mwaka-Rutare et al., 2020) reported relatively higher ACTIVLIM-Stroke scores in stroke survivors with a longer post-stroke recovery period (average of 38 months). Their sample's mean activity level was estimated to be 69%, whereas the overall level observed in our study was 51%. Given the similar socioeconomic contexts of the three studies, the differences in ADL ability levels might be attributed to baseline clinical characteristics of

the samples, such as disability level. Consistent with this possibility, the mean walking speed of Mwaka-Rutare et al.'s sample (0.9 m/s) was higher than that of both our sample (0.68 m/s) and Kossi et al.'s sample (0.73 m/s).

According to the ICF, walking is a critical component in enabling the performance of ADLs and social participation for stroke patients (Geyh et al., 2004). A limited ability to walk following a stroke restricts patients' independence and mobility at home and in the community (Schmid et al., 2007). In our study, walking speed distinguished between individuals who had different ADL levels well. High walking speed was associated with better ADL performance scores. Compared with household and limited-community ambulators, participants with full community ambulation status reported higher ADL levels. Similarly, in their study in the Democratic Republic of Congo with a socio-economic context similar to that of the present study, Mwaka-Rutare et al. (Mwaka-Rutare et al., 2020) likewise found that higher walking speeds were associated with better performance of basic ADLs. Additionally, our findings seem to be consistent with those of a 2007 study by Schmid et al. (Schmid et al., 2007) in a high-income context, wherein progression from one walking speed-based category to another was associated with ADL gains.

Walking speed in the present study did not discriminate among participants' social participation levels well, consistent with previous studies (Mwaka-Rutare et al., 2020; Schmid et al., 2007). This indicates that a high walking speed is no longer a priority for the patient in the chronic phase of the stroke, but a number of factors such as impairment, depression, social support etc. remain determinants of social

participation in both the acute and chronic phase (Elloker et al., 2018; Kossi et al., 2019). However, we obtained a lower optimal walking speed cut-off for distinguishing social participation (0.5 m/s) than was applied by Mwaka-Rutare et al. (Mwaka-Rutare et al., 2020) and Schmid et al. (Schmid et al., 2007) (>0.8 m/s). First, these differences in optimal walking speed cut-offs for social participation may be consequent to our sample being younger on average (52.1 ± 11.4 years) than the samples in these two prior studies (58.4 ± 12.9 years (Mwaka-Rutare et al., 2020) and 71.0 ± 10.64 years (Schmid et al., 2007). Young patients are likely to develop better active coping strategies that may contribute to limiting the impact of the reduced walking speed on social participation. Second, the nonsignificant associations of walking speed with social participation scores, in chronic stage of stroke, suggest that the optimal cut-off walking speed may be sufficient to enable good social participation, which would support the assumption that social support may be the main factor in enabling social participation without a strict dependence on a fluent walking speed (Elloker & Rhoda, 2018; Mairami et al., 2020). Third, the optimal walking speed cut-off of 0.5 m/s found in this study raises questions about the applicability of Perry et al.'s walking speed classification system in socioeconomic contexts that differ from the context where it was developed (i.e., the Los Angeles metropolitan area in the USA). In practice, requirements for safe community walking may differ across locations depending on contextual factors, such as environmental adaptations, the availability and affordability of technical assistance apparatuses, and social supports. Further studies should investigate walking speed cut-offs that are well-suited to an African context.

There are several implications of the present findings for clinicians involved in rehabilitation after stroke in low-income settings. Our findings suggest that interventions aimed at improving balance and enhancing walking speed may be useful in promoting long-term ADL abilities. Although our results did not affirm a clear association between walking speed and social participation, probably due to socioeconomic context, there is some evidence indicating that ADL level may be a key determinant of social participation in the subacute and chronic phases of stroke (Kossi et al., 2019).

Study strength and limitations

This study is the first to report the functional recovery of people post-stroke in Burundi, a low-income country. Functional recovery in our sample was evaluated with socioculturally adapted tools and in accordance with the ICF, considering impairment, activity limitations and participation restrictions. Nonetheless, our findings need to be interpreted in light of some potential limitations. Firstly, because we excluded patients with major cognitive impairments, severe disability, and/or with an unclear diagnosis, our findings may not be generalized to the whole stroke population in Burundi. Secondly, despite the statistical normality of the distributions, the unequal numbers of participants in the three groups could have influenced the statistical analyses. In addition, the use of patient-reported outcome tools to assess activity limitations and participation restrictions could generate a recall bias, but we believe that the use of culturally valid Rasch-based questionnaires limits this risk of bias. Finally, Perry's walking speed classification may not be well-suited to the context of low-income

countries given the relatively low average age of their populations and their poorer access to rehabilitation services compared to that in most developed countries.

1.6. Conclusion

Participants in the current study presented major balance impairments with a high risk of falling, low walking speed, moderate ADL limitations, and moderate social participation restrictions. Walking speed was confirmed to be associated with balance ability and ADL levels. A high walking speed was associated with better functional performance while a moderate speed was sufficient to enable social participation. During the rehabilitation process, particularly in chronic stage, a special emphasis should be placed on balance and walking speed. Training targeting walking speed and balance can be achieved at a low cost, making it well suitable for low-income settings.

Acknowledgments

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

All authors contributed to the study design and conception. J-L.T. and O.K. supervised the data collection. F.N., I.N. and A.S. undertook recruitment of participating centres and patients and managed the data,

including quality control. F.N., J.-L.T. and O.K. provided statistical advice on study design and analysed the data. F.N. drafted the manuscript, and all authors contributed substantially to its revision. O.K. takes responsibility for the paper as a whole. J.-L.T. and O.K. chaired the data oversight committee.

Data availability

Data are available from the corresponding author under reasonable request.

Disclaimer

The views expressed in this article are those of authors and not an official position of the institution

CHAPTER II (Study 2)[5]

Effectiveness of walking training on balance, motor functions, activities, participation and quality of life in chronic stroke survivors: A systematic review with meta-analysis and meta-regression of recent randomized controlled trials

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[5] As this chapter is already published, responses to the jury members were added to the manuscript as footnotes.

2.1. Abstract

Purpose*:* To review and quantify the effects of walking training for the improvement of various aspects of the functioning of people with chronic stroke.

Methods: We conducted a systematic search and meta-analysis of randomized controlled trials (RCTs) of chronic stroke rehabilitation interventions published from 2008 to 2020 in English or French. Of the 6476-screened articles collated from four databases, 15 RCTs were included and analyzed. We performed a meta-regression with the total training time as dependent variable in order to have a better understanding of how did the training dosage affected the effect sizes.

Results*:* Treadmill walking training was more effective on balance and motor functions (standardized mean difference (SMD)=0.70[0.02, 1.37], p=0.04) and 0.56[0.15, 0.96], p=0.007 respectively). Overground walking training improved significantly walking endurance (SMD=0.38[0.16, 0.59], p<0.001), walking speed (SMD=0.12[0.05, 0.18], p<0.001), participation (SMD=0.35[0.02, 0.68], p=0.04) and quality of life (SMD=0.46[0.12, 0.80], p=0.008). Aquatic training improved balance (SMD=2.41[1.20, 3.62], p<0.001). The Meta-regression analysis did not show significant effect of total training time on the effect sizes.

Conclusion: Treadmill and overground walking protocols consisting of ≥30 min sessions conducted at least 3 days per week for about 8 weeks are beneficial for improving motor impairments, activity limitations, participation, and quality of life in people with chronic stroke.

***KEYWORDS*:** walking training, overground walking, treadmill walking, physical activity, stroke.

Implications for Rehabilitation

- Treadmill walking training is effective for improving balance and motor functions.
- Overground walking training improved significantly walking endurance, walking speed, participation and quality of life.

Aquatic training improved balance.

CHAPTER II : Effectiveness of walking training on balance, motor functions, activities, participation and quality of life in chronic stroke survivors: A systematic review with meta-analysis and meta-regression of recent randomized controlled trials

2.2. Introduction

Stroke remains a major global health problem and its importance in public health is expected to increase (Adoukonou et al., 2020; Adoukonou et al., 2018; Adoukonou et al., 2021a; Feigin et al., 2014) as many countries are undergoing population aging and health transitions associated with economic development (Feigin et al., 2015; Thrift et al., 2017). According to the Global Burden of Stroke project, stroke is the second leading cause of death worldwide (11.8%) (Katan & Luft, 2018). Moreover, stroke is a leading cause of long-term disability that can disrupt the ability of affected patients to walk, get in and out of their beds and chairs, and dress themselves (Adoukonou et al., 2018; Kossi et al., 2016; Krishnamurthi et al., 2014). One of the main goals for patients who have suffered a stroke to enable them to regain independence and improve quality of life (QoL) is recovering the ability to walk. In the chronic phase of stroke, motor recovery stabilizes and patients need to develop compensatory adaptations to their environments (Falcon et al., 2016).

Physical inactivity due to poststroke disability can lead to an increased risk of cardiovascular diseases (Roger et al., 2012). The American Heart Association recommends that stroke survivors engage in 20–60 min of aerobic exercise at least 3 days per week, supplemented with resistance training as well as balance and stretching exercises, to improve muscular strength, gait, and balance, and to prevent cardiovascular complications (Gordon et al., 2004). Cardiorespiratory training and, to a lesser extent, mixed training have been shown to reduce disability and improve mobility, balance, and cardiorespiratory

fitness (Saunders et al., 2020). Moreover, a variety of physical exercises have been shown to be beneficial to chronic phase stroke survivors (Han et al., 2017), including walking trainings (Ilunga Tshiswaka et al., 2018; Kim et al., 2014), treadmill training (Drużbicki et al., 2015; Munari et al., 2018), progressive resistance training (Dorsch et al., 2018; Flansbjer et al., 2012) and cycling (S. J. Kim et al., 2015), among others.

Walking is a low to moderate intensity aerobic exercise that can be performed with or without equipment, alone or with a group, and at one's own pace, making it an ideal form of exercise for stroke survivors. Treadmill walking is highly modifiable owing to a wide range of speed and inclination settings with the presence of support handrails, whereas overground walking does not require equipment and can be easily incorporated into daily life. The use of the walking robot has shown its effectiveness especially in the acute and subacute stage but financial access may limit its use (Shakti et al., 2018; Watanabe et al., 2017). The advantages of robot-assisted training, compared to treadmill training were suggested to be a longer training duration, reproducible symmetrical gait kinematic patterns of the leg movements, hands-free operation by a single therapist, and reduction in the physical load imposed upon the therapist (Mehrholz et al., 2020; Peurala et al., 2014). A recent systematic review (Mehrholz et al., 2020), suggests that stroke patients who receive electromechanical-assisted gait training in combination with physical therapy are more likely to achieve independent walking than patients receiving gait training without these devices.

The relative benefits of treadmill walking, overground walking and robot-assisted walking trainings remains unclear in terms of the improvement of motor functions, activity, participation and quality of life in chronic stroke survivors. In 2014, Peurala and colleagues (2014) have explored the effectiveness of walking training on walking capacity and self-care in patients with stroke, but they did not assess the effect on motor functions, participation and quality of life that are important goals of rehabilitation in particular in people with stroke. Therefore, the purpose of the present systematic review, meta-analysis and meta-regression was to review and quantify the effects of various walking training protocols versus other physical exercises for the improvement of balance, motor functions, walking endurance, walking speed, participation, and quality of life in people with chronic stroke.

2.3. Methods

This study was performed in accordance with a previously established protocol registered on the international prospective register of systematic reviews, PROSPERO (https://www.crd.york.ac.uk/PROSPERO/; registration number: CRD42018092246). Our study complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Moher et al., 2009). Methodological issues were solved with the guidance of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2019).

Description of the intervention

Walking is a physical activity in which the body advances at a slow to moderate pace by moving the feet in a coordinated fashion (*PubMed*, *Mesh Database*) (Taylor et al., 1985). Walking training is therefore any activity/exercise that involves walking including recreational or free-living walking within the community, walking for fitness, and competitive race-walking as well as rehabilitative walking training (e.g., walking with expensive robotics, body weight supported training, aquatic pool floor walking).

Comparators/controls

We considered all active control groups different from walking training interventions, and nonactive control groups including stretching training, massage, social and educational class, nonintervention, etc.

Identification and selection of studies

We conducted systematic searches of four electronic databases (Cochrane Library, Sciences Direct, Medline/PubMed and Scopus) for articles published in English or French from January 2008 to December 2018 and updated the search in August 2020. The search included terms relating to or describing walking training or any physical exercise therapy in people post-stroke. The search strategy was adapted to each database, combining keywords and MeSH terms where applicable. Reviews and retrieved publication references were hand-searched for potentially suitable articles. The full search process is presented in supplementary material 2.

Inclusion criteria

Included studies were randomized controlled trials (RCTs) fulfilling the following criteria: Participants were adult people post-stroke (age ≥ 18 years) diagnosed according to the World Health Organization definition (WHO, 1989) or confirmed by imaging for which 6 months has passed after their stroke; physical exercise during recovery included walking training (intervention group) or any other conventional rehabilitation therapy treatment, physical exercise, or placebo (comparison group); and outcome data included impairment level (balance, motor impairment), activity level (walking endurance and speed, functional independence), community participation, and/or QoL. Functional independence is an individual's ability to perform activities of daily living (ADLs).

Data extraction and risk of bias assessment

The first and second authors screened titles and abstracts of all unique record for relevance independently. Full texts of selected papers were reviewed and extracted data were compiled in an Excel spreadsheet. Selections and ratings were compared for agreement and disagreement. Differences were discussed until consensus was reached between the first and second authors. If necessary, a third author was consulted. The corresponding authors of articles were contacted in cases of missing data. The risk of bias for each article was assessed by two reviewers using the Cochrane risk of bias tool (Higgins et al., 2011) which allow categorizing the risk of bias in RCTs in seven domains: random sequence generation, allocation concealment, performance

bias, detection bias, attrition bias, reporting bias, and other bias. For each item in the tool, the assessment of risk of bias is in two parts. The support for judgment provides a succinct free text description or summary of the relevant trial characteristic on which judgments of risk of bias are based and aims to ensure transparency in how judgments are reached. The second part of the tool involves assigning a judgment of high, low, or unclear risk of material bias for each item.

Data synthesis, subgroup and sensitivity analysis

We carried out subgroup analysis of comparable studies by stratifying the results by intervention type. Our subgroup analysis was focused on comparing different walking trainings. To ensure the robustness of evidence, we performed sensitivity analysis to assess the impact of studies with poor methodological quality by excluding them from the initial analysis. A pre-set cut-off point of ≥50% was used to select trials for the sensitivity analysis. We assessed how sensitive the results of the meta-analysis were in relation to quality of included trials.

Statistical analysis

Statistical analyses were performed in Review Manager version 5.3 software under a random effects model (Borenstein et al., 2010). Standardized mean differences (SMDs) with 95% confidence intervals (CIs) were reported (Ensor et al., 2018). The SMD is an index of intervention effect size relative to the variability observed in a study. A SMD of zero indicates no treatment effect compared to a control condition (equivalent effect). However, for the walking speed we calculated the mean differences (MDs). Thereby, the reader could have

a better understanding of the absolute effect of the walking trainings on walking speed. Sample heterogeneity is reported in terms of I^2, the variance percentage attributable to study heterogeneity. An I^2 value of 50% or higher indicates the presence of substantial heterogeneity. The criterion for statistical significance was $p<0.05$.

2.4. Results

A total of 6476 possibly relevant studies were identified in our electronic database searches. After removal of duplications, screening of titles and abstracts, and reviewing of full texts, 15 RCTs met the inclusion criteria and were included in the qualitative and quantitative analyses. A flowchart of the study selection process is presented in Figure 9.

