Universidade Federal de Minas Gerais

Université de Montréal

Nível de atividade física em indivíduos pós-acidente vascular encefálico

Le niveau d'activité physique chez les sujets après accident vasculaire cérébral

Physical activity levels in individuals after stroke

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Preface

This thesis was prepared in compliance with the rules of the Board of the Graduate Program in Rehabilitation Sciences of the Universidade Federal de Minas Gerais (UFMG)/Brazil and the standards established by Université de Montréal (UdeM)/Canada, according to pre-requisites established by the agreement reached by the two institutions (Appendix I - Agreement for a joint doctoral program). This thesis was conducted as a partial requirement for a jointly awarded degree of Doctor in Rehabilitation Sciences conferred by UFMG, and Doctor of Philosophy conferred by UdeM, through a cotutelle arrangement.

The requirements of the Graduate Program in Rehabilitation Sciences of the UFMG and the requirements of the doctoral program of UdeM comprise: (1) the fulfillment of academic credits; (2) a comprehensive exam; (3) the writing and development of a thesis; (4) the production of scientific papers; and (5) an oral defense of the thesis.

In order to meet the requirements of both institutions, this cotutelle arrangement comprised three phases. The first was held at UFMG from March 2015 to August 2016 and included (1) the completion of the required coursework and the fulfillment of academic credits (The completed courses are described in Appendix II), (2) the writing of the research project and submission to the Ethics Committee (Appendix III and IV), and acquisition of materials, (3) the writing of scientific papers of the protocols of two systematic reviews developed in partnership with the Ph.D. student Júlia Caetano Martins:

- ➤ AGUIAR L. T., MARTINS J.C., NADEAU S., BRITTO R. R., TEIXEIRA-SALMELA L. F., FARIA C. D. C. M. Efficacy of interventions to improve physical activity levels in individuals with stroke: a systematic review protocol. **BMJ Open**, v.7, n.1, p.e012479, 2017.

- ➤ MARTINS J.C., AGUIAR L. T., NADEAU S., SCIANNI A. A., TEIXEIRA-SALMELA L. F., FARIA C. D. C. M. Measurement properties of self-report physical activity assessment tools in stroke: a protocol for a systematic review. **BMJ Open**, v.7, n.2, p.e012655, 2017.

The second phase included the exchange period held at UdeM from September 2016 to August 2017. During this period, the required coursework was completed, academic credits fulfilled, and the comprehensive exam performed (The completed courses are described in Appendix V). I also participated in partnership with Noémie Duclos in her post-doctoral project "*Asymétrie locomotrice et capacités à marcher dans la communauté chez les personnes hémiparétiques*". My collaboration in this project resulted in the co-authorship of two papers:

> ➤ DUCLOS, N.C.; AGUIAR, L.T.; AISSAOUI, R.; FARIA, C.D.C.M.; NADEAU, S.; DUCLOS, C. Activity monitor placed at the non-paretic ankle is accurate in measuring step counts during community walking in post-stroke individuals: a validation study. Accepted for publication at **PM&R Journal**, 2019 (Appendix VI).

> ➤ DUCLOS, N.C.; AGUIAR, L.T.; AISSAOUI, R.; NADEAU, S.; DUCLOS, C. *Collecter des informations sur l'activité des personnes à l'aide d'accéléromètres et les analyser: Pertinence et implication de l'actimétrie en réadaptation*. Accepted for publication at the journal **Encyclopédie Médico-Chirurgicale** (EMC), 2019.

Also, during this period, the research design of the experimental study was refined, and the writing of the scientific paper of the protocol of the randomized controlled trial of this thesis and another one developed in partnership with the Ph.D. student Júlia Caetano Martins, and the systematic reviews were completed:

> ➤ AGUIAR, L.T.; NADEAU S.; BRITTO, R.R.; TEIXEIRA-SALMELA, L.F.; MARTINS, J.C.; FARIA, C.D.C.M. Effects of aerobic training on physical activity in people with stroke: protocol for a randomized controlled trial. **Trials,** v.19, n.1, p.446, 2018.

> ➤ MARTINS J.C., AGUIAR L. T., NADEAU S., SCIANNI A. A., TEIXEIRA-SALMELA L. F., FARIA C. D. C. M. Efficacy of task-specific training on physical activity levels of people with stroke: protocol of a randomized controlled trial. **Physical Therapy**, v.97, n.6, p.640-648, 2017.

- AGUIAR, L.T.; MARTINS, J.C.; NADEAU, S.; BRITTO, R.R.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Efficacy of interventions aimed at improving physical activity in individuals with stroke: a systematic review. **Disability and Rehabilitation**, v.19, p.1-16, 2018.

- MARTINS, J.C.; AGUIAR, L.T.; NADEAU, S.; SCIANNI, A.A.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Measurement properties of self-report physical activity assessment tools in stroke: a systematic review. Submitted to the **Brazilian Journal of Physical Therapy**, 2018.

The third phase was held at UFMG, from September 2017 to February 2019. During this period data collection regarding the randomized controlled trial was performed, processing of data, and writing of the thesis were carried out. In addition, in a partnership with the Ph.D. student Daniela Matos Garcia Oliveira a protocol of a randomized controlled trial was developed:

- OLIVEIRA, D.M.G.; AGUIAR, L.T.; LIMONES, M.V.; GOMES, A.G.; SILVA, L.C.; FARIA, C.D.C.M.; SCALZO, P.L. Aerobic Training Efficacy in Inflammation, Neurotrophins, and Function in Chronic Stroke Persons: Randomized Controlled Trial Protocol. **Journal of Stroke and Cerebrovascular Diseases**, v.28, n.2, p.418-424, 2019.

This thesis contains an abstract written in Portuguese, French and English, and is divided in nine chapters. The **first chapter** refers to the introduction of the general problem. The **second chapter** refers to a literature review, including the rationale of the studied topic, and the objectives of the four papers. The **third chapter** refers to the protocol of a systematic review on the effects of interventions on physical activity levels post-stroke, which was published at BMJ Open Journal. The **fourth chapter** refers to the complete paper of this systematic review with the aim to investigate the effects of any intervention on physical activity levels of individuals after stroke, which was published in Disability and Rehabilitation Journal. The **fifth chapter** refers to the protocol of the randomized controlled trial with the aim to investigate if aerobic training is effective to improve physical activity levels and sedentary behavior after stroke, published at Trials Journal. The **sixth chapter** refers to the

main study of this thesis, the randomized controlled trial, which will be submitted for publication to Neurorehabilitation and Neural Repair journal, after the oral defense. This study aimed to investigate whether aerobic training is effective on improving physical activity levels and time spent in low-energy expenditure activities of individuals after stroke. The **seventh chapter** contains a discussion of the results, and the **eighth chapter** contains the relevant final considerations. The references are included in the **ninth chapter** and the appendixes are included at the end of this thesis.

Preliminary results of the systematic review and the randomized controlled trial of this thesis were presented by me at the CRIR Student Colloquium/Canada, at the 2nd Quebec Congress in Adaptation-Rehabilitation Research/Canada, at the 3rd Annual PATH Symposium/Canada, at the XXII Congresso Brasileiro de Fisioterapia (COBRAF)/Brazil, and at the V Congresso Brasileiro de Fisioterapia Neurofuncional (COBRAFIN)/Brazil.

It is also worth mentioning that, during the first years of the Ph.D. Program, ten other scientific papers were developed related to data of the master's dissertation (2013-2015):

➢ AGUIAR, L.T.; CAMARGO, L.B.; ESTARLINO, L.D.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Strength of the lower limb and trunk muscles is associated with gait speed in individuals with sub-acute stroke: cross-sectional study. **Brazilian Journal of Physical Therapy,** v.22, n.6, p.459-466, 2018.

➢ AGUIAR, L.T.; MARTINS, J.C.;QUINTINO, L.F.; BRITO, S.A.F.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. A single trial may be used for measuring muscle strength with dynamometers in individuals with stroke: A cross-sectional study. **PM&R,** v.S1934-1482, n.18, p.30849-30859, 2018.

➢ AGUIAR, L.T.; MARTINS, J.C.; BRITO, S.A.F.; MENDES, C.L.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Knee extensor muscles strength indicates global lower-limb strength in individuals who have suffered a stroke: A cross-sectional study. **Brazilian Journal of Physical Therapy,** v.S1413-3555, n.17, p.30542-7, 2018.

➢ BENFICA, P.A.; AGUIAR, L.T.; BRITO, S.A.F.; BERNADINO, L.H.N.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Reference values for muscle strength: a systematic review with a descriptive meta-analysis. **Brazilian Journal of Physical Therapy,** v.22, n.5, p.1-8, 2018.

➢ AGUIAR, L.T.; LARA, E.M.; MARTINS, J.C.; QUINTINO, L.F.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Modified sphygmomanometer test for the assessment of strength of the trunk, upper and lower limbs muscles in subjects with subacute stroke: reliability and validity. **European Journal of Physical Rehabilitation Medicine**, v.52, n.5, p.637-49, 2016.

➢ AGUIAR, L.T.; ALBUQUERQUE, J.A.; MARTINS, J.C.; LARA, E.M.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Dynamometry for the assessment of grip, pinch, and trunk strength in subjects with subacute stroke: reliability and various sources of outcome values. **Brazilian Journal of Physical Therapy,** v.20, n.5, p.395-404, 2016.

➢ MARTINS, J.C.; AGUIAR, L.T.; LARA, E.M.; MOURA, J.B.; SOUZA, L.A.C.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Assessment of the strength of the lower limb muscles in subjects with stroke with portable dynamometry: a literature review. **Fisioterapia e Movimento,** v.29, n.1, p.193-208, 2016.

➢ MARTINS, J.C.; AGUIAR, L.T.; LARA, E.M.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Assessment of grip strength with the modified sphygmomanometer test: association between upper limb global strength and motor function. **Brazilian Journal of Physical Therapy,** v.19, n.6, p.498-506, 2015.

➢ MARTINS, J.C.; TEIXEIRA-SALMELA, L.F.; SOUZA, L.A.C.; AGUIAR, L.T.; LARA, E.M.; MOURA, J.B.; FARIA, C.D.C.M. Reliability and validity of the modified sphygmomanometer test for the assessment of strength of upper limb muscles after stroke. **Journal of Rehabilitation Medicine**, v.47, n.8, p.697-705, 2015.

➢ MARTINS, J.C.; FARIA, C.D.C.M.; AGUIAR, L.T.; SOUZA, L.A.C.; LARA, E.M.; TEIXEIRA-SALMELA, L.F. Assessment of the strength of the trunk and upper limb muscles in stroke subjects with portable dynamometry: a literature review. **Fisioterapia e Movimento**, v.28, n.1, p.169-86, 2015.

Besides the publication of scientific papers, other relevant activities developed during this period were (2015-2019):

- Courses taught as an invited professor at Graduate Programs (*latu-sensu*): 43 hours.
- Courses taught as an invited professor at Graduate Program (*stricto-sensu*): 10 hours.

- Professor at Universidade do Estado de Minas Gerais (UEMG), since March 2018 (20h/week). Courses Taught: 1) Physiotherapy in children's health; 2) Supervised Internship III (Neurology and Geriatrics); 3) Interdisciplinary Studies.
- Participation in short-term workshop: 11.
- Short-term workshop taught: 3.
- Presentations in scientific events: 16.
- Publications of abstracts in proceedings of conferences: 93.
- Participation in the jury of Final Conclusion Work (undergraduate students): 1.
- Participation in the jury of Final Conclusion Work (graduate students): 9.
- Supervisor (undergraduate student): 2.
- Supervisor (graduate student): 4 (2 completed, 2 in progress).
- Awards: 9.
- Event Production: 2.
- Participation in judging commission boards: 4.
- Journal reviewer: 6.
- Development of educational material: 2.

Finally, three dissertations, secondary to the present thesis, are being developed by three master's students who assisted in the data collections of the present thesis.

At the end of the thesis is the student's mini-curriculum, with some activities and productions developed only during the doctoral period (2015-2019) (Appendix VII).

Resumo

O aumento do nível de atividade física, definido como qualquer movimento corporal voluntário que requer gasto energético, pode melhorar a função e a saúde dos indivíduos após o acidente vascular encefálico (AVE). O objetivo geral dessa tese foi analisar o estado atual das evidências sobre intervenções com o objetivo de aumentar o nível de atividade física pós-AVE e desenvolver um estudo experimental que forneça evidências que possam auxiliar a prática clínica. O **primeiro estudo** teve como objetivo descrever um protocolo de uma revisão sistemática (PROSPERO 2016: CRD42016037750) sobre os efeitos de intervenções no nível de atividade física pós-AVE. O objetivo do **segundo estudo** foi realizar uma revisão sistemática de ensaios clínicos randomizados que examinaram quais intervenções foram empregadas para aumentar o nível de atividade física pós-AVE. Dezoito estudos foram incluídos (escores PEDro bons e GRADE muito baixo). Em sete estudos, os grupos experimentais (fortalecimento, exercícios aeróbios e domiciliares; aconselhamento, fortalecimento, exercícios aeróbios e domiciliares; estimulação elétrica; treino específico da tarefa; terapia robótica; feedback baseado em acelerômetro; e encorajamento à atividade física) mostraram aumento do nível de atividade física. Entretanto, o número limitado de estudos e a heterogeneidade das intervenções, dos desfechos mensurados e dos resultados limitam as conclusões. O **terceiro estudo** teve como objetivo descrever o protocolo de um ensaio clínico randomizado (ClinicalTrials.gov: NCT02798237) para investigar a eficácia do treinamento aeróbio na melhora do nível de atividade física e do tempo gasto em atividades de baixo consumo energético pós-AVE. O **quarto estudo**, um ensaio clínico randomizado, teve como objetivo investigar se o treinamento aeróbio melhora o nível de atividade física e o tempo gasto em atividades de baixo consumo energético (desfechos primários), a aptidão cardiorrespiratória, a depressão, a capacidade de caminhada, a mobilidade, a participação e a qualidade de vida (desfechos secundários) pós-AVE. Vinte e dois adultos residentes na comunidade pós-AVE crônico foram randomizados em dois grupos. O grupo experimental realizou treinamento aeróbio em esteira a 60-80% da frequência cardíaca de reserva. O grupo controle realizou caminhada no solo com intensidade inferior a 40% da frequência cardíaca de reserva. Ambos os grupos receberam 40 minutos de intervenção três dias por semana durante

12 semanas. Não houve diferença estatisticamente significativa no nível de atividade física e no tempo gasto em atividades de baixo consumo energético. Comparado ao grupo controle, o grupo experimental apresentou aumento da qualidade de vida (13 pontos; IC95%: 3,5-23 pontos). Ambos os grupos melhoraram a depressão (2,2 pontos; IC95%: 0,01-4,3 pontos), a capacidade de caminhada (31-55 m; IC95%: 3,8-107m) e a mobilidade (0,12 m/s; IC95%: 0,02-0,2 m/s). Não houve outras alterações significativas. Os resultados desta tese mostram que a evidência limitada disponível atualmente é insuficiente para fazer uma recomendação sobre intervenções para aumentar o nível de atividade física dos indivíduos pós-AVE. Ensaios clínicos futuros são necessários para determinar os benefícios do treinamento aeróbio no nível de atividade física e no tempo gasto em atividades de baixo consumo energético.

Palavras chave: Acidente Vascular Encefálico, Exercício Aeróbico, Atividade física, Comportamento sedentário, Reabilitação, Fisioterapia.

Résumé

L'augmentation du niveau d'activité physique, définie comme tout mouvement corporel volontaire nécessitant une dépense d'énergie, pourrait améliorer la fonction et la santé des personnes après un accident vasculaire cérébral (AVC). L'objectif général était d'analyser le niveau d'évidences des interventions visant à augmenter le niveau d'activité physique après un AVC et de comparer l'effets d'interventions. La **première étude** a proposé un protocole pour une revue systématique (PROSPERO 2016: CRD42016037750) des effets d'interventions sur les niveaux d'activité physique après un AVC. La **deuxième étude** a consisté en une revue systématique d'essais contrôlés randomisés qui ont examiné les interventions utilisées pour augmenter les niveaux d'activité physique après un AVC. Dix-huit études ont été incluses (bons scores PEDro et très bas scores GRADE). Dans sept études, les groupes expérimentaux (aérobique seulement, résistance et entraînement à domicile; conseils, aérobie, résistance et entraînement à domicile; stimulation électrique; entraînement aux tâches fonctionnelles; thérapie assistée par robot; rétroaction basée sur accéléromètre; et encouragement à réaliser de l'activité physique) ont montré une amélioration de l'activité physique. Cependant, le petit nombre d'études et l'hétérogénéité des interventions, des mesures de résultats et des résultats ont limité les conclusions. La **troisième étude** a décrit un protocole d'un essai contrôlé randomisé (ClinicalTrials.gov: NCT02798237) visant à déterminer l'efficacité de l'entraînement aérobique sur l'amélioration du niveau d'activité physique et du temps consacré aux activités à faible dépense énergétique après un AVC. La **quatrième étude** a comparé les effets de deux interventions (essai contrôlé randomisé) de marche sur le niveau d'activité physique, le temps consacré aux activités à faible consommation d'énergie, la condition cardiorespiratoire, la dépression, l'endurance, la mobilité, la participation et la qualité de vie. Vingt-deux adultes vivant dans la communauté après un AVC chronique ont été randomisé en deux groupes. Les participants du groupe expérimental ont suivi un entraînement aérobique sur tapis roulant de 40 minutes à 60-80% de sa fréquence cardiaque de réserve, trois jours/semaine pendant 12 semaines. Les participants du groupe contrôle ont reçu la même intervention mais en limitant l'effort à 40% de la fréquence cardiaque de réserve. Il n'y a pas eu de changements significatifs sur le niveau d'activité physique ou le temps consacré aux