Study 2 : Effectiveness of walking training on balance, motor functions, activities, participation and quality of life in chronic stroke survivors: A systematic review with meta-analysis and meta-regression of recent randomized controlled trials

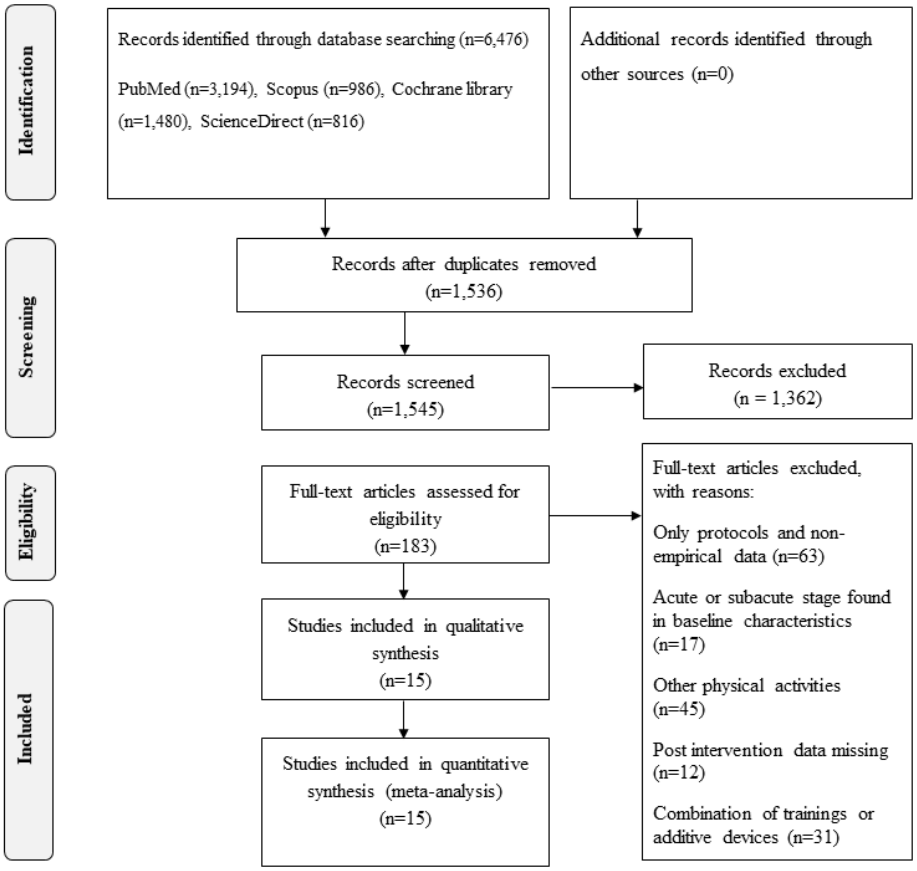


Figure 9: Flowchart of study selection.[6]

Study characteristics

The 15 included studies involved 653 participants (324 in walking training intervention groups and 329 in control groups). These studies investigated the effects of walking training on balance and motor function, activity (endurance, walking speed, and functional independence), community participation, and quality of life. The

[6] the deletion of more than 1500 duplicates is understandable given that 4 databases were consulted with an equation grouping several terms.

sample characteristics are summarized in supplementary materials 2, table 1. The studies' durations ranged from 2 weeks to 48 weeks, with a predominant interval in the range of 4–12 weeks. Mean participant ages for the studies ranged from 50 to 76 years. The 15 studies were divided into five subgroups based on walking training intervention type: treadmill, n = 4; overground, n = 7; robot-assisted, n = 3; and aquatic training, n=1.Table 3 presents the exercise modalities in the experimental group of the included studies. The median duration of sessions was 30 min, with a median frequency of 3 times per week. Protocols were conducted for a median period of 8 weeks.

Table 3: Exercise modalities of experimental interventions.

Authors (year)	**Volume/session,** min	**Frequency,** times/week	**Protocol duration,** weeks	**Total training time,** min
Ada (2013)	30	3	8	720
Fischer (2011)	60	3	8	1440
Globas (2011)	30	3	12	1080
Gordon (2013)	30	3	12	1080
Hornby (2008)	30	3	4	360
Kim (2014)	60	5	4	1200
Kim (2016)	30	5	6	900
Malagoni (2016)	20	6	10	1200
Mayo (2013)	30	6	52	9360
Mudge (2009)	30	3	4	360
Olawale (2011)	25	3	12	900
Park (2011)	60	3	4	720
Shaughnessy (2012)	40	3	24	2880
Stein (2014)	60	3	6	1080
Yen (2008)	60	3	4	720
Median [P25 ; P75]	30[30 ; 60]	3[3 ; 3]	8[4 ; 12]	1,000[720 ; 1200]

P= Percentile.

Methodological quality and risk of bias assessment

The methodological quality assessment data for each of the included studies are reported in Table 4. In summary, the study ratings were as follows: 3 (20%) excellent methodological quality (high quality); 6 (40%) good methodological quality (moderate quality); 4 (26.67%) fair methodological quality (low quality); and 2 (13.33%) poor methodological quality. Table 5 presents the risk of bias assessment in the included studies. Overall, 86.67% of studies presented low risk of bias with respect to random sequence generation, 73.33% with incomplete outcome data, 60% with allocation concealment, 40% with blinding of outcome assessment, 33.33% with selective reporting while 80% presented high risk of bias with respect to blinding of participants and personnel criteria.

Table 4: Methodological quality assessment of included studies with PEDro scale

Study	A	B	C	D	E	F	G	H	I	J	Score/10	Level
Ada et al. (2013)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9	1
Fischer et al. (2011)	Y	Y	Y	NC	N	Y	Y	Y	Y	N	7	2
Globas et al. (2012)	Y	Y	Y	NC	NC	Y	Y	Y	Y	Y	8	1
Gordon et al. (2013)	Y	Y	Y	N	N	Y	Y	N	Y	N	6	2
Hornby et al. (2008)	Y	Y	Y	N	N	N	Y	N	Y	N	5	3
Kim et al. (2014)	Y	Y	Y	N	N	Y	N	N	Y	N	5	3
Kim et al. (2016)	Y	Y	Y	N	N	NC	Y	Y	Y	N	6	2
Malagoni et al. (2016)	Y	Y	Y	N	N	N	Y	Y	Y	N	6	2
Mayo et al. (2013)	Y	Y	N	N	NC	Y	N	Y	Y	N	5	3
Mudge et al. (2009)	Y	Y	N	N	Y	Y	Y	Y	Y	N	7	2
Olawale et al. (2011)	Y	N	N	N	N	N	Y	N	Y	N	3	4
Park et al. (2011)	Y	Y	Y	N	NC	N	Y	N	Y	N	5	3
Shaughnessy et al. (2012)	Y	N	N	N	N	NC	Y	N	Y	N	3	4
Stein et al. (2014)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	1
Yen et al. (2007)	Y	Y	Y	N	N	N	Y	N	Y	Y	6	2

Y = yes; N = no; NC = not clear
A = random allocation; B = concealed allocation; C = groups similar at baseline; D = participant blinding; E = therapist blinding; F = assessor blinding; G = <15% dropout; H = intention-to-treat analysis; I = between group difference reported; J = point estimate and variability reported.
Levels: 1 = score 8–10 (excellent quality); 2 = score 6–7 (good quality); 3 = score 4–5 (fair); 4 = score < 4 (poor quality).

Table 5 : Evaluation of the risk of bias in the included studies by the Cochrane risk of bias assessment tool

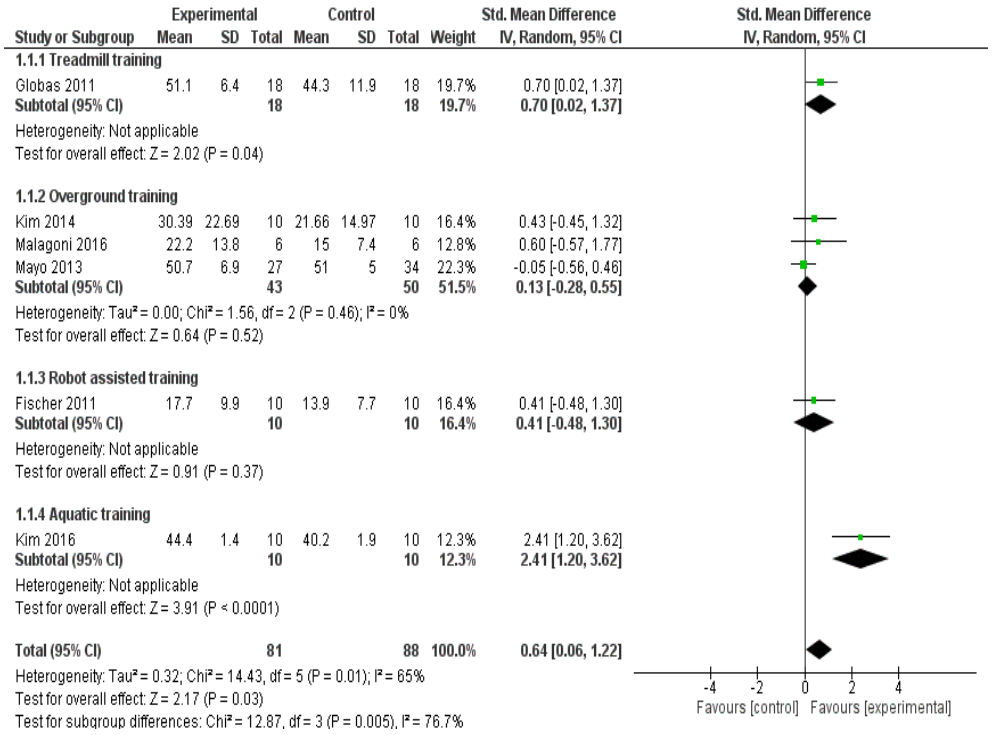
Studies	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Ada et al. (2013)	+	−	?	?	+	?	+
Fischer et al. (2011)	+	−	?	?	+	?	+
Globas et al. (2011)	+	+	−	?	+	+	+
Gordon et al. (2013)	+	?	−	+	+	+	+
Hornby et al. (2008)	+	+	−	−	?	+	?
Kim et al. (2016)	?	−	?	?	+	−	?
Kim et al. (2014)	+	+	−	+	+	?	+
Malagoni et al. (2016)	+	+	−	−	+	+	+
Mayo et al. (2013)	+	+	−	+	+	+	+
Mudge et al. (2009)	+	+	−	+	+	+	+
Olawale et al. (2011)	?	?	−	−	?	−	+
Park et al. (2011)	+	+	−	+	+	?	+
Shaughnessy et al (2012)	+	?	−	−	?	?	+
Stein et al. (2014)	+	+	−	+	+	?	+
Yen et al. (2008)	+	+	−	−	−	?	+

+, Low risk; −, High risk;?, Unclear

Effectiveness of walking training on body function

The effects of walking training on balance and motor function are shown in figures 10 and 11, respectively. A total of 6 studies involving 169 participants assessed balance impairments while a total of 3 studies involving 227 and participants assessed motor functions impairments. Balance was evaluated with the Berg Balance Scale (Globas et al., 2012; Hornby et al.2008, Mayo et al., 2013; Yen et al., 2008), Timed Up and Go or community walking balance test (Malagoni et al., 2016, Kim et al.2014 &2016), and/or Tinetti Balance Scale (Fisher et al., 2011) whereas motor functioning was assessed with the Motricity Index (Gordon et al., 2013), Stroke Impact Scale, hand function domain (Shaughnessy et al., 2012), and the 5-Chair Rise test (Globas et al., 2012). Our meta-analysis showed a significant overall beneficial effect of walking training on balance (SMD=0.64[0.06, 1.22], p=0.03; I^2=65%) and motor function (SMD=0.43 [0.16, 0.69], p=0.002; I^2=0%). Subgroup analysis showed that treadmill training improved significantly balance (SMD=0.70[0.02, 1.37]; p=0.04; I^2=0%) and motor function (SMD=0.56[0.15, 0.96]; p=0.007; I^2=15%) in people with chronic stroke.

Study 2 : Effectiveness of walking training on balance, motor functions, activities, participation and quality of life in chronic stroke survivors: A systematic review with meta-analysis and meta-regression of recent randomized controlled trials



<u>Figure 10</u>. Forest plot showing walking training effect on balance. The effect is shown by the standardized mean difference (SMD) of each subgroup and overall effect; significance at p < 0.05.[7]

[7] The data from Hornby and Stein's studies are not included in the forest plot of balance outcome because of their low methodological quality for sensitivity analyses.

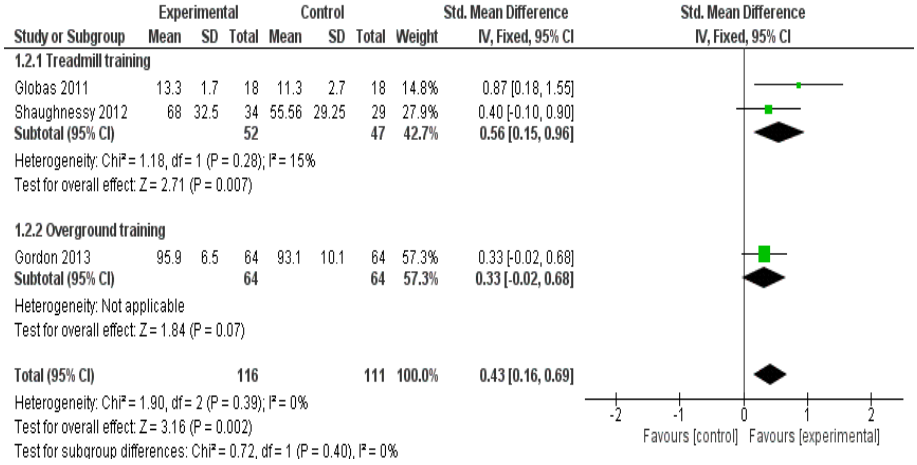


Figure 11. Forest plot showing walking training effect on motor function. The effect is shown by the SMD of each subgroup and overall effect; significance at $p < 0.05$.

Effect of walking training on activity limitation

The effects of walking training on endurance, walking speed, and functional independence are shown in figures 12-14, respectively. Walking endurance was measured by 6-minute walk test (Ada et al., 2013; Fisher et al., 2011; Globas et al., 2012; Hornby, 2008; Kim et al., 2014; Mayo et al., 2013; Mudge et al., 2009; Olawale et al., 2011; Park et al., 2011; Stein et al., 2014) and 3-minute walk test (Fisher et al., 2011) while walking speed was measured by 10-meter walk test (Ada et al., 2013; Fisher et al., 2011; Globas et al., 2012; Kim et al., 2016; Kim et al., 2014; Mayo et al., 2013; Mudge et al., 2009; Olawale et al., 2011; Park et al., 2011; Stein et al., 2014), 8-meter walk test (Fisher et al., 2011), and gait rite (Stein et al., 2014). Functional independence was evaluated by stroke impact scale, mobility and daily activities domains (Shaughnessy et al., 2012), instrumental activities of daily living “IADL” (Gordon,2013) Rivermead mobility Index (Park et al.,

2011), physical activity and disability scale (Mudge et al., 2009). Analysis of all walking training types together showed significant positive effects of the interventions on walking endurance (SMD=0.30[0.13, 0.47]; p<0.001; I^2=0%) and walking speed (SMD=0.09[0.04, 0.14]; p<0.001; I^2=0%). Subgroup analyses showed that overground training protocols improved walking endurance (SMD=0.38[0.16, 0.59]; p<0.001; I^2=0%) and walking speed (SMD=0.12[0.05,0.18]; p<0.01; I^2=0%). Our meta-analysis did not show a significant effect of walking training on functional independence (SMD=0.10[−0.14, 0.34]; p=0.4; I^2=0%).

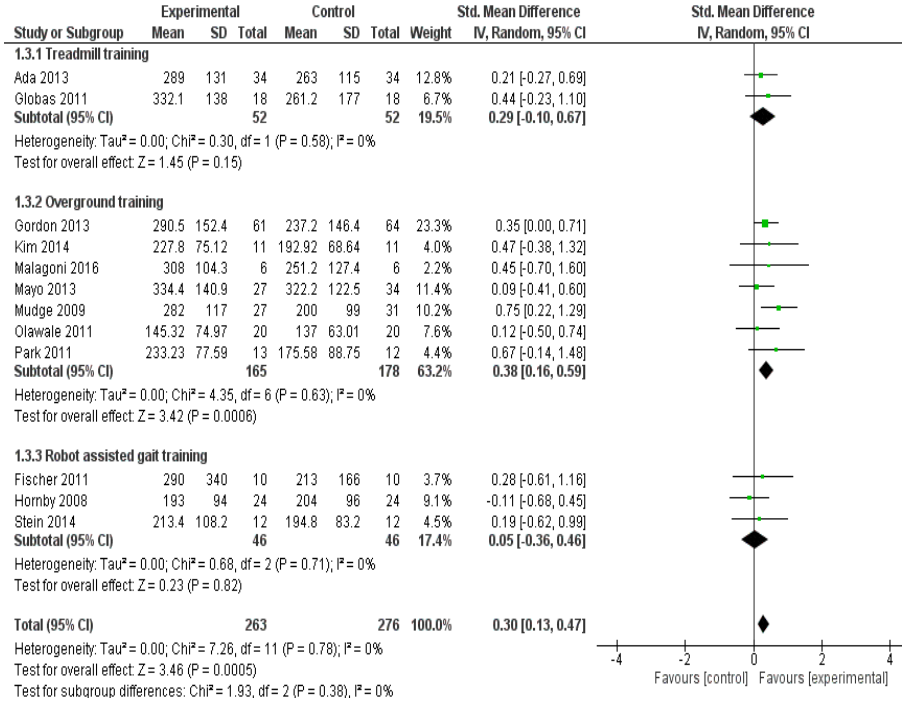
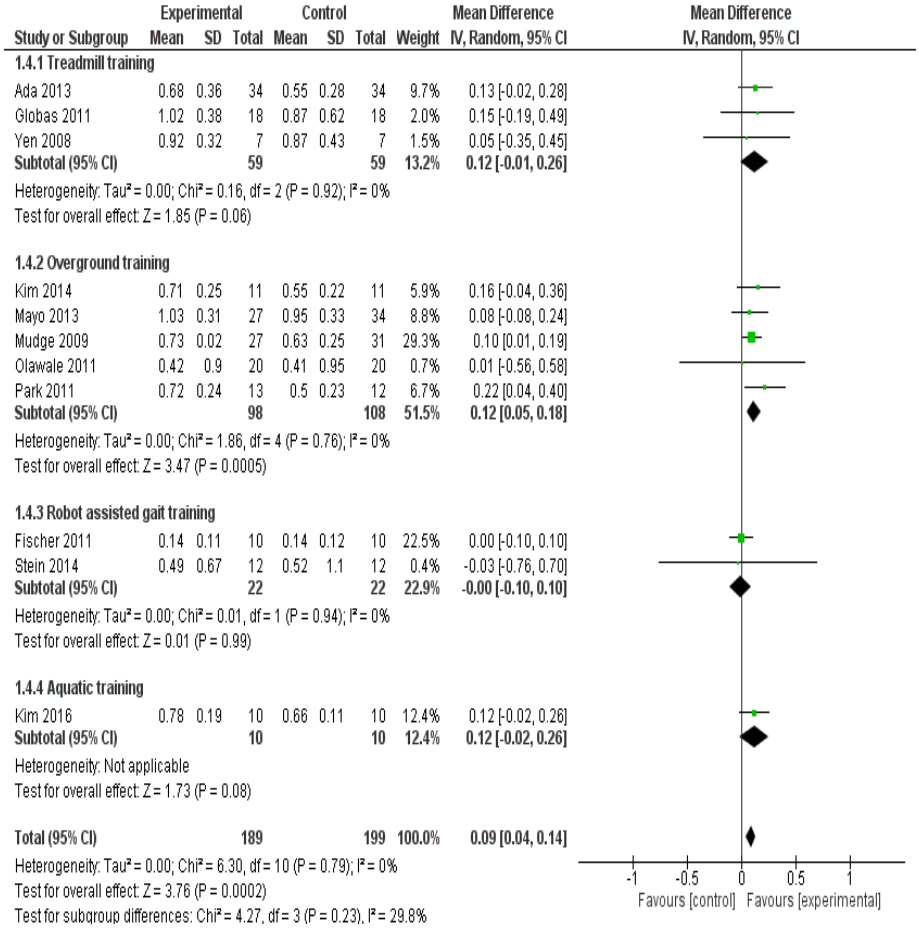


***Figure 12**. Forest plot showing walking training effect on walking endurance. The effect is shown by the SMD of each subgroup and overall effect; significance at p < 0.05.*



<u>Figure 13</u>. Forest plot showing walking training effect on walking speed. The effect is shown by the SMD of each subgroup and overall effect; significance at $p < 0.05$.