activités à faible consommation d'énergie. Seuls les participants du groupe expérimental ont amélioré leur qualité de vie améliorée (13 points; IC95%: 3,5-23 points). Les deux groupes ont amélioré la dépression (2,2 points; IC95%: 0,01-4,3 points), leur endurance (31-55 m; IC95%: 3,8-107 m) et leur mobilité (0,12 m/s; IC95% : 0,02-0,2 m/s). Il n'y a pas eu d'autres changements significatifs. Les résultats de cette thèse ont permis de démontrer l'insuffisance d'évidences pour recommander des interventions visant à augmenter les niveaux d'activité physique des individus après un AVC. Aussi, ils nous ont amené à conclure que d'autres études sont requises pour clarifier les avantages de l'entraînement aérobique sur l'activité physique et le temps consacré aux activités à faible consommation d'énergie.

Mots-clés : Accident vasculaire cérébral, Exercice aérobique, Activité physique, Sédentarité, Réadaptation, Physiothérapie

Abstract

The increase of physical activity levels, defined as any voluntary bodily movement that requires energy expenditure, might improve function and health in individuals after stroke. The general objective of this thesis was to analyze the current level of evidence about interventions to increase physical activity level after stroke and to develop an experimental study that could provide evidence that could help clinical practice. The **first study** had the objective to describe a protocol for the development of a systematic review (PROSPERO 2016: CRD42016037750) about the effects of interventions on physical activity levels after stroke. The objective of **second study was** to develop a systematic review of randomized controlled trials that examined which interventions have been employed for increasing physical activity levels after stroke. Eighteen studies were included (good PEDro and very low GRADE-scores). In seven studies, the experimental groups (aerobics, resistance, and home-based training; counseling, aerobics, resistance, and home-based training; electrical stimulation; functional-task training; robot-assisted therapy; accelerometer-based feedback, and physical activity encouragement) showed significant increases in physical activity. However, the small number of studies and the heterogeneity in the interventions, outcome measures, and results limit the conclusions. The **third study** had the objective to describe the protocol of a randomized controlled trial (ClinicalTrials.gov: NCT02798237) aimed to investigate if aerobic training is effective on improving physical activity levels and time spent in low-energy expenditure activities after stroke. The **fourth study**, a randomized controlled trial, aimed to investigate if aerobic training would improve physical activity levels and time spent in low-energy expenditure activities (primary outcomes), and cardiorespiratory fitness, depression, endurance, mobility, participation and quality of life (secondary outcomes) after stroke. Twenty-two community-dwelling adults with chronic stroke were randomized in two groups. The experimental group performed aerobic treadmill training at 60-80% of their heart rate reserve. The control group performed overground walking below 40% of heart rate reserve. Both groups received 40 minutes of intervention three days per week over 12-weeks. There were no significant changes on physical activity levels and time spent in low-energy expenditure activities. Compared to the controls, the experimental group showed increased

quality of life (13 points; 95%CI: 3.5 to 23 points). Both groups improved depression (2.2 points; 95%CI: 0.01 to 4.3 points), endurance (31-55 m; 95%CI: 3.8 to 107 m), and mobility (0.12 m/s; 95%CI: 0.02 to 0.2 m/s). There were no other significant changes. The results of this thesis showed that the limited evidence currently available is insufficient to make a recommendation about interventions to increase physical activity levels of individuals after stroke. Further studies are needed to clarify the benefits of aerobic training on physical activity and time spent in low-energy expenditure activities.

Keywords: Stroke, Aerobic exercise, Physical activity, Sedentary lifestyle, Rehabilitation, Physiotherapy

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List of abbreviations and glossary of terms

ACS: Activity Card Sort

ACSM: American College of Sports Medicine

CIHR: Canadian Institutes of Health Research

CONSORT: Consolidated Standards of Reporting Trials

CVDs: Cardiovascular diseases

DALYs: Disability-adjusted life-year

ECG: Electrocardiogram

EMBASE: Excerpta Medica

FAI: Frenchay Activities Index

GRADE: Grading of Recommendations Assessment, Development and Evaluation

HAP: Human Activity Profile

HR_{max}: Maximal heart rate

HRR: Heart rate reserve

HR_{rest}: Rest heart rate

LabCare: Laboratório de Avaliação e Pesquisa em Desempenho Cardiorrespiratório

LILACS: Latin American and Caribbean Literature in Health Sciences

MARCA: Multimedia Activity Recall for Children and Adults

MEDLINE: Medical Literature Analysis and Retrieval System Online

METs: Metabolic equivalents

NEUROLAB: *Laboratório de Estudos em Reabilitação Neurológica do Adulto*

PAS: Physical Activity Scale

PASE: Physical Activity Scale for the Elderly

PEDro: Physiotherapy Evidence Database

PHQ-2: Patient Health Questionnaire-2

PHQ-9: Patient Health Questionnaire-9

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis

PROSPERO: Prospective Register of Systematic Reviews

SCIELO: Scientific Electronic Library Online

SIS: Stroke Impact Scale

SpO$_2$: Peripheral oxygen saturation

SS-QOL: Stroke-Specific Quality of Life scale

SWT: Shuttle-Walk Test

UdeM: *Université de Montréal*

UFMG: *Universidade Federal de Minas Gerais*

VO$_{2max}$: Maximal oxygen uptake

VO$_{2peak}$: Peak oxygen consumption

6MWT: Six-Minute Walk Test

10MWT: Ten Meter Walk Test

Dedication

Dedico essa tese aos meus pais, Rita e Amancio, e à minha irmã, Tatiana, que sempre me apoiaram e permitiram que eu alcançasse os meus sonhos.

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environnement et avec une nouvelle langue a certainement été un défi pour moi. Je voudrai donc vous remercier d'avoir rendu mon parcours à Montréal plus tendre et doux.

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Chapter 1.   Introduction

Stroke can be defined as the sudden death of brain cells due to lack of oxygen when the blood flow to the brain is lost by obstruction or rupture of an artery to the brain (JOHNSON *et al.*, 2016). Stroke has a high prevalence worldwide, and projections indicate an increase of over 20% in the prevalence of this health condition between 2012 and 2030 (BENJAMIN *et al.*, 2018). Considering the population aging process, occurring specifically in under developed or developing countries, it is expected to observe a more significant increase in the prevalence of individuals after stroke (BENJAMIN *et al.*, 2018). The absolute number of people who are affected by stroke each year and disability-adjusted life-year (DALYs) lost has increased, especially in underdeveloped or developing countries (BENJAMIN *et al.*, 2018), such as Brazil. For these and other reasons, it is estimated that the direct costs related to the medical and hospital care of the individual who was affected by stroke will more than double by 2035 (BENJAMIN *et al.*, 2018).

Stroke is a leading cause of serious long-term disability, and along with ischemic heart disease account for most of the global burden of cardiovascular disease (ROTH *et al.*, 2017; BENJAMIN *et al.*, 2018). Individuals after stroke are more likely to receive help with mobility, self-care and household activities than sociodemographic and comorbidity-matched controls and are 40% more likely to have restriction in participation in activities that they valued (SKOLARUS *et al.*, 2014). In addition, individuals after stroke are at higher risk of being affected by other cardiovascular diseases (CVDs), such as myocardial infarction and recurrent stroke (BENJAMIN *et al.*, 2018). It is estimated that about a quarter of stroke events are recurrent (BENJAMIN *et al.*, 2018), and in these cases the total direct medical costs are 38% higher than with individuals who were affected by a first stroke (MOZAFFARIAN *et al.*, 2015). Furthermore, recurrent stroke is often associated with the worst severity of the disease (MOZAFFARIAN *et al.*, 2015). Thus, it is important to develop and implement interventions for prevention and treatment of the most commonly associated disabilities post-stroke, the secondary complications and risk factors associated with recurrent stroke and to promote functionality and health for these individuals (BILLINGER *et al.*, 2014). Intervention

strategies targeting key modifiable factors, such as hypertension and low physical activity levels, are necessary (JOHNSON *et al.*, 2016). Physical activity has the potential to influence several functional domains and health in individuals after stroke (BILLINGER *et al.*, 2014).