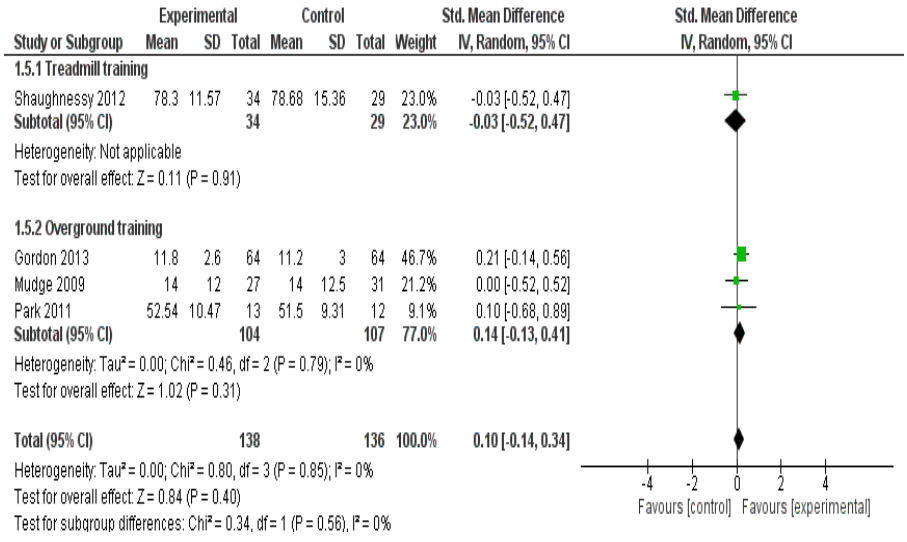


Figure 14. ***Forest plot showing the walking training effect on functional independence. The effect is shown by the SMD of each subgroup and overall effect; nonsignificant at p < 0.05.***

Effect of walking training protocols on social participation and quality of life

The effects of walking training on social participation and quality of life are shown in figures 15 and 16, respectively. Participation was measured in the included studies by the Adelaide Activity Profile (Ada et al., 2013), modified Emory Functional Ambulation Profile (Hornby et al., 2008), SF-36 (Mudge et al., 2009), and Stroke Impact Scale (Kim et al., 2014; Mayo et al., 2013; Shaughnessy et al., 2012), while quality of life was assessed by EuroQoL(Ada et al., 2013), short-form health survey SF-12 (Globas et al., 2012), SF-36 (Gordon et al.,

2013; Mayo et al., 2013), Stroke impact scale (Shaughnessy et al., 2012), and Physical functionning scale (Malagoni et al, 2016). Overall, no significant effect of walking training on participation was found (SMD=0.06[-0.40, 0.52], p=0.80, I^2=77%). Nevertheless, subgroup analyses showed a significant beneficial effect of overground training (SMD=0.35[0.02, 0.68] p=0.04, I^2=9%), but not treadmill or robot-assisted training. Overall, there was a significant effect of walking training on health-related quality of life (SMD=0.40[0.06, 0.75]; p=0.02, I^2=57%). In subgroup analyses, quality of life was significantly improved by overground training (SMD=0.46[0.12, 0.80], p=0.008, I^2=19%).

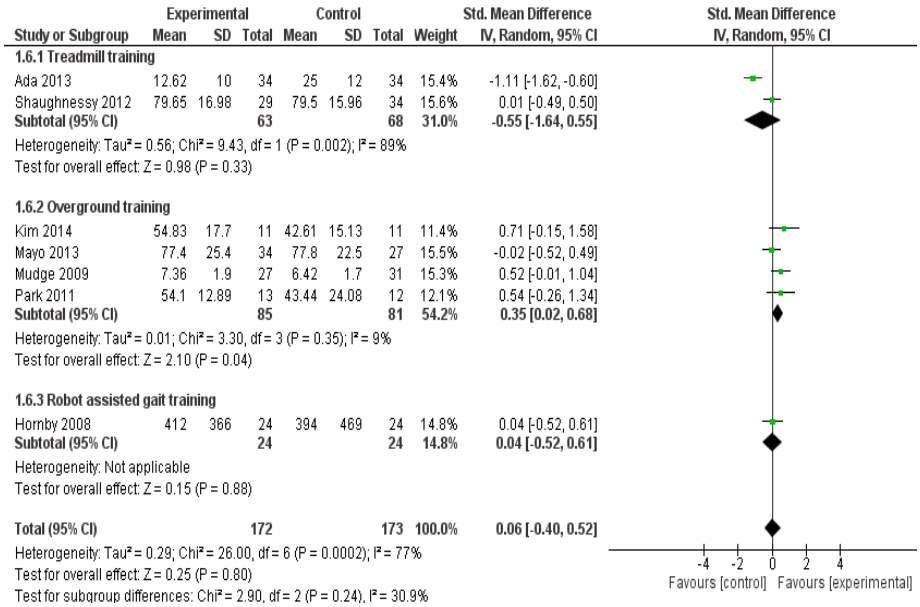


Figure 15. Forest plot showing walking training effect on participation. The effect is shown by the SMD of each subgroup and overall effect; nonsignificant at p < 0.05.

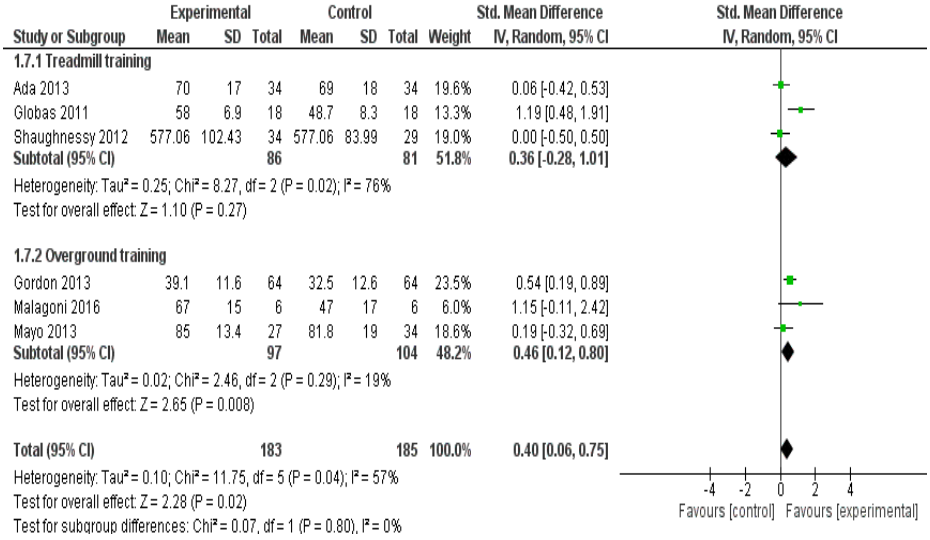


***Figure 16**. Forest plot showing walking training effect on quality of life (QoL). The effect is shown by the SMD of each subgroup and overall effect; significance at $p < 0.05$.*

Sensitivity and meta-regression analysis

Treatment significance effects remained similar across different analyses after excluding trials with PEDro scores <5 (Hornby et al., 2008; Kim et al., 2014; Mayo et al., 2013; Olawale et al., 2011; Park et al., 2011; Shaughnessy et al., 2012, Yen et al.2007). We conducted a meta-regression with the total training time as the independent variable in order to have a better understanding of how did the training dosage affected the effect size. Results of meta-regression analyses are summarized in Table 6. There is no evidence of a significant effect of total training time on the effect sizes.

Table 6. Main results for the meta-regression of the effect of total training time on the effect sizes

Variables & covariates	Coefficient	Standard error	95% CI	Z-value	p-value
Balance					
Intercept	1.02	0.38	0.27 - 1.76	2.68	0.007
Total training time	-0.01	0.01	-0.01 - 0.01	-1.29	0.196
Walking endurance					
Intercept	0.39	0.11	0.18 - 0.59	3.69	0.001
Total training time	0	0	-0.01 - 0	-1	0.316
Walking speed					
Intercept	0.09	0.03	0.04 - 0.16	3.27	0.001
Total training time	0	0	1.09 - 0.01	-0.37	0.713
Functional independence					
Intercept	0.15	0.21	-0.27 - 0.56	0.68	0.496
Total training time	0	0.01	-0.01 - 0.01	-0.17	0.868
Participation					
Intercept	0.56	0.21	0.15 - 0.98	2.66	0.008
Total training time	-0.01	0.01	-0.02 - 0	-1.24	0.216
Quality of life					
Intercept	0.56	0.27	0.04 - 1.09	2.12	0.034
Total training time	0	0.01	-0.02 - 0.01	-0.76	0.445

2.5. Discussion

This study provides an updated review of the current evidence related to the use of walking training protocols to improve functioning in chronic stroke patients and a foundation for developing evidence-based exercise prescriptions for this diagnosis group. We compared the effectiveness of walking training protocols with that of other physical exercises. Of the 15 RCTs (659 participants) included in this study, 4 evaluated treadmill training, 7 evaluated overground walking training, 3 evaluated robot-assisted gait training, and 1 evaluated aquatic training. Overall, Treadmill and overground walking protocols consisting of ≥30 min sessions conducted at least 3 days per week for at about 8 weeks are beneficial for improving motor impairments, activity limitations, participation, and quality of life in chronic stroke patients.

Our meta-analysis results indicated that treadmill-walking training can improve balance and motor function in the chronic stroke phase. Similarly, Ilunga Tshiswaka et al. (2018) found in their review that most studies evaluating overground or treadmill walking training demonstrated significant improvements in walking function. Furthermore, (Rensink et al., 2009) reported significant walking function improvement in their systematic review for groups of individuals using overground or treadmill training. In a systematic review by Pang et al. (Pang et al., 2013) found that aerobic exercise did not improve Berg Balance Scale scores; their findings are not in accordance with ours. Lloyd et al. (Lloyd et al., 2018) found no effect of training on motor impairments in a review involving only non-

ambulatory stroke survivors. All studies included in the present meta-analysis recruited patients with a minimal level of walking ability and therefore some minimal level of balance.

In the chronic stroke phase, patients can continue to develop motor-compensation strategies and walking training provides an opportunity to develop such compensatory skills. Treadmill and robot-assisted protocols enable walking with a reduced balance requirement relative to overground walking (Peurala et al., 2014). Fall prevention is an important clinical consideration in ambulatory stroke survivors (Bernhardt et al., 1998) and recovery of balance is essential for independence in daily living. Improvement of balance has been shown to be influenced by training intensity, with frequencies of at least five sessions a week of 30–60 min each producing significant improvements within 4 weeks (Hwang et al., 2015). Longer-term interventions (e.g. 12 weeks) appear to be needed to reduce the severity of motor impairments (Daly et al., 2011; Globas et al., 2012; Kossi et al., 2019).

Regarding activity limitations, our review showed that walking training programs improved walking endurance, walking speed, but not the functional independence. Specifically, only overground training protocols were found to be effective for improving both walking endurance and walking speed. These results underscore the fact that, even in the chronic stage of stroke, walking endurance can be improved. Recent studies issued similar conclusions (Lloyd et al., 2018; Pang et al., 2013; Saunders et al., 2020). Pang et al. (2013) concluded from their meta-analysis that aerobic training was more effective for enhancing walking endurance and maximum walking velocity than mixed

aerobic/strength training. Saunders et al. (2020) found that a fitness program led to increased walking capacity and self-selected speed. Lloyd et al. (2018) showed that assisted walking produced borderline significant improvement in walking endurance and walking independence. In a cohort study, (Karttunen et al., 2015) demonstrated that functional status and functional independence were improved by walking training. On the contrary, Pang et al. (2013) and Saunders et al. (2016) found no significant effect of walking training and cardiorespiratory training on Functional Independence Measure (FIM) scores, though studies using other assessment tools (e.g. Barthel Index, Frenchay Activities Index, Nottingham Extended Activities of Daily Living Scale) did find significant effects of walking training on functional independence (Globas et al., 2012; Letombe et al., 2010).

Walking endurance has been identified as a key area of difficulty for people with stroke (Mayo et al., 1999). Though any aerobic activity would be expected to improve cardiorespiratory endurance, overground walking appears to be more effective for improving walking endurance in this population than treadmill training, perhaps because the former is more challenging compared to the later that induces passive movements at speeds selected by patients in accordance with their individual comfort levels (Hwang et al., 2015).

The commonly used FIM scale measures independence level in the performance of a wide range of daily activities, some of which are less likely to be influenced by exercise training (e.g. eating, grooming, swallowing, and bowel and bladder management). (Katz-Leurer et al., 2006) reported treatment effects selectively on FIM motor sub scores without a significant effect on total FIM scores.

Finally, it is noteworthy that our meta-analysis detected a significant effect of overground walking training on both participation and quality of life. Recent systematic reviews did not draw conclusions as to whether training can improve self-perceived health status or quality of life after stroke (Pang et al., 2013; Saunders et al., 2020), both of which are under-evaluated variables, having been evaluated in a limited number of trials with inconsistent results. More research is required to clarify the effects of aerobic exercise on these important outcomes.

Walking remains a priority for functional independence in the chronic phase of stroke (Jørgensen et al., 1995). Thus far, most studies assessing walking interventions in chronic stroke populations have involved assisted programs, such as exercises supported by therapists, body-weight supporting equipment, and/or robotic equipment. The use of electromechanical devices may be feasible within a rehabilitation setting, though we could not find any reports that included the costs of such devices, and cost, space, and staff training requirements can pose barriers, particularly for community setting interventions. Of the 15 walking training studies reviewed here, only 2 were undertaken in a community setting, highlighting an important gap in post discharge continuation of fitness training, particularly in a group format (Billinger et al., 2014). Although none of the studies in our meta-analysis included cost estimations, one recent study demonstrated the cost-effectiveness (Collins et al., 2018) of a clinically effective community-based fitness training program for ambulatory stroke survivors. More health-economic data are needed to enable the development of such services.

Study strengths and limitations[8]

The present study provides an updated review of the current evidence related to the use of walking training protocols to improve functioning in chronic stroke patients. Our methodology complies with the Cochrane's guidelines for systematic reviews of interventions and the PRISMA statements. Period of twelve years considered in this study gives a possibility of thorough analyzes concerning walking training in stroke rehabilitation; thereby providing an opportunity for a detailed review of the literature on this particular topic.

However, this study had some limitations. Firstly, because we restricted our search to studies published in English or French, relevant studies in other languages may have been missed. Secondly, this meta-analysis did not include follow-up analysis because many of the reviewed studies did not report follow-up data. Therefore, our results do not provide evidence of long-term effects.

2.6. Conclusion

The present meta-analysis indicates that treadmill and overground walking training programs are effective for improving balance, motor functioning, walking speed, endurance, participation and quality of life in chronic stroke survivors. Hence, reductions in global disability indices following walking training may be mediated largely by mobility improvements. Walking training frequency should be fairly high (~3

[8] As the magnitude of change was not reported and still considered low, no clinical conclusion can be drawn.

times per week) for about 8 weeks and training sessions should last ≥30 min to be effective for improving walking performance.

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Author contributions

Conceptualization was done by Félix Nindorera, Ildephonse Nduwimana, Jean-Louis Thonnard, and Oyéné Kossi. Protocol draft was done by Félix Nindorera, Ildephonse Nduwimana, Jean-Louis Thonnard, and Oyéné Kossi. Development of the search strategy was done by Félix Nindorera, Ildephonse Nduwimana, and Oyéné Kossi. Data extraction and synthesis was done by Félix Nindorera, Ildephonse Nduwimana. Writing—review & editing was done by Félix Nindorera, Ildephonse Nduwimana, Jean-Louis Thonnard, and Oyéné Kossi. Supervision by Oyéné Kossi

Disclosure statement

The authors report no declarations of interest.

CHAPTER III (Study 3)

Effect of mixed and collective physical activity in chronic stroke rehabilitation: A randomized cross-over trial in low-income settings.[9]

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[9] As this chapter is already published, responses to the jury members were added to the manuscript as footnotes.

3.1. Abstract

***Background**:* The prevalence of physical inactivity after stroke is high and exercise training improves many outcomes. However, access to community training protocols is limited, especially low-income settings.

***Objective**:* To investigate the feasibility and efficacy of a new intervention: Circuit walking, balance, cycling and strength training (CBCS) on activity of daily living (ADL) limitations, motor performance, and social participation restrictions in people after stroke.

***Methods**:* Forty-six community-dwelling individuals with chronic stroke who were no longer in conventional rehabilitation were randomized into an immediate CBCS group (IG; initially received CBCS training for 12 weeks in phase 1), and a delayed CBCS group (DG) that participated in sociocultural activities for 12 weeks. In phase 2, participants crossed over so that the DG received CBCS and the IG performed sociocultural activities. The primary outcome was ADL limitations, measured with the ACTIVLIM-Stroke scale. Secondary outcomes included motor performance (balance: Berg Balance Scale [BBS], global impairment: Stroke Impairment Assessment Set [SIAS] and mobility: 6-minute and 10-metre walk tests [6MWT and 10mWT] and psychosocial health [depression and participation]). Additional outcomes included feasibility (retention, adherence) and safety.

***Results**:* ADL capacity significantly improved pre to post CBCS training (ACTIVLIM-stroke, +3,4 logits, $p < 0.001$; ES=0.87), balance (BBS, +21 points, $p < 0.001$; ES=0.9), impairments (SIAS, +11 points,

$p < 0.001$; ES=0.9), and mobility (+145 m for 6MWT and +0.37 m/s for 10mWT; $p < 0.001$; ES= 0.7 and 0.5 respectively). Similar improvements in psychosocial health occurred in both groups. Adherence and retention rates were 95% and 100%, respectively.

Conclusion*:* CBCS was feasible, safe and improved functional independence and motor abilities in individuals in the chronic stage of stroke. Participation in CBCS improved depression and social participation similarly to participation in sociocultural activities. The benefits persisted for at least 3 months after intervention completion.

Protocol Registration number: PACTR202001714888482

Keywords**:** community rehabilitation; group training; activities of daily living; motor performance; chronic stroke; low-income setting

CHAPTER III: Effect of mixed and collective physical activity in chronic stroke rehabilitation: A randomized cross-over trial in low-income settings

3.2. Introduction

Stroke is the second leading cause of death and the first cause of disability worldwide (Adoukonou et al., 2021b; Katan & Luft, 2018). Disability remains highly prevalent up to 3 years after stroke (Patel et al., 2006). More than 60% of people affected experience long-term balance and lower-limb impairments that interfere with their ability to complete activities of daily living (ADL) independently (Langhorne et al., 2009). Additionally, most stroke survivors continue to have reduced social participation, even after achieving relatively good recovery from their impairments (Kossi et al., 2019). Both ADL limitations and participation restrictions reduce the wellbeing of stroke survivors, and improvements in ADL and participation depend on several factors including access to rehabilitation (Mendis, 2013), socioeconomic context (healthcare coverage and social security) (Niama Natta et al., 2020), and cultural beliefs (Mbada et al., 2019).

Access to stroke prevention and treatment interventions is particularly challenging in low-resource settings (Brouwer et al., 2015), including in middle- to low-income countries where stroke tends to affect more young people in comparison with higher-income countries (Adoukonou et al., 2021b). The highest stroke incidence, prevalence, and case fatality rates are seen in sub-Saharan-Africa (Adoukonou et al., 2021b; Patel et al., 2006). Moreover, individuals in the chronic stage of stroke in low-income countries are at a high risk of dropping out of rehabilitation programs, mainly because of socio-economic factors (Brouwer et al., 2015; Mbada et al., 2019; Niama Natta et al., 2020).

Hence, there is an important unmet need for cost-effective community-based stroke rehabilitation strategies.

Physical inactivity is associated with an increased risk of cardiovascular disease and recurrent stroke (Roger et al., 2012). Physical activity is recommended for secondary prevention and rehabilitation (Billinger et al., 2014). Recreational, group-based community physical activity thus represents an attractive motivational and accessible strategy in stroke rehabilitation. Aerobic or mixed (aerobic and resistance) training programs have been shown to improve outcomes in people who are also participating in conventional rehabilitation programmes (Saunders et al., 2020). It is unclear how effective such training programs would be outside of a clinical environment with expensive equipment (walking robots, cycle-ergometers, treadmills, etc.) and how well multi-modal physical activity plans would be carried out in a group community setting with limited resources. Therefore, we set out to investigate the feasibility and efficacy of an inexpensive multimodal, structured group physical training program (Circuit walking, balance, cycling and strength; CBCS) in a sample of Burundian individuals in the chronic stage after stroke. Specifically, we aimed to assess the effect of CBCS training on impairments, balance, ADL limitations, participation restrictions and depression. We hypothesised that CBCS training would improve impairments, activity limitations and participation restrictions.

3.3. Methods

Study design, setting, and ethical considerations

This study was a two-arm, parallel-group, crossover and single-blind randomized controlled trial. It was conducted in a community facility attached to the National Teaching hospital (CHU Roi Khaled) in Burundi. The study protocol was approved by the National Ethics Committee (CNE/25/2019) and registered in the Pan African Clinical Trials Registry (https://pactr.samrc.ac.za/; no. PACTR202001714888482).

Participants

Potential participants were identified from hospitals and rehabilitation centres by consulting admission records. Identified persons who were living in the community and who had completed or dropped out of conventional physical therapy at the time of recruitment were invited to enrol. All invited participants were screened to ensure that they met our inclusion criteria: clinical diagnosis of primary or recurring unilateral stroke based on neuroimaging or a clinical neurological examination; chronic stroke stage (≥ 6 months since stroke); ≥ 18 years of age; ability to walk 10 m with or without an assistive device; and moderate disability (modified Rankin scale ≤ 3 (Banks & Marotta, 2007). People with a major cognitive impairment (Community Screening Interview for Dementia score ≥ 7) (Hall et al., 2000), aphasia, or with permanent degenerative damage were excluded. Participants were informed of the study objectives and that the

procedures conformed with the Declaration of Helsinki, and provided written consent.

Randomization and allocation

A public health researcher assistant not involved in the study used a computer-generated random allocation sequence to randomize the participants into 1 of 2 groups: immediate CBCS (IG) and delayed CBCS group (DG) using blocks according to age, disability, sex and study variables. The allocation was carried out with opaque, sealed envelopes.

Interventions[10]

The interventions were performed 2 hours/day, 3 times a week for 12 weeks (36 sessions: 72 hours). The content of the performed tasks is presented in the appendices.

Experimental intervention (CBCS)

The experimental group participants were split into 3 subgroups of 6-8 participants with similar within-subgroup disability levels for CBCS training. All participants performed a 15-min warm-up before training and a 15-min cool down with stretching after training. The training consisted of 30 min of circuit walking followed by 30 min of recreational activities intended to improve balance, coordination, and strength, as well as 30 min of cycling at 50–75% of their maximal heart rate (determined by Karvonen's formula) (Camarda et al., 2008). The

[10] As the full protocol of this study has not been published, the content of the exercises can be found in the appendices.

physical exercises included in CBCS are described in detail in the Supplementary Table. Disability level subgroups were trained concurrently, with each group randomly assigned to a CBCS component, such that while one group was walking, another was cycling, and the third was performing balance, strength, and coordination exercises. Shaping was adapted to each individual. To help increase the duration of targeted motor involvement, encouragement was given through verbal feedback, distance covered was tracked, and level of exertion was followed with heart rate monitors during walking and cycling. Activity intensity was increased as sessions progressed to promote energy expenditure.

Control intervention

While waiting to cross over to CBCS training, participants participated in a sociocultural intervention aimed to improve social interaction through 3 activities that did not involve energy expenditure: board games (Awalé and Checkers), cultural discourse and drama. The board game component was performed in randomly allocated subgroups of 6 to 7 participants. Awalé (a.k.a. awele) is an informal combinatorial board game created in Africa. It is the most widespread of the mancala family of games, a set of African count and capture games in which pebbles, seeds, or shells are distributed in bowls or holes, sometimes dug in the ground. Checkers is an informal combinatorial board game wherein each player captures the opponent's pieces. For each game, participants solely used their non-affected hand and progressed through learning, forming playoff groups, and competing phases. Playoff competitions for each game yielded top-four

finalists and then first and second place finishers were determined in a final match. After the board game period of each session, participants reformed groups of 4~6 people for the discourse and drama components. The drama "theatre" consisted of acting out cultural themes with the ultimate aim of making the audience laugh. Topics were offered for cultural discourse and drama (topic pools were updated every 2 weeks).

Assessment and outcome measures

Participants were assessed at four timepoints, T1–T4: T1, baseline (at enrolment); T2, at 3 mos. (immediately post-intervention); T3, at 6 mos. (after crossover); and T4, at 9 mos. (3-mo. follow-up). A blind assessor collected participant data according to each of the 3 International Classification of Functioning, Disability and Health (ICF) components, namely impairments, ADL limitations, and participation restrictions. Psychometric questionnaires were administered by face-to-face interview and clinical tests were conducted in the rehabilitation centre.

We used the Community Screening Interview for Dementia (CSI-D) and timed up-and go (TUG) test to evaluate baseline cognitive and mobility abilities. The CSI-D, was developed as a screening instrument for dementia. It consists of 2 components: a cognitive test for non-literate and literate populations and an informant interview regarding performance in everyday living (Hall et al., 2000). We administered only the former. Higher CSI-D scores reflect better cognitive abilities. The TUG test is an objective clinical measure of

functional mobility and balance, and thus the risk of falling. It measures the time taken for an individual to rise from a chair, walk 3 meters, turn, walk back and sit down (Chan et al., 2017).

Primary outcome: ADL limitations

The main endpoint was functional independence in ADL as measured by the ACTIVLIM-Stroke scale, a cross-cultural Rasch-built 20-item self-reported questionnaire instrument that is used to measure ADL limitations in people with stroke and presents good psychometric qualities (Charles Sèbiyo Batcho et al., 2014; Batcho et al., 2012). For each item, the participants rated a particular task on a 3-level scale: impossible (0), difficult (1), or easy (2). Total ACTIVLIM-Stroke raw scores (ranging from 0 "more limited" to 40 "normal") were subjected to logit and centile metric transformations via an online tool available at www.rehab-scales.org. The relationship between ordinal total score and linear measures (in %) was calibrated as described by Batcho et al. (Batcho et al., 2012). Higher scores indicate less difficulty with ADL.

Secondary outcomes of motor performance: global impairment, balance, and mobility

We evaluated global impairment with the Stroke Impairment Assessment Set (SIAS), a valid and reliable measure of global stroke impairment (Liu et al., 2002; Tsuji et al., 2000). It consists of 22 items that evaluate spasticity, aphasia, and motor impairment of the limbs on an ordinal scale. Each item was rated from 0 (severely impaired) to 3 (normal), except the limb motor function items, which were rated from 0 (severely impaired) to 5 (normal). The SIAS total score ranges from 0 (severely impaired) to 76 (normal).

The Berg Balance Scale (BBS), which is valid, reliable, and responsive, was used to assess balance impairment (Blum & Korner-Bitensky, 2008; Hiengkaew et al., 2012). The maximum total score on the BBS is 56 (higher score means better balance). The 95% confidence minimal detectable change (MDC_{95}) is 5 points (Hiengkaew et al., 2012). A BBS score ≤ 42 is predictive of risk of falling (Steffen et al., 2002).

The 6 min walk test (6MWT) and the 10 m walk test (10mWT) were used to assess mobility. Both are widely used as community walking indicators (Bohannon & Williams Andrews, 2011; Steffen et al., 2002). The 6MWT measures walking endurance based on the distance (recorded in m) walked within 6 min: participants are instructed to walk as fast as possible for 6 min on a 30 m pathway with the option to stop for fatigue at any point. For the 10mWT, participants were instructed to walk at a comfortable pace (Bohannon, 1997) over a 14 m marked pathway; they were timed over the middle 10 m distance. The fastest of 3 trials was used for the analysis.

Secondary outcomes of psychosocial health: depression and social participation

Depression was examined with the Hospital Anxiety and Depression Scale (HADS). The HADS is a questionnaire divided into an Anxiety and a Depression subscale both containing 7 intermingled items (Zigmond & Snaith, 1983). We considered a score of ≥ 8 on the depression subscale of the HADS to be indicative of the presence of at least mild depressive symptoms: that cut-off has good specificity (0.79) and sensitivity (0.83) (Bjelland et al., 2002).

Participation was measured with the Participation Measurement Scale (PM-Scale), a 22-item Rasch-built stroke-specific scale that refers to daily situations encountered by stroke survivors in Africa and has good psychometric qualities (Kossi et al., 2018; Kossi & Thonnard, 2018). Participants were asked to rate their perceived participation in item-specified activities on a 3-level scale: not at all (0); weakly (1); or strongly (2). PM-Scale raw scores were converted into logits and centiles at www.rehab-scales.org. Total PM-Scale raw scores range from 0 to 44; logit transformed scores ranged from –6.56 to 6.51 logits, corresponding to 0 to 100 centiles. Higher raw scores, logits, and centiles indicate greater participation.

Additional outcomes: feasibility and safety

Adherence was determined by session participation rate (attended sessions / total number of sessions × 100). Retention rate was the percentage of participants who completed the final follow-up assessment at T4. Adherence and retention were considered acceptable if the percentages were ≥ 80%. The percentage of participants who experienced adverse effects was recorded as a measure of safety.

Statistics

Sample size estimation

Sample size calculation was based on ACTIVLIM-Stroke scale scores derived from earlier studies (Batcho et al., 2014; Batcho et al., 2013). A mean improvement of 0.45 logits after a walking training intervention (Batcho et al., 2013) and a minimal clinically important difference (MCID) of 2.6 logits [2.63;3.62; 95% confidence interval of

mean] (Batcho et al., 2014) have been reported. With $\alpha = 0.05$ and $1-\beta = 0.8$, a minimum sample of 21 and a maximum of 27 per group were required. Considering a dropout rate of around 8%, we needed to include between 44 and 60 participants.

Data analysis

Descriptive statistics were used to summarize group characteristics. Quantitative variables with a normal distribution are reported as means with standard deviations (SDs), while ordinal and non-normally distributed data are reported as medians with interquartile ranges. Independent t-tests and non-parametric tests were used to compare baseline characteristics between the groups. Between-group differences over time were detected with two-way repeated-measures (2 × 4) analyses of variance (ANOVAs), the findings of which are reported as *p* values with post-hoc test results. The Benjamin-Hochberg test was used to confirm the Bonferroni post-hoc significance. Because homoscedasticity was sustained, the ANOVAs were conducted without transformation. The effect size was estimated using the value of the η^2, rated as small (0.01); medium (0.06) or large (≥0.14). Individual changes were analysed using the t-value (Anselmi et al., 2015) and the number (rate) of participants with an increase in score greater than the minimal detectable change (MDC) or the MCID was calculated. The participants were divided into 4 classes according to their t score significance limits: large improvement ($t \geq 1.96$), improvement ($0 < t < 1.96$), no change ($t = 0$), deterioration ($t < 0$). All analyses were performed in SPSS for Windows® (version 25.0, IBM, Chicago, IL) and the significance was set at <5%.

3.4. Results

Flow of participants and sample characteristics

Figure 17 shows the flow of participants. Of 336 potential participants who were identified, 103 were screened, and 58 matched the eligibility criteria. Among those, 46 were available to participate, were randomized into the immediate and delayed CBCS training groups and completed the study. The groups did not differ in demographic characteristics, baseline primary outcome values or secondary outcome measures (Table 8).