Physical activity, a complex construct, is reduced in quantity, duration, and intensity after stroke (FIELD *et al.*, 2013; FINI *et al.*, 2017). While, on average, individuals in the subacute phase post-stroke took 5,535 steps per day, and those in the chronic phase post-stroke took 4,078, matched healthy individuals took 8,338 steps per day (FINI *et al.*, 2017). In addition, on average, walking duration of individuals in the chronic phase post-stroke was 88 minutes per day, while matched healthy controls spent 115 minutes on walking activities (FINI *et al.*, 2017). It was already reported that energy expenditure is also reduced in people in the chronic phase post-stroke (1,257-1,500 kcal/day) when compared to matched healthy individuals (2,041-2,109 kcal/day) (FINI *et al.*, 2017; MENDES *et al.*, 2018). In addition, individuals in the subacute and chronic phase post-stroke spent, on average, 88% and 79% of their daily time in low-energy expenditure activities, respectively (JOSEPH *et al.*, 2017; FINI *et al.*, 2017). Considering that physical inactivity is linked with various comorbidities (i.e.: stroke and heart attacks), many agree that there is a need to improve this outcome targeting better quality of life and participation in social roles after stroke (BILLINGER *et al.*, 2014; BENJAMIN *et al.*, 2018). Thus, it could be concluded that it would be relevant to examine the current evidence about interventions planned to increase physical activity levels after stroke and to propose and investigate new intervention in participants post-stroke.

Chapter 2.   Literature review

2.1 Physical activity

2.1.1 Physical activity and sedentary behavior

Physical activity is a complex concept defined as any bodily movement produced by skeletal muscles that result in energy expenditure above basal level (CASPERSEN; POWELL; CHRISTENSON, 1985). Thus, physical activity is associated to the movements that an individual performs (CASPERSEN; POWELL; CHRISTENSON, 1985). Sedentary behavior, which is part of the physical activity continuum and has an independent impact on health, is defined as any behavior performed while awake that involves energy expenditure ≤1.5 metabolic equivalents (METs) (low energy expenditure activities) while in a sitting, reclining, or lying posture (TREMBLAY *et al.*, 2017). Exercise is a type of physical activity which is performed repeatedly, in a planned and structured way, in order to improve or maintain physical fitness components (CASPERSEN; POWELL; CHRISTENSON,1985). Physical fitness is a set of characteristics that people have or attain (CASPERSEN; POWELL; CHRISTENSON, 1985). Some of the components of physical fitness are cardiorespiratory fitness, muscular endurance and strength (CASPERSEN; POWELL; CHRISTENSON, 1985).

There has been an increase in research about the effects of time spent in low-energy expenditure activities (SAME *et al.*, 2016). According to a recent review, results of studies in the general population shows that sedentary behavior has a negative effect on health, which is independent of physical activity levels (SAME *et al.*, 2016). It is possible for a person to be considered physically active while also having a high amount of time spent in low-energy expenditure activities (SAME *et al.*, 2016). Thus, it seems that sedentary behavior and low physical activity levels represents distinct constructs in the physical activity continuum and have independent impacts on health (TIEGES *et al.*, 2015; VERSCHUREN *et al.*, 2015; SAME *et al.*, 2016).

Physical activity can be categorized in different ways (CASPERSEN; POWELL; CHRISTENSON, 1985). One type of classification of physical activity is on domains of daily

life during which the activity occurs: occupational (i.e.: manual labor tasks, walking, carrying or lifting object); domestic (i.e.: housework, child care, self-care, shopping); transportation (i.e.: walking or bicycling with the purpose of going somewhere, climbing stairs to public transportation, standing while using transportation); and leisure time (i.e.: sports, hobbies, exercise, volunteer work) (CASPERSEN; POWELL; CHRISTENSON, 1985; STRATH *et al.*, 2013). Physical activity can also be categorized in four dimensions: mode or type (i.e.: walking or cycling, or aerobic or anaerobic); frequency (i.e. number of sessions per day or per week), duration (i.e.: minutes or hours), and intensity (i.e.: metabolic demand of an activity) (CASPERSEN; POWELL; CHRISTENSON, 1985; STRATH *et al.*, 2013). Every person performs physical activity during daily life, however, the amount of physical activity each one performs may vary largely from person to person as well as over time (CASPERSEN; POWELL; CHRISTENSON, 1985). Current guidelines state that adults should perform at least 150 minutes to 300 minutes a week of moderate-intensity, or 75 minutes to 150 minutes a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and intensity aerobic activity (PIERCY *et al.*, 2018).

2.1.2 Physical activity measurement instruments

The instruments used to measure physical activity are varied in their complexity, precision and the amount of information provided (STRATH *et al.*, 2013). The instrument chosen for physical activity measurement will depend on the aims of the assessment and the resources available (FINI *et al.*, 2015). Physical activity measurement instruments can be categorized in subjective or objective. Subjective measuring methods are those in which the person needs to record or recall their physical activities (STRATH *et al.*, 2013). Objective methods are those that directly measure one or more bio signals (i.e.: heart rate or acceleration) and include all wearable monitors and direct observation (STRATH *et al.*, 2013).

The utility of the measurement process and research results depends on the extent that the measurement instrument shows adequate measurement properties for the assessment of an outcome measure in a specific population (PORTNEY; WATKINS, 2015). Therefore, an important aspect of an ideal physical activity assessment tool is the accuracy (validity) and

reproducibility (reliability) in its estimation of physical activity levels (AINSWORTH *et al.*, 2015).

2.1.2.1 Subjective instruments

Questionnaires and diaries are two subjective or self-report methods of measuring physical activity (STRATH *et al.*, 2013). The advantages of questionnaires are that, in general, they have low cost, low burden of individuals, are easy to administer, can assess different domains and dimensions of physical activity, and are usually performed in a single time point (STRATH *et al.*, 2013). However, there is a possibility of recall or social desirability bias (STRATH *et al.*, 2013; APARICIO-UGARRIZA *et al.*, 2015). Diaries, on the other hand, are not subjected to memory bias as much as questionnaires, also have low cost, and can provide information about physical activity domains and dimensions (STRATH *et al.*, 2013). Nevertheless, as mentioned by Strath *et al.*, (2013), diaries put very high burden on individuals and are time-consuming.

A recent systematic review had the aim to summarize the measurement properties and the clinical utility of self-report instruments to measure physical activity of individuals after stroke (MARTINS *et al.*, 2018). Only six self-report instruments had their measurement properties investigated for physical activity measurement in individuals after stroke: Activity Card Sort (ACS), the Coded Activity Diary, the Frenchay Activities Index (FAI), the Human Activity Profile (HAP), the Multimedia Activity Recall for Children and Adults (MARCA), and the Nottingham Leisure Questionnaire (original and short versions) (MARTINS *et al.*, 2018). The methodological quality of the studies that performed the investigation of the measurement properties ranged from "poor" to "good", and most of the results regarding the quality of the measurement properties were considered doubtful (MARTINS *et al.*, 2018). The instruments with the highest clinical utility scores were the FAI and the HAP (MARTINS *et al.*, 2018).

The FAI is a questionnaire that measures 15 activities associated with everyday life (MARTINS *et al.*, 2018). It is divided in three subscales: domestic, leisure/work and outdoor activities (MARTINS *et al.*, 2018). The dimension of physical activity assessed is frequency: the participant scores 0 if he never does the activity, 1 if he does it less than once a week, 2 if he does it one or two times per week, or 3 if he does it most days (MARTINS *et al.*, 2018).

The scale provides a summed score from 0 to 45 points (MARTINS *et al.*, 2018). This instrument has not been translated/adapted for Portuguese-Brazil.

The HAP covers a wide range of familiar physical activities for daily living and thus has acceptable face validity (TEIXEIRA-SALMELA *et al.*, 2007). In addition, it has adequate concurrent validity (TEIXEIRA-SALMELA *et al.*, 2007) and responsiveness (TEIXEIRA-SALMELA *et al.*, 1999) for the measurement of physical activity levels of individuals after stroke. The scoring of HAP includes both very low and high levels of physical activity and does not present ceiling or floor effects (TEIXEIRA-SALMELA *et al.*, 2007). In addition, it has been translated and adapted for Portuguese-Brazil (SOUZA *et al.*, 2006).

2.1.2.2 Objective instruments

There are different methods of assessing physical activity with objective instruments, such as, indirect calorimetry, doubly labeled water, observation and wearable monitors (STRATH *et al.*, 2013; FINI *et al.*, 2015; KENNEY *et al.*, 2015; APARICIO-UGARRIZA *et al.*, 2015). The advantages of some of these methods includes high accuracy and reliability and provision of detailed information on intensity, frequency, and duration of physical activity (STRATH *et al.*, 2013; APARICIO-UGARRIZA *et al.*, 2015). The disadvantages can include high cost, increased burden of wear for some devices, possibility of measurement only for short periods, and depending on instrument, technical equipment and expertise is necessary (STRATH *et al.*, 2013; APARICIO-UGARRIZA *et al.*, 2015).