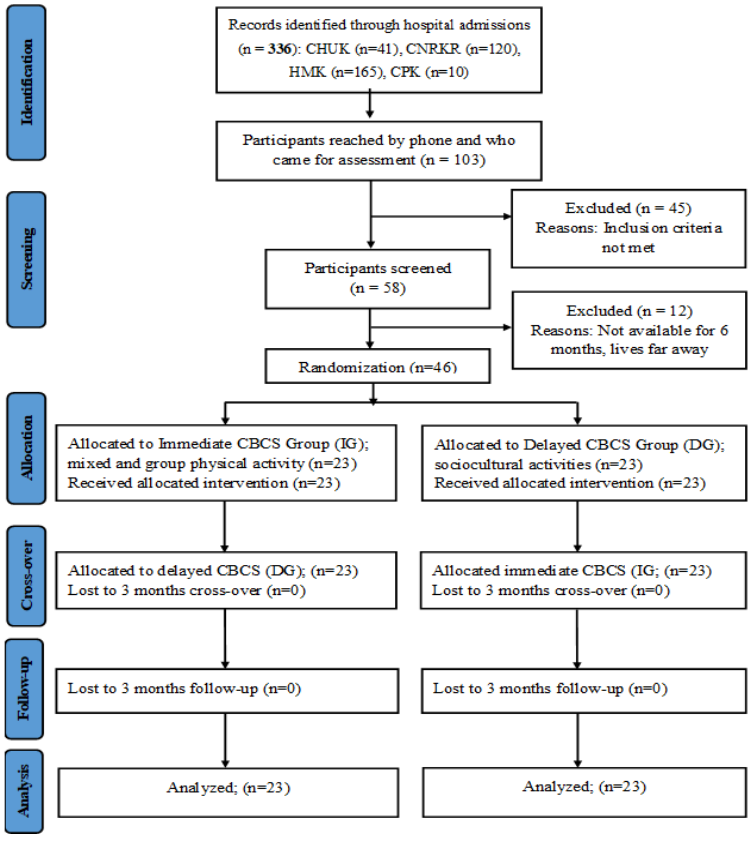


Figure 17: Consort diagram of eligibility and participant inclusion

Table 8: Baseline characteristics of participants (n = 46) in the immediate (IG) and delayed CBCS (DG) groups.

Characteristic	**IG n=23**	**DG n=23**	***p-value***
Mean age (SD), y	50.9 (10.7)	50.1 (11.2)	0.8†
Mean BMI (SD), Kg/m^2	25.57 (5.17)	25.09 (4.35)	0.74†
Median post-stroke duration (Q1; Q3), mo.	24 (11; 37)	21 (9; 32)	0.17‡
Sex, N			0.64 ††
Females/ Males	5 /18	5 /18	
Affected side, n (%)			0.12 ††
Right	15 (65%)	10 (44%)	
Left	8 (35%)	13 (56%)	
Type of stroke, n (%)			0.12††
Ischemic	11 (48%)	8 (35%)	
Hemorrhagic	11 (48%)	9 (39%)	
Undetermined	1 (4%)	6 (26%)	
Disability; MRS median score (Q1; Q3)	2 (2; 3)	3 (2; 3)	0.33 ‡
Impairment severity, median scores (Q1; Q3)			
SIAS	30 (23; 33)	29 (26; 31)	0.76 ‡
HADS	8 (6; 10)	8 (6; 9)	0.6 ‡
CSI-D	8 (7; 9)	8 (7; 9)	0.8 ‡
Balance/fall risk, median score (Q1; Q3)			
TUG	15 (11; 35)	15 (9; 28)	0.54 ‡
BBS	30 (20; 33)	28 (21; 33)	0.72 ‡
Activity limitations, mean (SD)			
ACTIVILIM-Stroke scale in logits	0.45 (1.64)	0.69 (1.19)	0.5†
6MWT in m	221 (112.61)	207 (120.57)	0.68†
10mWT in m/s	0.64 (0.34)	0.7 (0.35)	0.56†
Participation, PM-Scale in logits, mean (SD)	0.71 (1.19)	0.31 (1.41)	0.3†

†Independent t-test; ††Chi-square and Fisher's exact tests; ‡Mann-Whitney U test

Abbreviations: CBCS: Circuit walking, balance, cycling and strength; 6MWT, 6 Minute Walk Test; 10mWT, 10 metre Walking Test; ACTIVLIM-Stroke, Activity limitation for stroke; BBS, Berg Balance Scale; BMI, Body Mass Index; CSI-D, Cognitive Screening Instrument for Dementia; HADS, Hospital Anxiety and Depression Scale; mo. Months; MRS, Modified Rankin Scale; PM-Scale, Participation Measurement Scale; Q1; Q3, 25$^{th\%tile}$ and 75$^{th\%tile}$ quartiles; SD, standard deviation; SIAS, Stroke Impairments Assessment Set; TUG, Timed-Up and Go test; y, years.

Primary outcome: Overall activity limitations

Group-averaged ADL limitations, represented by ACTIVLIM-Stroke scale scores, assessed at each timepoint are shown relative to the expected response in figure 18. The change in functional independence is shown in Figure 18 and individual change after CBCS training (post-intervention and post-cross-over) is shown in supplementary material 3, figure1. At baseline (T1), the immediate (52 [12] %) and delayed group (55 [12] %) had similar mean scores. These baseline scores indicate that the participants were able to perform at least the 8-9 easiest items easily but were unable to perform the 4 most difficult items.

After the 3 month intervention period, at T2, ACTIVLIM-Stroke scale score improved significantly in the immediate group (81 [19] %; $p < 0.001$ vs. T1) but not in the delayed group (59 [11] %; $p = 0.30$). Mean ACTIVLIM-Stroke scale score at T2 of the immediate group was significantly greater than that of the delayed group ($p < 0.001$). This high score in the immediate group indicates that the participants could easily perform all ACTIVLIM-Stroke activities including basic tasks and motor skill-dependent ADLs items (e.g., “getting up from a chair”, “taking off a t-shirt”) but they encounter difficulties in performing activities involving substantial walking (e.g., “walking more than 1 km”, “walking upstairs”).

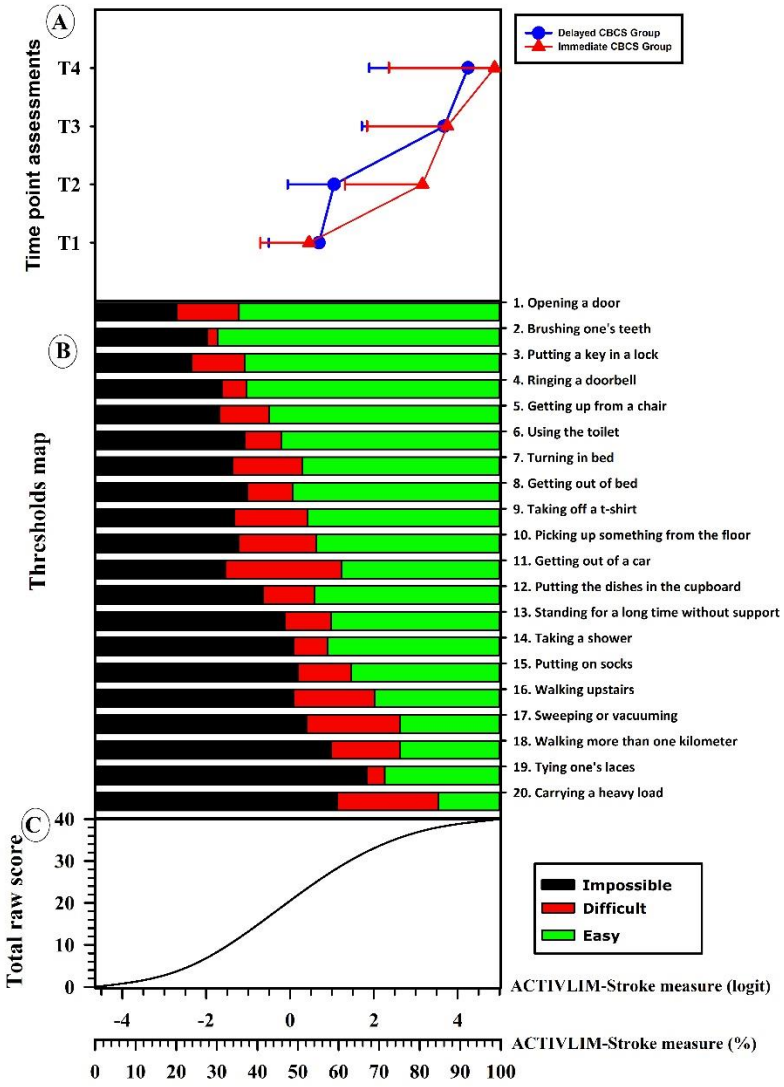
After the 3 month crossover period, at T3, ADL abilities improved significantly in the delayed group, which completed the CBCS protocol during the crossover period [ACTIVLIM-Stroke measure (86 [20] %; $p < 0.001$ vs. T2). During the cross over period, no significant improvement occurred in the immediate group, which

participated in CBCS in the pre-crossover phase and sociocultural activities during the crossover period [ACTIVLIM-Stroke measure, 87 (20) %; $p = 0.50$ vs. T2]. At T3, after the crossover period, ACTIVLIM-Stroke scale scores did not differ between groups ($p = 0.30$) and, on average, the participants in both groups were able to perform all assessment tasks easily.

After the 3 months follow up period, at T4, mean ACTIVLIM-Stroke scale score centiles tended to increase in both groups, though the change from T3 to T4 was not significant: immediate group (98 [24] %; $p = 0.40$) and delayed group (92 [24] %; $p = 0.50$). ADL abilities at T4 did not differ between groups ($p = 0.40$) and, on average, the participants in both groups could perform all items.

The results of the two-way ANOVA of ACTIVLIM-Stroke scale scores are detailed in Table 9. Significant session effects were found within each group, with a significant group × session interaction (pre-post training and interaction effect sizes ES; η^2 =0.87 and 0.31, respectively). ADL performance improved after CBCS training and the improvement was maintained at follow-up. Within-group comparisons of logit scores across assessment time points confirmed that the immediate group's mean performance improved significantly from T1 to T2 (+2.7 logits, ES = 0.33) and T3 (+3.8 logits). The delayed group's scores only changed significantly from T2 to T3 (+2.99 logits). The overall pre-post training mean change for the sample was 3.4 logits (SD, 1.4), equal to 35 centiles. Large improvements occurred in > 80% of participants, as shown by the t-scores and the fact that changes in scores between T1 and T2 (intervention) and between T2 and T3 (cross over) were above the MCID (Tables 9 and 10). The effects were maintained

at follow-up, as indicated by non-significant differences between T3 and T4. In summary, CBCS training improved functional independence by ~41% (Fig. 18) or ~4 logits (mean change from pretraining to follow up).



***<u>Figure 18</u>**: ADL limitations at four evaluation times (T1, T2, T3, T4) according to ACTIVLIM-Stroke scale scores of functional ability. (A) Mean ACTIVLIM Scores at each time point. (B) ACTIVLIM-Stroke scale item-threshold map showing expected responses to each item as a function of the participant's functional ability. (C) Illustration of the relationship between ordinal raw scores and corresponding linear measures in logits and centiles (%).*[11]

[11] This figure has been modified to fit the partial credit model originally used to develop the scale.

Table 9. Mean (SD) scores for outcomes at each assessment time point for the immediate (IG,) and the delayed CBCS (DG) groups.

Outcome	IG n=23				DG n=23				S × G, $p(\eta^2)$	Between-group effects, *p-value* (η^2)		
	T1	T2	T3	T4	T1	T2	T3	T4		T2	T3	T4
ACTIVLIM-Stroke score	0.45 (1.16)	3.16 (1.85)	4.28 (1.95)	4.87 (2.52)	0.69 (1.19)	1.05 (1.1)	3.68 (1.97)	4.24 (2.35)	≤0.001 (0.31)	<0.001 (0.33) **IG>DG**	>0.05 (0.02)	>0.05 (0.02)
	p < 0.001; MCID: 20 (87%)				*p < 0.001; MCID: 19 (83%)*							
SIAS score	28.5 (6.1)	37.2 (6.73)	39.9 (7.66)	41.6 (7.8)	28.3 (4.7)	28.3 (4.9)	40.4 (4.1)	42.7 (6.5)	<0.001 (0.54)	<0.001 (*0.37*) **IG>DG**	0.7 (0.00)	0.61 (0.01)
	P < 0.001				*P < 0.001*							
BBS score	27 (9)	47 (7)	49 (7)	51 (7.4)	26 (10)	26 (10)	48 (8)	52 (5)	<0.001 (0.76)	<0.001 (0.62) **IG>DG**	0.69 (0.0)	0.75 (0.00)
	p < 0.001; MDC: 23 (100%)				*p < 0.001; MDC: 23 (100%)*							
HADS score	7.87 (2.47)	2 (1.16)	0.74 (0.68)	1.7 (2.22)	7.74 (2.47)	2.74 (2.28)	0.91 (1.5)	1.35 (2.16)	0.28 (0.03)	0.21 (0.04)	0.62 (0.01)	0.59 (0.01)
	p < 0.001				*p < 0.001*							

Note: ACTIVLIM-Stroke is shown in logits. Within-group effects of session T1–T4 are shown in the group column sets. Between-group effects are shown as p values obtained in post hoc analyses and pre-post training effect size (η^2). MCID: Number (percentage) of participants in each group who achieved the MCID/MDC for each variable after the cross-over period.

Abbreviations: CBCS: Circuit walking, balance, cycling and strength; ACTIVLIM-Stroke, Activity limitation stroke scale; BBS, Berg Balance Scale; HADS, Hospital Anxiety and Depression Scale; MCID, Minimal Clinically Important Difference; SIAS, Stroke Impairments Assessment Set; S × G, session × group interaction; T1, baseline; T2, after the intervention period; T3, after the crossover period; and T4, after 3 mo. follow-up period.

Table 9. Mean (SD) scores for outcomes at each assessment time point for the immediate (IG,) and the delayed CBCS (DG) groups (continued).

Outcome	IG n=23				DG n=23				S × G, $p(\eta^2)$	Between-group effects, *p-value* (η^2)		
	T1	T2	T3	T4	T1	T2	T3	T4		T2	T3	T4
6MWT, m	221 (112.6)	346.3 (147.3)	359.1 (161.5)	340.3 (167.9)	207 (120.6)	205.8 (117.5)	359.6 (147.8)	360.8 (144.8)	<0.001 (0.4)	<0.01 (0.22) **IG>DG**	0.9 (0.00)	0.6 (0.01)
	p < 0.001; MCID: 16 (70%)				*p < 0.001; MCID 20 : (87%)*							
10mWT, m/s	0.64 (0.34)	1.01 (0.51)	1.01 (0.48)	1.04 (0.53)	0.70 (0.35)	0.75 (0.38)	1.07 (0.55)	1.07 (0.50)	<0.001 (0.25)	<0.05 (0.08) **IG>DG**	0.7 (0.004)	0.8 (0.003)
	p < 0.001; MCID: 21 (91%)				*p < 0.001; MCID: 20 (70%)*							
PM-Scale	0.71 (1.19)	2.57 (1.36)	3.49 (1.18)	5.54 (1.85)	0.31 (1.42)	1.96 (1.57)	3.58 (1.87)	4.93 (2.51)	>0.05 (0.04)	>0.05 (0.04)	>0.05 (0.00)	>0.05 (0.02)
	p < 0.001; MCID: 21 (91%)				*p < 0.001; MCID: 23 (100%)*							

Note: PM-Scale scores is shown in logits. Within-group effects of session T1–T4 are shown in the group column sets. Between-group effects are shown as p values obtained in post hoc analyses and pre-post training effect size (η^2). MCID: Number (percentage) of participants in each group who achieved the MCID/MDC for each variable after the cross-over period.

Abbreviations: CBCS: Circuit walking, balance, cycling and strength; 6MWT, 6-Minute Walk Test; 10mWT, 10-metre Walk Test; MCID, Minimal Clinically Important Difference; PM-Scale, Participation Measurement Scale; S × G, session × group interaction; T1, baseline; T2, after the intervention period; T3, after the crossover period; and T4, after 3 mo. follow-up period

Table 10: Analysis of change at the individual level for all outcomes and for each group (immediate and delayed CBCS groups) reported as the number of participants (percentage) according to the t score significance limits.

	Large improvement (t≥1.96)		Improvement (0<t<1.96)		No change (t=0)		Decrease (t<0)	
Outcomes	T2 vs T1	T3 vs T2	T2 vs T1	T3 vs T2	T2 vs T1	T3 vs T2	T2 vs T1	T3 vs T2
Activlim-Stroke score (logit)								
• Immediate CBCS	23 (100%)	12 (52%)	0	6 (26%)	0	4 (17%)	0	1 (4%)
• Delayed CBCS	0 [12]	21 (91%)	1(4%)[13]	0	0	2 (9%)	5 (22%)	0
SIAS score								
• Immediate CBCS	21 (91%)	9 (39%)	1 (4%)	10 (43%)	0	2 (9%)	1 (4%)	2 (9%)
• Delayed CBCS	0	23 (100%)	10 (43%)	0	5 (22%)	0	8 (35%)	0
BBS score								
• Immediate CBCS	23 (100%)	1 (4%)	0	17 (74%)	0	4 (17%)	0	1 (4%)
• Delayed CBCS	0	23 (100%)	8 (35%)	0	4 (17%)	0	11 (48%)	0

Note: t values (correspond to effect size), which consider self-relative scores and their associated errors for a person at 2 different time points, were calculated as follows: t value==(Pj-Pi)/(√(〖SE〗_J^2+〖SE〗_(I)^2)) where pi and pj represent the person's participation level at 2 time points, and SEj and SEi are the respective associated standard errors of measurement.

[12]A mistake in the numbers was slipped in by the publisher and is now corrected.

Table 10: Analysis of change at the individual level for all outcomes and for each group (immediate and delayed CBCS groups) reported as the number of participants (percentage) according to the t score significance limits (continued).