The indirect calorimetry estimates energy expenditure through the measurement of the respiratory exchange of oxygen and carbon dioxide, and it is considered the criterion method for measuring physical activity in laboratory environment (STRATH *et al.*, 2013; KENNEY *et al.*, 2015; APARICIO-UGARRIZA *et al.*, 2015). However, it is an expensive method, that requires a high degree of technical expertise, and allows for assessment for only a short time period (STRATH *et al.*, 2013; KENNEY *et al.*, 2015; APARICIO-UGARRIZA *et al.*, 2015). Additionally, respiratory gas measurements might not reflect all metabolic processes depending on the extent of the contribution of anaerobic metabolism for energy production (STRATH *et al.*, 2013; KENNEY *et al.*, 2015; APARICIO-UGARRIZA *et al.*, 2015).

The doubly labeled water method estimates total energy expenditure by measuring the elimination rate of the isotopes of oxygen (^{18}O) and hydrogen (^{2}H) over time after ingestion of

a dose of water labeled with known quantities of both isotopes (WARREN *et al.*, 2010; STRATH *et al.*, 2013). The ^2H is eliminated as water, and the ^{18}O is lost as both water and carbon dioxide (byproduct of energy metabolism) (WARREN *et al.*, 2010; STRATH *et al.*, 2013). The difference between the elimination rates of both isotopes in some body fluid (i.e.: urine) is used to estimate the production of carbon dioxide, which by equations, is converted to energy expenditure (WARREN *et al.*, 2010; STRATH *et al.*, 2013). The doubly labeled water method is considered the criterion method for measuring physical activity in free-living environment (WARREN *et al.*, 2010; STRATH *et al.*, 2013; APARICIO-UGARRIZA *et al.*, 2015). However, it is an expensive method, that requires specific technical equipment and qualified assessors (WARREN *et al.*, 2010; STRATH *et al.*, 2013; APARICIO-UGARRIZA *et al.*, 2015). In addition, to obtain energy expenditure related to physical activity it is necessary to measure resting metabolic rate and thermic effect of food (WARREN *et al.*, 2010; STRATH *et al.*, 2013).

In a systematic review with the aim to describe how physical activity levels is assessed post-stroke, it was reported that from the 91 studies included, 31 employed observational methods and 60 used wearable monitors (FINI *et al.*, 2015). Observational methods (i.e.: videotape observation or counting repetitions of activities) can detect low threshold of activity (STRATH *et al.*, 2013; FINI *et al.*, 2015). However, they are feasible for evaluation of physical activity on clinical settings only and are usually used in individuals in the subacute phase post-stroke (STRATH *et al.*, 2013; FINI *et al.*, 2015). Observational methods are time-consuming, do not allow for intensity measurement, and might not accurately estimate physical activity because of low sampling rate (STRATH *et al.*, 2013; FINI *et al.*, 2015). Wearable monitors are usually costly, but they have the advantage of measuring physical activity of individuals in their own environment, for long periods of time, and are frequently used to assess physical activity of individuals living in the community (STRATH *et al.*, 2013; FINI *et al.*, 2015).

There is no single gold-standard wearable monitor to assess physical activity levels (AINSWORTH *et al.*, 2015; FINI *et al.*, 2015; 2017). However, according to the systematic review with the aim to describe how physical activity levels is assessed post-stroke, two wearable monitors are capable of measuring intensity, frequency, and duration of physical activity levels in individuals after stroke: the SenseWear Armband (BodyMedia, Pittsburgh,

PA, USA) and the Step Activity Monitor (Modus Health LLC, Washington, DC, USA) (FINI *et al.*, 2015). Although the accelerometer Step Activity Monitor was the device most commonly used in the studies included in this review (FINI *et al.*, 2015), this equipment presents limitations regarding the measurement of low intensity or non-ambulatory activities, such as upper-limbs activities (STRATH *et al.*, 2013; AINSWORTH *et al.*, 2015). On the other hand, the SenseWear Armband is able to estimate energy expenditure of low intensity and non-ambulatory physical activities (HIREMATH *et al.*, 2013; REECE *et al.*, 2015).

The SenseWear Armband is a portable, small, lightweight, and non-invasive equipment that is easily used on the back of the non-paretic arm (APARICIO-UGARRIZA *et al.*, 2015; FINI *et al.*, 2015). It allows the measurement of physical activity levels for seven consecutive days, which is considered an adequate duration of assessment to reduce the possibility of bias related to differences in physical activity levels between days (TOUILLET *et al.*, 2010; DEAN *et al.*, 2012; RIDGERS *et al.*, 2016). The SenseWear Armband uses multiple sensors to measure the heat flux (rate at which heat is dissipated from the body), skin temperature, galvanic skin response (electrical conductivity of skin), and motion (triaxial accelerometer) (APARICIO-UGARRIZA *et al.*, 2015; FINI *et al.*, 2015). Data acquired by the sensors is integrated with clinical characteristics (age, height, weight, sex, and smoking habits) into a proprietary algorithm to provide the estimation of physical activity levels (APARICIO-UGARRIZA *et al.*, 2015; FINI *et al.*, 2015). Multisensor tools, such as the SenseWear Armband, have as an advantage the potential for improved precision for measuring physical activity levels, that might result from the estimative of physical activity levels from multiple sensors (AINSWORTH *et al.*, 2015). In addition, the SenseWear Armband was considered the best device to estimate total energy expenditure when compared to other accelerometers frequently employed in studies with individuals after stroke (COMPAGNAT *et al.*, 2016; MANDIGOUT *et al.*, 2017). One study assessed test-retest reliability of the SenseWear Armband for the measurement of energy expenditure in individuals after stroke (> three months post-stroke), and the correlations between the measurements were significant, positive and classified as high to very high magnitude ($0.76 \leq$ Intraclass Correlation Coefficient ≤ 0.98) (VANROY *et al.*, 2014). In three studies (MOORE *et al.*, 2012; MANNS; HAENNEL, 2012; MANDIGOUT *et al.*, 2017), the SenseWear Armband showed adequate validity for the measurement of energy expenditure of individuals after stroke. For individuals in the acute or

subacute phase post-stroke, the association between the energy expenditure measured by the SenseWear Armband and by indirect calorimetry, were significant, positive and classified as moderate magnitude (Intraclass Correlation Coefficient = 0.56) (MANDIGOUT *et al.*, 2017). For individuals in the chronic phase post-stroke, in one of these studies, the correlations between the SenseWear Armband and indirect calorimetry, were significant, positive and classified as high magnitude (Intraclass Correlation Coefficient = 0.70) (MANNS; HAENNEL, 2012). In the other study, the correlations between the energy expenditure measured by the SenseWear Armband and by the doubly labeled water, were also significant, positive and classified as high magnitude ($r = 0.85$) (MOORE *et al.*, 2012).

2.1.2.2.1 Parameters of physical activity

There are different parameters for the measurement of physical activity (FINI *et al.*, 2015; 2017; LYNCH *et al.*, 2018). For example, the SenseWear Armband (BodyMedia, Pittsburgh, PA, USA; software version 8.1) provides different parameters to describe the physical activity levels: energy expenditure, number of steps, average metabolic equivalents (METs), total distance, and physical activity duration per activity intensity (i.e. light, moderate, vigorous, and very vigorous). In addition, for each of these parameters this instrument provides the total per day, the daily average and the total during all the evaluation period.

The parameters of physical activity levels employed in previous studies differed, and usually no justification for these choices were reported (FINI *et al.*, 2015; 2017; LYNCH *et al.*, 2018). For example, Chasens *et al.*, (2014) measured physical activity of individuals with type 2 diabetes using the number of steps per day while (BOND *et al.*, 2017) also reported daily total duration at moderate-to-vigorous physical activity for individuals after bariatric surgery. Van Hoye *et al.* (2012) reported number of steps, minutes of physical activity (sedentary, light, moderate, vigorous, and very vigorous intensity physical activity) and daily energy expenditure.

In studies that measured physical activity levels post-stroke, step count is the parameter most frequently reported (ENGLISH *et al.*, 2014; FINI *et al.*, 2015; 2017; LYNCH *et al.*, 2018). However, though this is an easily understandable measure, there is some questioning if number of steps alone is an adequate physical activity measure (ENGLISH *et al.*, 2014; FINI

et al., 2015). The number of steps is not informative about the intensity or duration of physical activity (ENGLISH *et al.*, 2014). The same number of steps may be accumulated in a high or low intensity activity, or in a short or long period of activity (ENGLISH *et al.*, 2014). Furthermore, number of steps only gives information about ambulatory activities while physical activity levels, as defined previously, includes any body movement produced by skeletal muscles (CASPERSEN; POWELL; CHRISTENSON, 1985), such as upper limbs activities or cycling. Thus, the parameter "number of steps" may not be the best single parameter to characterize physical activity levels in individuals after stroke (ALZAHRANI *et al.*, 2011).