	Large improvement (t≥1.96)		Improvement (0<t<1.96)		No change (t=0)		Decrease (t<0)	
Outcomes	T2 vs T1	T3 vs T2	T2 vs T1	T3 vs T2	T2 vs T1	T3 vs T2	T2 vs T1	T3 vs T2
6MWT, m	17 (74%)	2 (9%)	6 (26%)	16 (70%)	0	0	0	5 (22%)
• Immediate CBCS								
• Delayed CBCS	0	20 (87%)	0	3 (13%)	12 (52%)	0	11 (48%)	0
10mWT, m/s								
• Immediate CBCS	22 (96%)	0	1 (4%)	10 (43%)	0	7 (30%)	0	6 (26%)
• Delayed CBCS	0	21 (91%)	18 (78%)	0	3 (13%)	0	2 (9%)	2 (9%)
PM-Scale score (logit)								
• Immediate CBCS	19 (83%)	15 (65%)	2 (9%)	4 (17%)	1 (4%)	2 (9%)	1 (4%)	2 (9%)
• Delayed CBCS	19 (83%)	19 (83%)	1 (4%)	3 (13%)	2 (9%)	1 (4%)	1 (4%)	0

Note: t values (correspond to effect size), which consider self-relative scores and their associated errors for a person at 2 different time points, were calculated as follows:

t value==(Pj-Pi)/(√(〖SE〗_J^2+〖SE〗_(I)^2)) where pi and pj represent the person's participation level at 2 time points, and SEj and SEi are the respective associated standard errors of measurement.

Secondary outcomes of motor performance

The results of the two-way ANOVA are presented in detail in table 9 and in figure 19.

Global impairment

Regarding global motor impairments assessed with the SIAS (Fig. 19A), the two-way ANOVA revealed a significant effect of session within each group and a group × session interaction (all $p < 0.001$; pre-post training and interaction ES 0.9 and 0.54). For the immediate group, mean SIAS scores were significantly higher at T2 (+9 points, $p < 0.001$, ES=0.37) and T3 (+11 points) than at T1. For the delayed group, mean SIAS scores were significantly higher at T3, after the crossover phase, than at T1 and T2 (+12 points). By T3, after the crossover phase, there was no longer a significant difference between the groups ($p = 0.80$) because the delayed group performance had increased to that of the immediate group. A clinically important improvement occurred in over 90% of participants (Table 10). CBCS training effects were maintained at T4 (no difference between T3 and T4 scores in either group).

Balance

The two-way ANOVA demonstrated significant effects of session within each group and a group × session interaction (all $p < 0.001$; pre-post training and interaction ES 0.9 and 0.76, table 9) on balance measured by the BBS (Fig. 19B). Post-hoc analysis showed that the immediate group's mean BBS scores improved significantly from T1 to T2, whereas scores for the delayed group improved significantly

from T2 to T3. Mean BBS scores were much higher for the immediate group (+20 points) than for the delayed at T2 ($p < 0.001$, ES 0.62). This difference was no longer present after the crossover phase at T3 ($p = 0.70$) because the delayed group's balance performance increased (+22 points) to that of the immediate group. The improvements in all participants exceeded the MDC and were large (tables 9 and 10). In both groups, the improvement in balance was maintained ($p > 0.05$ vs. T3) through the follow-up period at T4.

Mobility

As shown in Figures 19C and D, two-way ANOVAs revealed session effects within each group and a group × test session interaction for both walking endurance measured with the 6MWT and for walking speed measured with the 10mWT (all $p < 0.001$; pre-post training and interaction ES 0.5 to 0.7 and 0.25 to 0.4 respectively). Post-hoc analysis revealed that the immediate group had a greater mean walking distance (+125 m, ES=0.22) and speed (+0.37 m/s, ES=0.08) at T2 than at T1. For the delayed group, similar respective improvements were observed from T2 to T3 (+154 m distance and +0.32 m/s speed). Multiple comparisons of between-group differences showed that mean 10mWT and 6MWT outcomes were much higher for the immediate than for the delayed group at T2 ($p < 0.001$). This difference no longer existed after the crossover phase at T3 ($p = 0.70$) because the delayed group's distance and speed increased to those of by the immediate group. More than 70% of participants achieved at least the MCID and large t-score improvements (Tables 9 and 10) for both the 6MWT and 10mWT. For

both groups, the effects were maintained at T4 after the follow-up period.

Outcomes of psychosocial health

There were no significant group effects or interactions for depression or participation, assessed with the HADS and PM-Scale respectively. Significant improvements in depression symptoms and participation occurred in both groups over time ($p < 0.001$, Table 9). There were no statistical differences between the mean scores of the 2 groups at each time point (Figures 19F and D). Post-hoc analysis of within-group effects showed that for both groups, depression symptom levels decreased sharply from T1 to T3 (approximately -7 points in each group, ES = 0.9) and participation scores increased gradually from T1 to T4 (total changes: immediate group +4.83 logits; delayed group +4.62 logits, ES = 0.8). The greatest improvements in participation were seen in the immediate group data, from T1 to T2 (+1.86 logits) and from T2 to T3 (+0.92 logits) respectively. The changes in the delayed group scores were quite steady over time (+1.65, +1.62, and +1.35 logits).

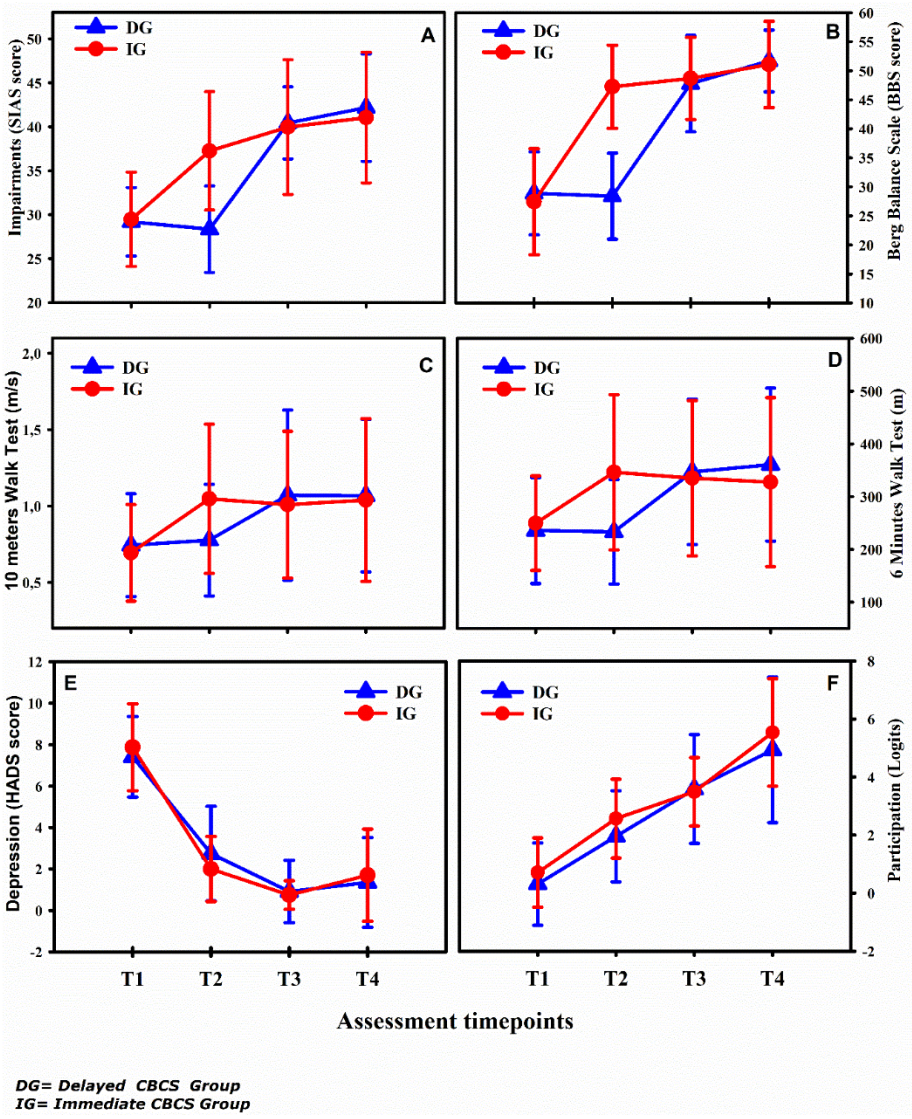


***Figure 19**: Mean (SD) values observed for overall and balance impairments as measured with the SIAS (A) and the BBS (B), respectively. Mean (SD) values observed for mobility as measured by the 10mWT (C) and 6MWT(D). Mean (SD) values observed for depression symptoms and social participation restrictions as measured with the HADS (E) and the PM-Scale (F). The immediate CBCS (experimental) group and delayed CBCS (socio-cultural activities) group data are shown as solid and dotted lines, respectively, with SD errors bars for each group.*

Additional outcomes of feasibility and safety

No participants dropped out at any stage: the retention rate was 100%. Of the 36 sessions in phase 1, the mean number of sessions completed was 34.8 (SD 1.5) and 34.8 (1.3) respectively for the immediate and delayed groups. In phase 2, the mean number of sessions completed was 33.3 (2.4) and 34.2 (1.7) respectively for the immediate and delayed groups. In phase 1, adherence was similar between the two groups (97%). In phase 2, the immediate and delayed group participants attended 93% and 95% of the sessions respectively. Minor adverse effects were reported in 11% of participants during CBCS training, all of which resolved within short periods of time (minutes, hours, or days). Two participants experienced low back pain, 2 reported knee pain after walking, and 1 reported hypotension and dizziness during the second session.

1.6 Discussion

This study demonstrated the safety, feasibility, and efficacy of a CBCS training protocol in individuals with chronic stroke living in a low-resource setting who were not participating in a formal rehabilitation program at the time of study enrolment. Completion of the CBCS training protocol was associated with reductions in ADL limitations together with improvements in motor performance outcomes (global impairment, balance and mobility). Furthermore, depression symptoms reduced and social participation increased in response to both CBCS training and sociocultural activities (the control

condition). All improvements were maintained 3 months after the end of the interventions.

Motor performance improvements

Physical activity has well-established benefits on mobility. In their recent systematic review and meta-analysis, Pogrebnoy and Dennett (Pogrebnoy & Dennett, 2020) concluded that combined aerobic and resistance training exercise programs improved habitual walking speed (mean difference, 0.07 m/s) and walking endurance (mean difference, 39.2 m). Improvements in mobility (speed and distance) and balance have also been highlighted in other physical activity studies conducted in rehabilitation or laboratory settings (Marzolini et al., 2018; Nindorera et al., 2021; Saunders et al., 2020). In a Cochrane review of group-based interventions (circuit classes) in developed countries, English et al. (English et al., 2017a) reached similar conclusions noting moderate improvements in walking distance (60–70 m), walking speed (0.15–0.19 m/s), balance, and overall functional independence (English et al., 2017a). The Cochrane review by English et al. included studies conducted in community or hospital settings and participants at all stages of stroke. Although no other studies of group community physical training with which to compare our findings are available, our results are consistent with those of several community-based studies conducted in developed countries (Diermayr et al., 2020; Malagoni et al., 2016; Tang et al., 2020). The recent, multicentre "LAST Study" (Askim et al., 2018) concluded that regular individualized coaching was safe and improved physical activity levels but did not improve the maintenance of motor function

or mobility outcomes more than standard care. Other findings (Mandigout et al., 2021; Tesio et al., 2020) support the low effectiveness of individualized coaching programs after hospital discharge, particularly the lack of tailoring of exercises to each individual. In contrast with the different context in terms of income with the LAST study, our intervention was supervised, group-based and targeted functional exercises of progressive difficulty adapted to each individual. In addition, our sample was relatively young (mean age 50 vs. 72 years).

Relative to the various aerobic, mixed, and circuit training interventions that have been shown to improve mobility, balance, and functional independence in inpatients and outpatients, the present study demonstrates an apparent advantage of multimodal, structured, and collective physical activity for these outcomes. Compared to prior studies, we observed quite robust improvements in ACTIVLIM-Stroke scale scores [>2.4 logits, MCID (Charles Sèbiyo Batcho et al., 2014)] and BBS [>5 points, MDC_{95} (Hiengkaew et al., 2012)], which exceeded the MCID for the 6MWT [71 m (Fulk & He, 2018)] and 10mWT [0.10–0.20 m/s (Bohannon & Glenney, 2014)]. Large changes occurred in more than 70% of participants. Global impairments, especially lower extremity motor function, were improved in the majority of participants. We attribute the relatively substantial improvements documented here to the intensive and functional aspects of our supervised intervention that enabled continuous motor learning (Schmidt et al., 2019), together with the fact that younger people tend to show greater improvements in motor performance than older people (Berghuis et al., 2016). The mix of aerobic and resistance training and

the implementation of relatively long (120 min), regular sessions (3 times/week, with ≥ 85% motor involvement, for 12 weeks) and adapted functional exercises with repetition, shaping, and feedback, make this CBCS training program effective as it meets the recommendations for stroke rehabilitation (Billinger et al., 2014). Furthermore, the activities included playful aspects to help keep the participants engaged. Additionally, the intervention was conducted in groups in a community environment, which may serve to increase participant motivation while promoting mutual support (Clark et al., 2020) as the participants engage in real-life challenges with clear functional benefits (e.g. crossing a gutter, climbing a slope, etc.). Compared to one-on-one physiotherapy sessions, group-based physical activity programs are more cost effective, requiring little supervision and allowing social integration in real life. The relatively young age of our sample (mean age ~50 years) and generally moderate (as opposed to severe) disability levels may have facilitated motor learning and performance (Berghuis et al., 2016; Clark et al., 2020; Schmidt et al., 2019).

Psychosocial health improvements

Our experimental CBCS training intervention and the control sociocultural program improved depression and social participation to similar extents. These findings are not surprising given that social games and social interactions facilitate socialization. Importantly, social support (friendship and social interaction) has been associated with improvement in post-stroke depression symptoms (Lin et al., 2019) and high levels of social support have been associated with better

participation (Elloker & Rhoda, 2018). Given that physical function has been shown to be an important predictor of community participation in young adults (Chang et al., 2022), it is clear that that exercise-based interventions (motor relearning program, cognitive-based exercise, community walking training program and home-based combined exercise) are highly effective for improving social participation (Zhang et al., 2020).

Overall, consistent with a Delphi study (Mahmood et al., 2022), the functional and playful aspect of the exercises, the motivation linked to the peer-support within the group, feedback, training intensity, the grading of exercises according to capacity and adapted to the individual (or to the group of individuals with similar disabilities) were the main strategies used to increase adherence and improve outcomes in the chronic phase of the stroke.

Study strengths

We conducted an assessor-blinded, crossover, randomized study of the effectiveness of a CBCS training intervention. We used a sociocultural program as the control intervention in the crossover design. This study was the first to investigate the effectiveness of a community group and multimodal physical activity program in chronic stroke rehabilitation in a low-resource setting within a sub-Saharan country, namely Burundi. Multiple aspects of post-stroke stroke disability were examined, including ADL limitations, impairments, and participation restrictions and we used socio-culturally suitable tools to assess the outcomes. Importantly, our post-intervention follow-up data

demonstrated that intervention benefits were maintained on (at least) a mid-term timescale. All participants completed both the intervention and crossover phases of the study (no drop-outs), which lends confidence to the credibility of our statistical analyses.

Study limitations

Because the CBCS training intervention was not compared directly to conventional rehabilitation or to a different physically active intervention, we cannot make conclusions regarding whether CBCS training is superior to conventional rehabilitation programs. Indeed, in low-income settings, many people in the chronic post-stroke stage drop out of rehabilitation or abandon it early due to the high cost of care since the onset of the stroke. Nevertheless, we used a cross-over design to overcome this issue. Future multicentre studies should compare CBCS training with conventional rehabilitation and include long-term follow-up analyses. In addition, we did not specifically assess each impairment, which may affect the overall rationale for functional recovery, but we believe that the main goals of people in the chronic phase of stroke are necessarily functional independence and cardiorespiratory capacity. Finally, we included people with moderate disability and further studies could investigate the effect of this program on people with severe disability.

3.5. Conclusion

The results of the present study showed that a community, collective and multimodal physical activity program for stroke rehabilitation was safe, feasible, and effective in a low-resource setting.

The 12-week CBCS training protocol significantly reduced ADL limitations and global impairments and improved balance and mobility. Additionally, CBCS training improved depression symptoms and participation significantly and similarly to a sociocultural activities program. Importantly, the benefits were maintained 3 months after the interventions ended.

Overall, our study demonstrated the value of combined, group and community-based training for improving impairments, ADL limitations, and social participation in individuals at the chronic stage after a stroke in low-income countries, where its ease of administration and local accessibility may be key to improving adherence and long-term outcomes due to limited geographical and financial access to rehabilitation [7-9]. The CBCS training intervention is cost-effective compared to conventional therapy because it can be delivered in the community in a group format with minimal supervision. An important consideration for people in the chronic stage after a stroke is also the promotion of reintegration into social settings outside of the hospital.

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Data sharing

Data (e.g., demographics, clinical characteristics, and detailed participant results) are accessible upon request via e-mail to the corresponding author.

Disclosures

The author(s) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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CHAPTER IV

GENERAL DISCUSSION

GENERAL DISCUSSION

This thesis aimed to contribute to stroke management and access to rehabilitation in low-income settings by better defining population's needs and identifying and implementing an efficient intervention.

Many existing studies in developed countries have contributed to stroke prevention (Kleindorfer et al., 2021), management and the establishment of guidelines for care (Powers et al., 2019; Winstein et al., 2016), and this has led to a significant decrease in the stroke incidence, prevalence and disability in these countries. In the field of rehabilitation, much evidences demonstrated the effectiveness of physical activity (treadmill, robot-assisted gait training, resistance training, cycling and so on…) (Mehrholz et al., 2017; Saunders et al., 2020) and other rehabilitative techniques (virtual reality, CIMT, brain stimulation, telerehabilitation…) (Laver et al., 2017) on stroke, but research on stroke management remains relatively poor in low-income countries. Stroke survivors in Africa continue to face numerous barriers related to care such as policy, social, attitudinal and physical barriers (Urimubenshi et al., 2018) but the main challenge is access to care, especially rehabilitation. To overcome this, the WHO agenda 2030 highlighted that developing and delivering cost-effective, equitable-access rehabilitation services must be addressed in low-income countries (Bernhardt et al., 2020).

It is within this context that this thesis, with data collected from the Republic of Burundi, aimed to contribute to stroke rehabilitation, by (1) describing the health-related functional status of chronic stroke

survivors in Burundi, (2) studying the effectiveness of walking training protocols on stroke outcomes through literature, and (3) implementing a cost-effective and culturally suitable program, called "CBCS; **C**ircuit walking, **B**alance, **C**ycling and strength training" and investigating its feasibility and effectiveness on impairments, ADL limitations and restrictions in participation.

The first study aimed to describe the clinical profile of post-stroke people by using well-designed and socio-culturally suitable tools, the ACTIVLIM-Stroke scale for activity limitation and PM-Scale for participation restrictions. Specifically, we assessed the level of balance impairments, ADL limitations, and participation restrictions and investigated their relationships with walking speed. We recruited a sample of 58 participants in the chronic stage of stroke, mean±SD age of 52±11.4 years. The study mainly showed a high proportion of participants with limitations in community ambulation. Most participants experienced poor balance indicative of a risk of falling, low walking speed, moderate ADL limitations and social participation restrictions. In addition, low walking speed was associated with high ADL limitations and moderate restriction in social participation. Walking speed was significantly correlated with balance and ADL limitation scores. These findings are consistent with many studies from low-income countries highlighting the large impact of stroke in these countries, especially regarding the young age of the patients (Mwaka-Rutare et al., 2020, Kossi et al., 2019). This highlights the vital need for access to care (Bernhardt et al., 2020; Urimubenshi et al., 2018;

Wasserman et al., 2009), especially rehabilitation to prevent/limit the impact of impairments, activity limitations and participation restrictions, thus preventing disability. Consequently, developing and implementing a cost-effective physical rehabilitation training for individuals with stroke in Sub-Saharan Africa low-income countries is a crucial need. Our results suggested that balance and walking should be targeted in such an intervention, but the exact components and their characteristics, notably dosage, needed further investigation through a comprehensive review of the literature.

In the *second study*, we conducted a meta-analysis of existing literature and quantified the effects of walking training for the improvement of various aspects of the physical function of people with chronic stroke. In this study, we also performed a meta-regression to understand the effect of training dosage better . We included and analyzed 15 randomized controlled trials (RCTs). The study mainly showed that treadmill and overground walking protocols consisting of ≥30 min sessions and conducted at least 3 days per week for about 8 weeks are beneficial for improving impairments, activity limitations, participation, and quality of life in people with chronic stroke. Consequently, developing a rehabilitation program that includes walking training with these modalities, especially overground training, would have a positive effect on stroke survivors in low-income countries like Burundi.

In *the third study*, we designed and implemented a new intervention, the “CBCS” a community, mixed and collective physical activity. We

investigated its feasibility and efficacy on activities of daily living (ADL) limitations, motor performance, and social participation restrictions in chronic stroke survivors. We randomized 46 community-dwelling post-stroke people, no longer in conventional rehabilitation into two groups: a waiting list performing socio-cultural activities and a CBCS therapy group performing mixed and collective physical activity. Both interventions were delivered at the same high dosage of 72 hours (2 hours/sessions, 3/wk for 12 weeks). After the first period of intervention, participants were crossed-over to allow the waiting list group to attend physical activity intervention for the same dosage. The assessment outcomes included ADL limitations, measured by ACTIVLIM-Stroke scale (main endpoint), motor performance (balance, global impairment and mobility) and psychosocial health (depression and participation). Additional outcomes included feasibility (retention, adherence) and safety. Participants were assessed before, immediately after the intervention and the cross-over, and at 3 months after interventions (Follow up). The results of this *3rd study* showed that mixed, community and group-based physical activity effectively improves functional independence and motor abilities. All participants exhibited clinically significant improvements in functional independence, balance, global impairments, and walking distance. Moreover, this physical activity program improved depression and social participation in a similar way to socio-cultural activities attendance. Furthermore, this intervention was feasible as none of the patients dropped out and the participants showed a high attendance rate. Ultimately, this procedure was safe because minor adverse effects

(dizziness, fatigue, …) were observed in a few participants for a few days.

To address the specific needs in stroke management and secondary prevention in low-income countries, it is critically important to be aware of the functional health status

According to World Health Organization (Dahl, 2002), functional disability is a multidimensional concept that involves an interaction of impairments, activity limitations and participation restrictions. Improvement of each of these components depends on several factors, including the economic situation (Lekander et al., 2017), access to rehabilitation and cultural beliefs (Mbada et al., 2019; Mendis, 2013). Hence, understanding the challenges faced by patients from low-income countries would be helpful in identifying the long-term issues that care-based services will need to address.

This unique study to report the functional recovery of Burundian people post-stroke confirmed gaps in stroke management that persist in low-income countries. Indeed, this study found that most patients experienced poor balance indicative of a risk of falling, low walking speed, moderate ADL limitations and social participation restrictions. Our findings are consistent with other studies conducted in similar settings. Chang (2015) and Kossi (2021) reported high prevalence rates of impairments (around 83%), which leads to a slow walking speed (fear of falling) and this limit functional independence and participation. These poor outcomes are probably linked to limited early

stroke management (medical and rehabilitation) and access to rehabilitation (Pandian et al., 2020; Urimubenshi et al., 2018). According to stroke management guidelines, early care and continuing specialized care after discharge from the hospital are sufficient to reduce mortality and disability by more than 60% (Lindsay et al., 2014). Stroke care in Africa fell below the recommended standards (Urimubenshi et al., 2018); African-policy makers and health care professionals need to combine efforts to improve equitable access to organized stroke care and quality service.

Low-income countries, particularly sub-Saharan Africa, need appropriate stroke rehabilitation interventions.

The management of stroke involves many fields, notably prevention strategies, cost-effective rehabilitative interventions , and community education. As stroke is a well-documented global burden, it is imperative to be aware of the most effective rehabilitation strategies and to determine the most cost-effective among them, which can be suitable for under-resourced settings. The first step is therefore to systematically search the literature for what has been done elsewhere and identify what is appropriate for low-income settings.

The contribution of our *second study* (Chapter 2) was to search the existing literature to identify effective interventions to improve functional outcomes, particularly mobility, and this study showed that overground walking training, an easy to implement and quite

inexpensive intervention, could improve balance, motor impairments, activity limitations, participation, and quality of life in people with chronic stroke. The main goals for individuals who have suffered a stroke are to enable them to regain independence and improve quality of life (QoL), especially the ability to walk (Kossi et al., 2019). This ability has been pointed out as a main long-term disability, disrupting ADL (Kossi et al., 2016). Although motor recovery seems stable or slow in the chronic phase of stroke (Falcon et al., 2016), walking ability remains a priority for functional independence in developed and low-income countries. High-income countries have a wide range of walking training equipment, such as classic treadmills, body weight support treadmill, robotic assisted gait training (Baronchelli et al., 2021; Mehrholz et al., 2017; Nascimento et al., 2021) and so on.... In addition to their high cost for low-income countries, these devices are mainly used in clinical settings and are not easily transferable in the community. In the perspective of effective interventions to promote stroke rehabilitation in Sub-Saharan Africa, the focus should be cost-effective interventions that can easily be implemented in the community.

Delivering a cost-effective and evidence-based rehabilitation approach to promote equitable-access to rehabilitation services: the community, mixed and collective physical activity

Study 1 revealed the strong need for effective rehabilitation to improve balance impairments, walking speed, activity limitations and participation restrictions among Burundians stroke survivors. *Study 2* suggested that overground walking training could be valuable therapy among others for stroke rehabilitation. Furthermore, during the 2030 rehabilitation agenda, the WHO launched a call to action based on 10 goals (Gimigliano & Negrini, 2017). Among these goals, the 5th goal refers to equitable access to rehabilitation while the 9th call for building research capacity and expanding the availability of robust evidence for rehabilitation.

It is in this context that we designed and carried out the intervention of the *3rd study* whose objective was to investigate the feasibility and efficacy of an inexpensive multimodal, mixed and collective physical training "CBCS". The multimodal and mixed aspects of this intervention involve the combination of overground walking, cycling and resistance trainings which are aerobic and anaerobic components of physical activity. Overground walking training consists of walking on different ground surfaces, resistance training consists of putting away, moving, and exchanging objects of different weights in different positions and cycle training consists of cycling on a fixed bicycle at a progressive resistance and intensity. In addition, the balance and coordination training components complement these exercises for the

specific needs of balance during ambulation. The "group" aspect of this intervention in an open-ground community keeps costs low as it requires little supervision, infrastructure and equipment. We specifically assessed the effect of this training on impairments, balance, ADL limitations, participation restrictions and depression. Results demonstrated the feasibility and safety of this mixed and group-based physical exercise training. In addition, this training improved clinically and significantly independence in ADL, motor performance outcomes, depression and participation. More importantly, mobility domain and independence in ADL were improved with large effect size, a greater effect compared to a physical activity program (treadmill and overground) conducted in sub-Saharan Africa (Olawale, O. A. et al. 2011). Furthermore, the benefits persist after 3 months follow-up. These results suggest that for motor abilities and, more importantly for ADL, a significant improvement can be induced with this very cost-effective procedure in an African country.

The significant results obtained here raise further the question of the potential generalization of the proposed intervention. The CBCS program seems easily transferrable to community health care, as it requires little equipment and few physiotherapists' supervision. The present study was conducted in an urban area of a low-income African country. Our process could probably be transferred to other African cities, provided that at least a few trained professionals can offer the intervention. However, even in this urban population, reaching the rehab center (i.e.transportation) was too expensive for the patients and costs were completely managed by the study. Therefore, is it likely that

such an intervention would be implemented in rural areas? This would request much longer displacements for the patients and/ or far numerous well-trained professionals to run multiple small group interventions in the villages, which does not seem economically realistic. Therefore, the development/ generalization of such an intervention would probably depend on the use of the community-based rehabilitation (CBR) system. We believe the CBCS program can be transferred to the community health care, as part of CBR. The healthcare system in most countries is organized as a three-level pyramid, with a local level at the bottom, a regional level in the middle and a national level at the top (Faberon & Marliac, 2017). The local level, a community level led by community health workers, has health centres and first referral hospitals called districts. The local level would therefore be possible to accommodate groups of participants with disability 2 to 3 times a week with a small financial contribution from each group.

As stated in the introduction, so far, the efficiency of this CBR system has been questioned (Pathak et al., 2021). Implementing an evidence-based intervention such as this would require a training framework for the community health workers (who are not health professionals). In addition, a system of remote follow-up by a trained therapist for multiple groups of CBR would be to consider to ascertain the quality of the intervention and specially to balance correctly intensity and shaping of the proposed exercises.

Interestingly, participation and depression were similarly improved by physical activity and socio-cultural activities. This highlights the value of social interactions that do not require supervision by a therapist

within communities. Recent work showed that social isolation is linked to depression and lack of social connection is associated with an increased risk of premature death from stroke (Boden-Albala et al., 2005; Venna & McCullough, 2015). Implementing community meeting centres, potentially through the existing CBR network, without motor training objective would already be an extraordinary low-cost measure to decrease depression and favour participation. Proposing for instance 3 times a week some activities such as the ones of our active control group (e.g. theatre, awalé, etc…) is inexpensive and would considerably improve the participation and well-being of stroke patients.

Overall the findings of our RCT are consistent with the evidences from HICs highlighting that aerobic or aerobic+resistance training provide many benefits, including biological (Mang et al., 2013; Penna et al., 2021), mobility (English et al., 2017), functional capacity and strength (Saunders et al., 2020; Veldema & Jansen, 2020), psychosocial and quality of life effects (Han et al., 2017; Lin et al., 2019; Zhang et al., 2020).

While the effectiveness of neurodevelopmental-based interventions approaches, which are most commonly used in rehabilitation in Africa, is still unclear (Scrivener et al., 2020), this study developed a cost-effective alternative. The effectiveness of this intervention can be attributed to its ingredients, which meet international recommendations for physical activity and stroke rehabilitation (Billinger et al., 2014; Winstein et al., 2016). Physical activity recommendations suggest aerobic training at moderate to high intensity and resistance, or circuit

training (Billinger et al., 2014). Regarding stroke rehabilitation, the ASA guidelines recommend intensive, repetitive, mobility-task training, home-based program and balance training (Winstein et al., 2016). In addition, the functional, group-based and fun aspect of this intervention with the progressive difficulty of the exercises allows an exemplary motor commitment with good motivation, which are ingredients of motor learning (Clark et al., 2020; Schmidt et al., 2019). In the context of low-income countries with lack of human resources and a poor geographical distribution of the few rehabilitation services that exist, this intervention could alleviate this constraint because it is accessible in the community and requires little supervision.

However, it should be noted that this intervention mainly addressed the mobility domain, which puts more emphasis on the lower extremity. This intervention has thus the potential to have a great impact, but not to induce recovery of the upper extremities. We deliberately chose not to address the upper extremities challenges in this study, as identified effective interventions for upper extremity recovery require more supervision by trained professionals (Pollock et al., 2014, Corbetta et al., 2015) and often require more materials, which makes it not accessible in the context of low-income communities. It is thus a limitation of our work and in the future, we should further consider how a low-cost effective intervention for upper extremity could be designed for patients whose possibility to go back to work is related to the recovery of upper extremity motor function.

CONCLUSION

CONCLUSION, SUGGESTIONS, AND PERSPECTIVES

Stroke is commonly the leading cause of disability worldwide, especially in low-income African settings where access to rehabilitation remains challenging. Despite the availability of suitable assessment tools, little is known about the functional level of chronic stroke survivors in Burundi, in addition to the lack of effective rehabilitation interventions. This thesis contributed by mapping the clinical profile of stroke survivors from sub-Saharan Africa low-income countries to raise awareness of a critical need for cost-effective and accessible rehabilitation intervention. Furthermore, this thesis demonstrated the feasibility and effectiveness of a diverse community and group-based physical activity intervention, one of the responses to the 2030 WHO's call for action agenda. The findings of the studies reported in this thesis have substantially enhanced the understanding of stroke management with physical activity in low-income settings.

Far from solving the challenges of stroke management in low-income countries, this thesis contributes to enhancing rehabilitation. From both the literature and the findings of the present work, we strongly suggest: (i) the development of a public information and education strategy on recognizing the stroke signs and seeking immediate care rather than prayers or witchcraft, (ii) the development of stroke prevention strategies at all levels and especially ongoing management of risk factors, (iii) the improvement of patient transport, coordination and continuity of care and especially the development of specialised stroke

care, (iv) the need for large-scale political management to improve access to rehabilitation (health insurance, equipment supply, assessment of CBR efficiency and development of strategies to improve efficiency).

Perspectives

The three studies provided in this thesis raise three main insights likely to have implications for future research. First, comprehensive knowledge of stroke prevalence, incidence and disability at the national level provides useful information regarding prevention and management. Although epidemiological studies on stroke exist in low-income countries and particularly in sub-Saharan Africa, no study of these important variables has been conducted in Burundi. Future studies could investigate this disease burden in Burundi to understand its trend and make recommendations for prevention and management. Second, our findings demonstrated immediate and short-term effects of group-based physical activity in post-stroke people at the chronic stage. Future studies could investigate the long-term effect, the effects in the sub-acute phase of stroke and the reliability of implementing a CBCS program in a CBR network supervised by trained community health workers. In addition, sedentary behaviour and physical activity level are important indicators for secondary stroke prevention that need to be investigated. Our ongoing work aims to describe the level of physical activity, and sedentary behaviour in the stroke population and their relationships with functional independence. Finally, the mixed and group-based physical activity intervention (CBCS) was not compared to conventional rehabilitation; therefore no conclusion can be drawn

regarding its superiority or inferiority. Future studies could compare this intervention to conventional physiotherapy. Taken together, these perspectives are likely to enhance comprehensive stroke knowledge and management strategies using physical activity.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY MATERIAL 1

GENERAL INTRODUCTION- Table 1: Definitions of stroke, adapted from (Sacco et al., 2013)

Type of stroke	**Definitions**
ischaemic stroke	"An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction"
silent CNS infarction	"Imaging or neuropathological evidence of CNS infarction, without a history of acute neurological dysfunction attributable to the lesion".
intracerebral hemorrhage	"A focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma".
stroke from intracerebral hemorrhage	"Rapidly developing clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma"
Silent cerebral hemorrhage	"A focal collection of chronic blood products within the brain parenchyma, subarachnoid space, or ventricular system on neuroimaging or neuropathological examination that is not caused by trauma and without a history of acute neurological dysfunction attributable to the lesion".
subarachnoid hemorrhage	"Bleeding into the subarachnoid space (the space between the arachnoid membrane and the pia mater of the brain or spinal cord)."
stroke from subarachnoid hemorrhage	"Rapidly developing signs of neurological dysfunction and/or headache because of bleeding into the subarachnoid space (the space between the arachnoid membrane and the pia mater of the brain or spinal cord), which is not caused by trauma"
stroke from cerebral venous thrombosis	"Infarction or hemorrhage in the brain, spinal cord, or retina because of thrombosis of a cerebral venous structure. Symptoms or signs caused by reversible edema without infarction or hemorrhage do not qualify as stroke"
Unspecified stroke	"An episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥24 hours or until death, but without sufficient evidence to be classified as one of the above."