Since physical activity results, by definition, in an increase in energy expenditure (CASPERSEN; POWELL; CHRISTENSON, 1985; STRATH *et al.*, 2013), the evaluation of physical activity levels usually included the quantification of energy expenditure (AINSWORTH *et al.*, 2015; APARICIO-UGARRIZA *et al.*, 2015). Energy expenditure is used to quantify the total amount (total volume) of physical activity accomplished during a period of time (WOOD; ZHU, 2006). The energy expenditure of each activity might be estimated by multiplying the frequency, duration, and intensity of the activity (WOOD; ZHU, 2006). The total energy expenditure associated with performance of different physical activities might be estimated by the sum of energy expenditure of all physical activities (WOOD; ZHU, 2006). Considering that the definition of physical activity implies in an increase in energy expenditure, and that energy expenditure is a result of the frequency, duration, and intensity of the physical activity, it seems that the measurement of energy expenditure would be the single best parameter to objectively assess physical activity levels.

2.1.3 Physical activity and sedentary behavior after stroke

Globally, physical activity levels of adults are low and are associated with mortality rate and higher risk of cardiovascular diseases, including stroke and heart attacks (BENJAMIN *et al.*, 2018). Physical inactivity also results in higher economic burden (BENJAMIN *et al.*, 2018). Higher physical activity levels are associated with reduced incidence of stroke and risk of cardiovascular diseases, thus being physically active is one of the American Heart Association's seven components of ideal cardiovascular health for adults (BENJAMIN *et al.*, 2018).

Physical activity levels of community-dwelling individuals after stroke are low in quantity, duration, and intensity (FIELD *et al.*, 2013; FINI *et al.*, 2017). According to a population-based study developed in Canada, community-dwelling individuals after stroke are more physically inactive than older adults with diabetes, musculoskeletal, cardiovascular, respiratory, or other neurological chronic diseases (ASHE *et al.*, 2009). According to meta-analyses, factors associated with physical activity after stroke are cardiorespiratory fitness, depression, fatigue, endurance, and quality of life (THILARAJAH *et al.*, 2018). Physical inactivity after stroke is explained by several factors related directly and indirectly to the stroke and has been pointed out as cause and consequence of their functional and health problems (DUNCAN *et al.*, 2012; HILL *et al.*, 2012; BILLINGER *et al.*, 2014). After stroke, one of the main consequences of the concomitant presence of cardiovascular diseases and impairments such as muscle weakness (HILL *et al.*, 2012), reduced cardiorespiratory fitness (MARSDEN *et al.*, 2013; SAUNDERS *et al.*, 2016), depression (BILLINGER *et al.*, 2014), physical mobility limitations (FARIA *et al.*, 2013) as well as low perception of quality of life (POLESE *et al.*, 2014), and reduced social participation (SKOLARUS *et al.*, 2014) is low physical activity levels. Besides contributing to a physically inactive lifestyle, these disabilities can also be aggravated by the low level of physical activity (BILLINGER *et al.*, 2014) creating a vicious cycle, that dramatically impact the healthy life style of individuals post-stroke.

Little is known about sedentary behavior of individuals after stroke (ENGLISH *et al.*, 2014). However, the results of recent studies showed that sedentary behavior is highly prevalent in individuals after stroke (TIEGES *et al.*, 2015; EZEUGWU *et al.*, 2016). When compared with individuals without stroke and matched by age, ethnicity and sex, individuals after stroke spend more time in low-energy expenditure activities (BUTLER; EVENSON, 2014; PAUL *et al.*, 2016). The consequences of this augmented sedentary behavior of individuals post-stroke on function and health are not well known yet (BUTLER; EVENSON, 2014). However, understanding if sedentary behavior is as relevant as physical activity levels for the function and health of individuals after stroke is one of the future research directions identified in the Scientific Statement of the American Heart Association and American Stroke Association about physical activity and exercise recommendations for individuals' after stroke (BILLINGER *et al.*, 2014). Although there is not much knowledge about the impact of high

levels of sedentary behavior in individuals after stroke, it is believed to impede recovery (BUTLER; EVENSON, 2014). Therefore, interventions aiming to modify sedentary behavior might be of relevance for individuals after stroke (GIBBS *et al.*, 2015; TIEGES *et al.*, 2015).

The possible effective interventions to modify sedentary behavior of individuals after stroke are unknown (EZEUGWU *et al.*, 2016). However, considering that the barriers to reducing sedentary behavior, reported by individuals after stroke, include physical deficits (EZEUGWU *et al.*, 2016), and that the results of a study with more than two thousand individuals without known heart disease showed that sedentary behavior have an inverse association with cardiorespiratory fitness, independent of physical activity (KULINSKI *et al.*, 2014), aerobic training might represent a treatment option for reducing sedentary behavior of individuals after stroke. Taking into account the importance of developing interventions to modify sedentary behavior, and the potential positive effect of aerobic training on this outcome, it is important to investigate if aerobic training can reduce time spent in low-energy expenditure activities after stroke. Only one randomized controlled trial investigated the effects of an intervention specifically with the aim to reduce sedentary behavior in individuals after stroke (ENGLISH *et al.*, 2016). Four counselling sessions were not effective to decrease sedentary behavior, however, the authors reported that the study was not powered to detect statistically significant intervention effects (ENGLISH *et al.*, 2016).

2.2 Aerobic exercise

2.2.1 Aerobic exercise definition

Aerobic exercise is any physical activity that involves the repetitive activation of large muscle groups in a rhythmic manner for a prolonged period (i.e.: walking, stepping, running, swimming, cycling or rowing) (PANG *et al.*, 2013; BILLINGER *et al.*, 2014; PIERCY *et al.*, 2018). For some authors the definition of aerobic exercise also includes an intensity threshold: aerobic intensity above 39% heart rate reserve (HRR) or peak oxygen consumption (VO_{2peak}), or above 63% maximal heart rate (HR_{max}) (BOYNE *et al.*, 2016). The components of aerobic exercise are intensity (amount of effort), frequency (days/week), duration (minutes), and type or modality (BILLINGER *et al.*, 2014; PIERCY *et al.*, 2018).

2.2.2 Physiologic determinants of cardiorespiratory fitness for healthy adults

Cardiorespiratory fitness is related to the ability to perform dynamic, moderate-to-vigorous intensity exercise that involves large muscles for a long duration (PESCATELLO *et al.*, 2014; KENNEY *et al.*, 2015; SAUNDERS *et al.*, 2016). It depends on the integrated adequate function of the respiratory and cardiovascular systems to maintain oxygen delivery to active muscles, and of the musculoskeletal system to use energy aerobically during exercise (NEDER, 2002; PESCATELLO *et al.*, 2014; KENNEY *et al.*, 2015; ROSS *et al.*, 2016). The maximal oxygen uptake (VO_{2max}) is the highest rate of oxygen consumption measured during maximal exercise and is considered the best single indicator of cardiorespiratory fitness (PESCATELLO *et al.*, 2014; KENNEY *et al.*, 2015; SAUNDERS *et al.*, 2016). The VO_{2max} is the result of the maximal cardiac output and the maximal arterial-venous oxygen difference (NEDER, 2002; PESCATELLO *et al.*, 2014; KENNEY *et al.*, 2015). The cardiac output is the result of the heart rate and stroke volume (NEDER, 2002; PESCATELLO *et al.*, 2014; KENNEY *et al.*, 2015).

The VO_{2max} represents an individual's physiologic limit (PESCATELLO *et al.*, 2014). Thus, a plateau in VO_{2max} is observed at the end of a progressive exercise test even with further increase in workload (PESCATELLO *et al.*, 2014). However, an individual might reach volitional fatigue before this plateau occurs (KENNEY *et al.*, 2015). In this case, the highest oxygen uptake attained is more correctly termed the peak oxygen uptake (VO_{2peak}) (KENNEY *et al.*, 2015). As a plateau is rarely observed in individuals with cardiovascular diseases during a progressive exercise test, the term peak oxygen uptake (VO_{2peak}) is more commonly used than the term maximal oxygen uptake (VO_{2max}) to describe cardiorespiratory fitness in populations with diseases, such as stroke (MARSDEN *et al.*, 2013; PANG *et al.*, 2013; PESCATELLO *et al.*, 2014; SAUNDERS *et al.*, 2016).