GENERAL INTRODUCTION - Table 2: Stroke semiology in the carotid territory of stroke

Involved artery	**Location**	**Symptoms**
Middle cerebral artery infarction	anterior or superior superficial territory	• Isolated frontal syndrome, transcortical motor aphasia/Broca's aphasia/conduction aphasia, ideomotor apraxia, motor alexia or hemineglect. • Brachial predominant or faciobrachial distal predominant motor hemicorporeal syndrome; cheiro-oral or pseudo thalamic sensory hemicorporeal syndrome
	posterior or inferior superficial territory	Facial-brachial sensory hemicorporeal syndrome, lateral hemianopsia or superior quadranopsia, transcortical sensory aphasia, Wernicke's alexia and agraphia/aphasia or spatial hemineglect, asomatognosia, confusional state
	Deep territory (lenticulostriate arteries):	• Proportional motor hemicorporeal syndrome pure or associated with a facio-brachial sensory hemicorporeal syndrome; subcortical type aphasia (transcortical motor) or spatial hemineglect, anosognosia, asomatognosia • Partial motor spectrum of various types (pure hemicorporeal motor syndrome, hemicorporeal motor and ataxic syndrome, hemicorporeal motor and sensory syndrome)
	Both superficial and deep territories	Proportional motor hemicorporeal syndrome, facio-brachial sensory hemicorporeal syndrome; lateral hemianopsia, combined head and eye deviation; global aphasia or spatial hemineglect, anosognosia, asomatognosia.
Anterior cerebral artery infarction		Motor hemicorporeal syndrome predominantly crural or more rarely facio-brachial, facio-brachial sensory hemicorporeal syndrome; hypertonia in flexion; limitation of voluntary lateral eye movements; forced grasping phenomenon; sphincter disorders; frontal syndrome; transcortical motor aphasia preceded by mutism or spatial motor hemineglect, confusional state
anterior choroidal artery		• Full spectrum: proportional hemicorporeal motor syndrome, facio-brachial sensory hemicorporeal syndrome; lateral hemianopia; subcortical aphasia or spatial hemineglect, anosognosia • Partial spectrum: motor and ataxic hemicorporeal syndrome; pure proportional motor hemicorporeal syndrome.

GENERAL INTRODUCTION - Table 3: Stroke semiology in the territory of the vertebro-basilar arteries…

Involved artery	Location	Symptoms
Brainstem infarction	Mesencephalic territory	Isolated disturbance of vigilance; oculomotor paralysis (III) associated with a complete hemicorporeal motor syndrome (Weber's syndrome) or cerebellar syndrome (Claude's syndrome) or contralateral choreoathetosis movements (Benedikt's syndrome); paralysis of verticality of gaze; pedunculated hallucinosis.
	Protuberance territory	Various oculomotor paralyses (internuclear, lateral gaze, VI, Bobbing); peripheral facial paralysis; associated or not with contralateral incomplete motor and sensory hemicorporeal syndromes.
	Bulbar territory	• Lateral: paralysis of the last cranial pairs (IX, X, XI), Claude Bernard-Horner, vestibular syndrome (lateropulsion, nystagmus), kinetic cerebellar syndrome, facial hypoesthesia and contralateral thermoalgesic sensory hemicorporeal syndrome (Wallenberg syndrome). • Median: XII paralysis, and contralateral incomplete motor hemicorporeal syndrome.
Cerebellar infarction	Superior cerebellar territory	Cerebellar kinetic syndrome (dysmetria, hypotonia, adiadocokinesia, dysarthria, nystagmus), Claude Bernard-Horner, abnormal movements and contralateral hemicorporeal sensory thermoal syndrome and IV palsy.
	Anteroinferior cerebellar territory	Cerebellar kinetic syndrome (dysmetria, hypotonia, adiadocinesia, dysarthria, nystagmus), Claude Bernard-Horner, cranial pairs (VI, VII, VIII) and contralateral thermoalgesic sensory hemicorporeal syndrome. Sometimes isolated vertigo.
	Posteroinferior territory	Isolated lateropulsion; isolated vertigo; ataxia on walking; associated Wallenberg syndrome.

Posterior cerebral artery infarction		• lateral hemianopia, quadranopia with central vision: visual hallucinations; loss of motion perception; alexia, color anomia, transcortical sensory aphasia or prosopagnosia, confusional state, visual hemineglect. • Rarely: complete middle cerebral artery infarction.
Thalamic infarcts	Thalamo-geniculate territory (lateral) and tuberothalamic territory	• Sensory hemicorporeal syndrome, asterixis, ataxia. • Discrete sensory hemicorporeal syndrome; aphasia, amnesia or visuo-spatial hemineglect.
	Paramedian and posterior choroidal territory	• Superior quadranopsia, rarely incomplete sensory or motor hemicorporeal syndrome. • Disturbance of vigilance; partial hemicorporeal motor and sensory syndrome; abnormal movements (asterixis, choreoathetosis); oculo-motor verticality disorders; subcortical aphasia or hemineglect, confabulation, confusional state, antero and retrograde memory disorders.

SUPPLEMENTARY MATERIAL 2

CHAPTER II - Search strategy

Pubmed Search strategies

#1	stroke[MeSH Terms]
#2	"chronic stroke"[Title/Abstract] OR "cerebrovascular accident"[Title/Abstract] OR "cerebrovascular accidents"[Title/Abstract] OR "brain vascular accident"[Title/Abstract] OR "brain vascular accidents"[Title/Abstract]
#3	#1 OR #2
#4	walking[MeSH Terms]
#5	walking[Title/Abstract] OR walk*[Title/Abstract] OR Gait[Title/Abstract] OR "gait training"[Title/Abstract]
#6	#4 OR #5
#7	exercise[MeSH Terms]
#8	exercise[Title/Abstract] OR exercises[Title/Abstract] OR "physical activity"[Title/Abstract] OR "physical activities"[Title/Abstract] OR "aerobic exercise"[Title/Abstract] OR "exercise training"[Title/Abstract
#9	#7 OR #8
#10	recovery of function"[MeSH Terms]
#11	(function[Title/Abstract] OR function recover*[Title/Abstract] OR activity[Title/Abstract] OR "activity limitation"[Title/Abstract] OR "physical fitness"[Title/Abstract] OR "quality of
#12	
#13	

	life"[Title/Abstract] OR "Community Participation"[Title/Abstract] OR participation[Title/Abstract] #10 OR #11 #3 AND #6 AND #9 AND #12

MeSH: Medical Subject Heading.

Cochrane library search strategy

ID	Search Hits
#1	(stroke OR "chronic stroke" OR "cerebrovascular accident" OR "cerebrovascular accidents" OR "brain vascular accident" OR "brain vascular accidents"):ti,ab,kw (Word variations have been searched)
#2	MeSH descriptor: [Stroke] explode all trees
#3	walking OR walk* OR gait OR "gait training"
#4	MeSH descriptor: [Walking] explode all trees
#5	exercise OR exercises OR "physical activity" OR "physical activities" OR "aerobic exercise" OR "exercise training"
#6	MeSH descriptor: [Exercise] explode all trees
#7	"recovery of function" OR function OR function AND recover* OR activity OR "activity limitation" OR "physical fitness" OR "quality of life" OR "Community Participation"

#8	MeSH descriptor: [International Classification of Functioning, Disability and Health] explode all trees
#9	#7 OR #8
#10	#5 OR #6
#11	#3 OR #4
#12	#1 OR #2
#13	#9 AND #10
#14	#11 AND #12
#15	#13 AND #14

Scopus search strategy: (TITLE-ABS-KEY (stroke OR "chronic stroke" OR "cerebrovascular accident" OR "cerebrovascular accidents" OR "brain vascular accident" OR "brain vascular accidents") AND TITLE-ABS-KEY (walking OR walk* OR gait OR "gait training") AND TITLE-ABS-KEY (exercise OR exercises OR "physical activity" OR "physical activities" OR "aerobic exercise" OR "exercise training") AND TITLE-ABS-KEY ("recovery of function" OR function OR function AND recover* OR activity OR "activity limitation" OR "physical fitness" OR "quality of life" OR "Community Participation" OR participation)) AND PUBYEAR > 2007 AND PUBYEAR < 2019

Sciences direct: stroke, stroke rehabilitation, walking, exercise, physical activity

CHAPTER II -Table 1: Characteristics of included studies[14]

Study	N	Intervention			Control			Duration (weeks)	Outcomes	Reported results
		Mean age, year	**Stroke severity at baseline**	**Type**	**Mean age**, year	**Stroke severity at baseline**	**type**			
Ada et al., (2013)	102	70±11	NR	Treadmill and overground trainings	68±12	NR	No intervention	16	Gait ability, participation, and health status	Four months of treadmill training resulted in better walking
Fisher et al., (2011)	20	60±14	NR	Robot assisted gait training	60±14	NR	Usual care	8	Walking ability and balance	Both groups showed significant improvement but no significant difference
Globas et al., (2012)	38	68.6±6.7	NIHSS score (0-42; mean±SD): 4.2±2.5	High intensity treadmill training	68.7±6.1	NIHSS score (0-42; mean±SD): 4.7±2.9	Usual care	12	Endurance, speed, balance, strength, QoL	Experimental intervention improves cardiovascular fitness and gait.
Gordon et al., (2013)	128	64.9±11.1	Barthel Index (mean±SD): 94.3±8.1	Walking overground trainings	63.4±9.4	Barthel Index (mean±SD): 91.5±9.7	Massage	12	Functional status, QoL	Aerobic walking improves the physical health component of quality of life and endurance
Hornby et al., (2008)	48	57±10	NR	Robotic-assisted locomotor training (LT)	57±11	NR	Therapist assisted usual care	2	Walking speed, participation, QoL	Therapist-assisted training facilitates greater improvements in walking ability

[14] This table has been adapted regarding the comments made about the assessment of stroke severity.

CHAPTER II -Table 1: Characteristics of included studies[15] (continued)

Study	N	Intervention			Control			Duration (weeks)	Outcomes	Reported results
		Mean age, year	**Stroke severity at baseline**	**Type**	**Mean age**, year	**Stroke severity at baseline**	**type**			
Kim et al., (2014)	22	50.1±10.2	NR	Community walking training program (overground trainings)	50.7±7.2	NR	usual care	4	Walking speed and endurance, participation	overground trainings is effective on walking function and social participation
Kim et al., (2016)	20	69.1±3.2	NR	Walking aquatic dual task training	68±3.1	NR	Usual care	6	Balance and gait ability	Aquatic dual-task training has a positive effect on balance and gait.
Malagoni et al., (2016)	12	62.5±13.8	NR	Structured home-based exercise	70.7±9.0	NR	Standard care	10	Walking ability, balance,	Experimental group improved balance, walking ability, QoL
Mayo et al., (2013)	87	67.7±14.4	NR	Mobility exercise and brisk walking	67.8±12.3	NR	Stationary cycling	48	Endurance, physical function, participation, QoL	Both programs were equally effective in maintaining walking capacity
Mudge et al., (2009)	60	76	NR	Circuit class training	71	NR	social and educational class	4	Gait speed, endurance, confidence and	Circuit-based rehabilitation leads to improvements in gait endurance

[15] This table has been adapted regarding the comments made about the assessment of stroke severity.

CHAPTER II -Table 1: Characteristics of included studies[16] (continued)

Study	**N**	**Intervention**			**Control**			**Duration** (weeks)	**Outcomes**	**Reported results**
		Mean age, year	**Stroke severity at baseline**	**Type**	**Mean age**, year	**Stroke severity at baseline**	**type**			
Olawale et al., (2011)	60	56.8±6.4	NR	Treadmill walking trainings	57.2±5.9	NR	Usual care	12	Walking ability (speed and endurance)	Experimental training improved walking function
Park et al., (2011)	25	59.3±8.4	NR	Community-based ambulation training	56.9±7.7	NR	Usual care	4	Walking ability and balance confidence	Community-based ambulation training can improve walking ability
Shaughnessy et al., (2012)	64	64.3±9.2	NR	Treadmill training	64.3±9.2	NR	Stretching training	24	Self-efficacy and outcome expectations for exercise, QoL	No statistically significant between-group differences
Stein et al., (2014)	24	57.6±10.7	NR	Robotic-device walking training	56.6±15.1	NR	Exercise group program	6	Gait velocity, gait endurance, balance and functional ambulation profile	No significant differences between the two groups
Yen et al., (2008)	14	57.3±16.4	Brunstrom stage of lower extremity: 4 - 5	Usual body weight supported treadmill training	56±12.6	Brunstrom stage of lower extremity: 4 – 5	Usual care only	4	Balance, walking speed	Additional gait training may improve balance and gait performance

[16] This table has been adapted regarding the comments made about the assessment of stroke severity.

SUPPLEMENTARY MATERIAL 3

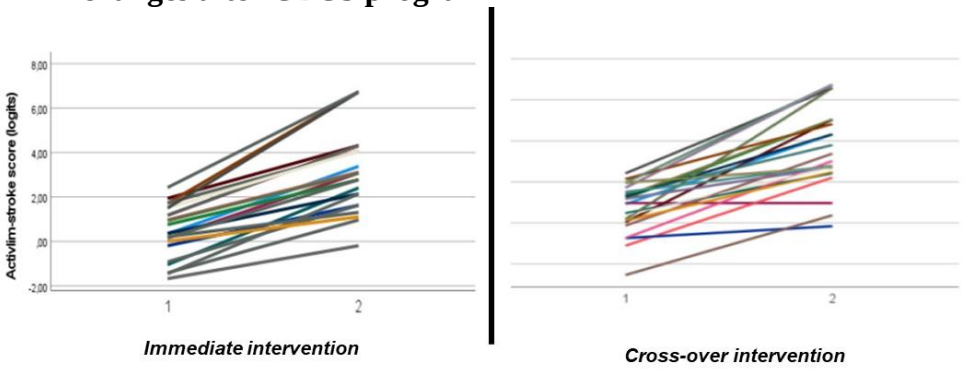
Chapter 3 (Table 1) : Overview of tasks in each Circuit walking, Balance, Cycling and Strength trainings (CBCS) session.

Training component	**Activities**	**Challenge**
Circuit walking, 30 min	Circuit 1: Walking on flat ground Circuit 2: Walking on slightly sloped path with right and left turns Circuit 3: Long distance walking with contour, slope, up steps, and down steps. Circuit 4: Walk on an elevated contour ground, cross small water swales Circuit 5: Go up and down a high slope, walking on rough ground	Distance, speed, number of rounds
Balance, coordination and strength exercises, 30 min	a. Sit-to-stand (from chair, from stool, from swiss ball) b. Weight shift side to side (right and left leg) c. Standing reaching for objects within or outside of base of support d. Weight bearing when crossing short obstacle with each leg e. Weight bearing when walking on foam surface (with or without arm swing) f. Load a cart with objects and move the load by pushing the cart g. Trunk control during bimanual coordination of objects varying in shape and weight: Simple task h. Trunk control during bimanual coordination using different objects (weight, shape ...): behind the back, behind the neck, front of the chest i. Weight bearing when crossing a large obstacle with one and another leg (+/-arm swing) j. Step over an obstacle and go back k. Sitting on a ball (playing ball in a group, moving and storing heavy objects) l. Crossing a long series of obstacles (on foam surfaces, on uneven ground, add bimanual tasks, dual tasks…) m. Walk on a line with feet together (with and without dual task: count numbers, sing, answer a call)	Modify base of support, position of foot, adding bimanual task and dual task Gradually increase the difficulty

Supplementary materials

Chapter 3 (Table 1) : Overview of tasks in each Circuit walking, Balance, Cycling and Strength trainings (CBCS) session (continued).

Training component	**Activities**	**Challenge**
Cycling, 30 min	Stage 1: Low resistance (1–3), Low intensity training (≤50% max heart rate) Stage 2: Middle resistance (2–4), Moderate intensity training (55–65% max heart rate) Stage 3: High resistance (5–8), Moderate or High intensity training (55–75% max heart rate)	Speed, distance reached

Structure: Week. 1 & 2: walking Circuit 1 + balance, coordination, and strength (BCS) a–c + cycling stage 1. Week. 3 & 4: walking Circuits 1 & 2 + BCS a–f + cycling stages 1 & 2. Weeks 5–8: walking Circuits 1–4 + BCS a–i + cycling stages 1 & 2. Weeks. 9–12: all walking circuits + all BCS activities + all cycling stages.

CHAPTER III - Figure 1: spaghetti chart of individual changes after CBCS program