During a single bout of aerobic exercise, the cardiovascular and respiratory systems adjust their function to provide the oxygen required to actively contract the muscles (NEDER, 2002; KENNEY *et al.*, 2015). With aerobic exercise training, these systems are challenged repeatedly, thus, they adapt and there is an improvement on VO_{2max} (MARSDEN *et al.*, 2013; PANG *et al.*, 2013; KENNEY *et al.*, 2015; SAUNDERS *et al.*, 2016; BOYNE *et al.*, 2016).

This improvement is the result of multiple physiologic adaptations within the cardiovascular, musculoskeletal and, to a lesser extent, the respiratory system (NEDER, 2002; KENNEY *et al.*, 2015). As maximal levels of exercise are achieved, factors in all these systems may potentially limit the maximal ability to transport and use oxygen (NEDER, 2002; KENNEY *et al.*, 2015).

2.2.2.1 Cardiovascular system

During a single bout of aerobic exercise, cardiac output is increased due to a combined increase in heart rate and stroke volume (NEDER, 2002; KENNEY *et al.*, 2015). Thus, there is an increase in systolic blood pressure, which facilitates the increase in blood flow through the active muscles (NEDER, 2002; KENNEY *et al.*, 2015). In addition, there is a redistribution of blood, with an increase to the tissues with greatest metabolic need and hemoconcentration occurs as plasma volume decreases (result of increased blood pressure), which increases oxygen-carrying capacity (NEDER, 2002; KENNEY *et al.*, 2015). Moreover, hemoglobin desaturation is enhanced to better respond to the increased oxygen demand and there is also an increased extraction of oxygen from the blood for use by the active tissues, resulting in an amplified arterial-venous oxygen difference (KENNEY *et al.*, 2015).

After aerobic exercise training, heart rate at rest and at submaximal exercise decreases, however, at maximal exercise it does not change. Thus, increases in VO_{2max} depend on changes in stroke volume and arterial-venous oxygen difference. Stroke volume is augmented at rest, during submaximal, and maximal exercise (NEDER, 2002; KENNEY *et al.*, 2015). One of the reasons for this is the increase in plasma volume, and a longer diastolic filling time (KENNEY *et al.*, 2015). In addition, the left ventricle force of contraction is augmented, due to cardiac muscle hypertrophy, and greater elastic recoil caused by increased preload (Frank-Starling mechanism) (KENNEY *et al.*, 2015). Moreover, the diminished systemic vascular resistance also contributes to greater stroke volume (KENNEY *et al.*, 2015). Although the increase in VO_{2max} of healthy individuals is mainly the result of the higher stroke volume and muscle blood flow, there is also an increase in arterial-venous oxygen difference that contributes to it (KENNEY *et al.*, 2015). This change is the consequence of increased muscle blood flow, and an increase in: number of capillaries, capillary recruitment, blood volume, and increased active muscle ability to extract oxygen (KENNEY *et al.*, 2015). It is estimated that

70–85% of the limitation in VO_{2max} is linked to maximal cardiac output (BASSETT; HOWLEY, 2000).

2.2.2.2 Musculoskeletal system

The maximal capacity of the muscles to use oxygen can be measured by their oxidative capacity, which depends on its oxidative enzyme concentration, fiber type composition, and oxygen availability (KENNEY *et al.*, 2015). The musculoskeletal adaptations to aerobic exercise training include an increase in the type I fibers cross-sectional area and percentage, and a shift from type II_x to II_a fibers (shift from low-to-medium oxidative capacity). In addition, there is an increase in the number of capillaries per muscle fiber, which results in improved muscle perfusion and oxygen diffusion (KENNEY *et al.*, 2015). Aerobic training increases muscle myoglobin (responsible for the transport of oxygen from cell membranes to the mitochondria), the number and size of muscle fiber mitochondria, and the quantity of oxidative enzymes. Thus, aerobic training results in increased capacity for oxidative metabolism (KENNEY *et al.*, 2015).

2.2.2.3 Respiratory system

During a single aerobic exercise bout, there is an immediate increase in ventilation. In addition, oxygen exchange at the alveoli is facilitated since there is a greater partial pressure gradient as venous oxygen is depleted (NEDER, 2002; KENNEY *et al.*, 2015). Aerobic exercise training does not have an important influence on lung structure and function (KENNEY *et al.*, 2015). However, some adaptations that might explain the augmentation of the VO_{2max} are an increase in: 1) maximal pulmonary ventilation (as a result of tidal volume and respiratory rate increase), and 2) maximal pulmonary diffusion (NEDER, 2002; KENNEY *et al.*, 2015). The respiratory system is not usually a VO_{2max} limiting factor even during maximal effort, however, it may limit VO_{2max} performance in individuals with different respiratory disorders (BASSETT; HOWLEY, 2000; NEDER, 2002; KENNEY *et al.*, 2015).

2.2.2.4 Individual characteristics

There are some individual characteristics that might influence the response to aerobic training, such as baseline cardiorespiratory fitness, genetics, sex, age, and health condition

(BOUCHARD *et al.*, 1999; BASSETT; HOWLEY, 2000; KENNEY *et al.*, 2015). For the same volume of training, an individual with high cardiorespiratory fitness will have a smaller relative improvement in VO_{2max} than a person with lower cardiorespiratory fitness. In addition, the ability to increase the VO_{2max} seems to be genetically limited and is lower in women than in men. Moreover, there is a decrease in VO_{2max} with aging, due to decreased blood flow and cardiac output (mainly due to decreased maximum heart rate) (BASSETT; HOWLEY, 2000; KENNEY *et al.,* 2015). However, maximal arterial-venous oxygen difference usually does not change with aging (BASSETT; HOWLEY, 2000; KENNEY *et al.,* 2015). Physical activity levels also seem to be an important factor in the decreased VO_{2max}, since many of the deleterious changes of aging are attenuated in older athletes who continue to perform exercise training (BASSETT; HOWLEY, 2000; KENNEY *et al.*, 2015). After aerobic training, older individuals still can achieve an increase in VO_{2max}. Although, different from younger individuals, it results mostly from improvement in the muscles' oxidative enzyme activities than from an increased maximal cardiac output (BASSETT; HOWLEY, 2000; KENNEY *et al.,* 2015).

2.2.3 Cardiorespiratory fitness post-stroke

One of the common disabilities post-stroke is reduced cardiorespiratory fitness compared to healthy individuals (MARSDEN *et al.*, 2013; PANG *et al.*, 2013; DUNN *et al.*, 2015; KAMINSKY *et al.*, 2015; VAN DE PORT *et al.*, 2015; SALTYCHEV *et al.*, 2016; SAUNDERS *et al.*, 2016). Even independently ambulant community-dwelling individuals after stroke showed reduced cardiorespiratory fitness when compared to healthy age- and gender-matched controls (DUNN *et al.*, 2015). This reduced cardiorespiratory fitness post-stroke may have a negative impact on daily activities, since it might be lower than the energy expenditure needed for some activities of daily living (IVEY *et al.*, 2008; BAERT*, et al.*, 2012; ENGLISH *et al.*, 2014; BOSS *et al.*, 2017). In addition, individuals after stroke show higher energy cost to perform common activities, such as walking (KRAMER *et al.*, 2016). Thus, for example, walking slowly around the house, based on healthy subject's data, is classified as light physical activity (requires on average two metabolic equivalent of tasks). However, individuals after stroke require approximately three metabolic equivalents to perform this same activity, thus it can be considered moderate intensity (KRAMER *et al.*,

2016). Therefore, individuals post-stroke needs to exert a great effort to perform some activities of daily living and might not be able to perform or to sustain other activities (IVEY *et al.*, 2008). Improving cardiorespiratory fitness post-stroke is important, as it might enable activities of daily living to be performed at a lower percentage of aerobic capacity (BILLINGER *et al.*, 2014).

2.2.4 Physiologic determinants of cardiorespiratory fitness after a stroke

2.2.4.1 Cardiovascular system

Two transversal studies have reported opposing views on the physiological basis of the low VO_{2peak} post-stroke. Tomczak *et al.* (2008) assessed cardiovascular function of 10 individuals in the chronic phase post-stroke and 10 healthy age, gender, and activity-matched controls (TOMCZAK *et al.*, 2008). At rest, only the stroke volume was significantly reduced in individuals after stroke when compared to healthy individuals (TOMCZAK *et al.*, 2008). However, VO_{2peak}, power output, heart rate, stroke volume, and cardiac output were statistically lower at peak exercise in individuals' post-stroke whereas no difference was observed for the arterial-venous oxygen difference, systolic, or diastolic blood pressure (TOMCZAK *et al.*, 2008). Thus, the authors concluded that the reduction on the VO_{2peak} post-stroke was probably secondary to a decline in cardiac output (TOMCZAK *et al.*, 2008). On the other hand, Jakovljevic *et al.* (2012) compared 28 men in the chronic phase post-stroke with 25 healthy age-matched men during the performance of a maximal cardiopulmonary exercise test (JAKOVLJEVIC *et al.*, 2012). They found that, besides a low VO_{2peak}, the peak arterial-venous oxygen difference was reduced in individuals after stroke when compared to healthy individuals. However, the peak exercise cardiac power and cardiac output were not significantly different between individuals after stroke and healthy individuals. Thus, for the authors of this study (JAKOVLJEVIC *et al.*, 2012), it seems that in individuals after stroke the ability of skeletal muscles to extract oxygen was reduced, although cardiac function was maintained. Jakovljevic *et al.* (2012) concluded that the low VO_{2peak} of individuals after stroke was probably due to a reduced ability of the working muscles to extract oxygen.

These latter findings are supported by the results of a recent randomized controlled trial with community-dwelling individuals in the chronic phase post-stroke, which aimed to

investigate the physiological factors affecting the changes in VO_{2peak} after a multimodal intervention (aerobic/strength/balance/flexibility) or a control home stretching program (MOORE *et al.*, 2016). After the intervention, there was a statistically significant increase in the VO_{2peak} and peak arterial-venous oxygen difference in the experimental group whereas there were no significant differences in the cardiac output or cardiac power output in either group (MOORE *et al.*, 2016). In addition, a significant association was observed between change in VO_{2peak} and change in peak arterial-venous oxygen difference ($r=0.507$), though no significant correlation was found with cardiac output (MOORE *et al.*, 2016). Thus, according to Moore *et al.* (2016), the improvement in VO_{2peak} post-intervention was related to the ability of the skeletal muscles to extract oxygen, rather than cardiac function. Tang *et al.* (2014) also performed a randomized controlled trial with the aim of comparing the effects of aerobic exercise training with a balance and stretching program for six months duration on fitness, cardiovascular risk factors, and cardiac function in individuals with chronic stroke. There were no changes in VO_{2peak} or in the majority of the variables related to cardiac function (left ventricular ejection fraction, left atrial emptying fractions, mitral and tricuspid annular velocities) in any of the groups, though the group that performed aerobic exercise demonstrated greater improvement in right atrial emptying fraction (TANG *et al.*, 2014). The absence of significant change in cardiac function might be due to the fact that this study only assessed cardiac function at rest. Performing this evaluation at peak exercise may be more representative of the adaptability of the cardiovascular system to increased demand. Additionally, this trial presents limitations to the interpretation of the determinants of VO_{2peak}, since there were no changes in VO_{2peak}.

2.2.4.2 Musculoskeletal system

The reduced central neural drive, and thus altered neurological input to the periphery, associated to the high levels of physical inactivity post-stroke and other concomitant cardiovascular diseases may contribute to alter skeletal muscle tissue composition, thereby, contributing to low cardiorespiratory fitness (IVEY *et al.*, 2008; BILLINGER *et al.*, 2012; BILLINGER *et al.*, 2014). In addition to the muscular atrophy, and increased intramuscular fat, there is also a modification of fiber-type proportions (slow-to-fast fiber type conversion)

post-stroke (RYAN *et al.*, 2002; DE DEYNE *et al.*, 2004; IVEY *et al.*, 2008; ENGLISH *et al.*, 2010; RYAN *et al.*, 2011; BILLINGER *et al.*, 2014).

In addition, there is evidence of a reduction of capillaries per muscle fiber and exercise blood flow in the paretic leg, when compared to the nonparetic limb (IVEY *et al.*, 2008; BILLINGER *et al.*, 2012; BILLINGER *et al.*, 2014). Other significant differences between the paretic and non-paretic limb were a reduced femoral artery diameter and blood flow speed, and a greater femoral artery wall thickness (BILLINGER; KLUDING, 2009; BILLINGER *et al.*, 2012). These changes probably contribute to impaired flexibility of the artery wall to vasodilate during exercise to allow for adequate oxygen delivery to the active muscles (BILLINGER *et al.*, 2012). According to a review, the lean mass of the paretic limb was a predictor (r=0.61) of VO$_{2peak}$ in individuals in the chronic phase post-stroke (HAFER-MACKO *et al.*, 2008). Thus, these skeletal muscle changes post-stroke might contribute to a reduction of cardiorespiratory fitness and related health changes (BILLINGER *et al.*, 2012). Nevertheless, one study reported a significant increase in rest and reactive hyperaemic blood flow in both lower limbs after aerobic training for individuals after stroke (IVEY *et al.*, 2010).

2.2.4.3 Respiratory system

According to a review of the literature, individuals after stroke may demonstrate reduced pulmonary diffusion capacity, ventilation-perfusion mismatching, and decreased lung volumes (e.g., maximal inspiratory capacity, and expiratory reserve volume) (BILLINGER *et al.*, 2012). Moreover, when compared to healthy individuals, individuals after stroke usually show reduced inspiratory and expiratory muscle strength (BRITTO *et al.*, 2011; MESSAGGI-SARTOR *et al.*, 2015; LISTA PAZ *et al.*, 2016). Individuals after stroke also presented lower peak minute ventilation, and peak tidal volume (TOMCZAK *et al.*, 2008). However, there was no difference regarding breathing frequency (TOMCZAK *et al.*, 2008). Thus, it suggests that the low VO$_{2peak}$ post-stroke might be secondary to a decline in peak ventilation (due to a reduced peak tidal volume).

2.2.4.4 Individual characteristics

Lower baseline VO$_{2peak}$ values are associated with greater improvements in VO$_{2peak}$ in individuals after stroke (TANG *et al.*, 2013). In addition, Baert *et al.* (2012), in a longitudinal

study, measured VO_{2peak} at 3, 6, and 12 months post-stroke and observed that older individuals with diabetes were less likely to improve their VO_{2peak}. Nevertheless, Globas *et al.* (2012) reported that age was not associated with the aerobic training response. This latter result is in accordance with healthy individual data that, as stated previously, older individuals can still achieve an increase in VO_{2max} after aerobic training (KENNEY *et al.*, 2015). Thus, age might have an influence on VO_{2peak} in individuals after stroke who did not specifically get involved in aerobic exercise training but does not seem to affect the gains with aerobic training. Four studies investigated the longitudinal changes, without specific aerobic training, in VO_{2peak} after stroke (FUJITANI *et al.*, 1999; MACKAY-LYONS; MAKRIDES, 2004; POHL *et al.*, 2004; BAERT *et al.*, 2012). Although substantial limitations in cardiorespiratory fitness persisted, three studies found a significant increase in VO_{2peak} with time (FUJITANI *et al.*, 1999; MACKAY-LYONS; MAKRIDES, 2004; POHL *et al.*, 2004), whereas Baert *et al.* (2012) showed that on average VO_{2peak} did not significantly change over time (BAERT *et al.*, 2012). This difference in results might be explained by a difference in daily activities performed by participants, since individuals who walked more showed greater improvement of VO_{2peak} than those who did not (FUJITANI *et al.*, 1999).

2.2.5 Aerobic exercise training for persons after stroke

The results of different meta-analyses has shown that aerobic exercise training is effective to increase cardiorespiratory fitness (VO_{2peak}), endurance (usually measured by the Six-Minute Walk Test (6MWT)), maximum and comfortable gait speed (frequently measured by the Ten Meter Walk Test (10MWT) in individuals after stroke (MARSDEN *et al.*, 2013; PANG *et al.*, 2013; SALTYCHEV *et al.*, 2016; SAUNDERS *et al.*, 2016; BOYNE *et al.*, 2017). According to our search, there are less consistent reports regarding the efficacy of aerobic training to improve depression, balance, other measures of mobility (i.e.: Timed-Up and Go Test), quality of life, and physical activity levels in individuals after stroke (PANG *et al.*, 2013; SAUNDERS *et al.*, 2016). Current clinical guidelines strongly recommend, based on the positive study results, that individuals after stroke perform aerobic exercises regularly (BILLINGER *et al.*, 2014).

2.2.6 Explanations for peak oxygen uptake change (or not) with aerobic exercise training for persons with chronic stroke

Individual responses to aerobic exercise training are highly variable (BAERT *et al.*, 2012; TANG *et al.*, 2013; KENNEY *et al.*, 2015). As mentioned before, the response to aerobic exercise training is, in part, genetically determined (KENNEY *et al.*, 2015). For individuals participating in the same aerobic training program, there will be individuals who show a large improvement, and those who show little or no improvement (KENNEY *et al.*, 2015). Individual changes in VO_{2peak} of participants of a trial about cardiac rehabilitation after stroke ranged from 32% decline to 56% improvement (TANG *et al.*, 2013).

Additionally, as also mentioned previously, another factor that can also influence an individual response to aerobic exercise training is baseline cardiorespiratory fitness (KENNEY *et al.*, 2015). For healthy individuals, the higher the baseline cardiorespiratory fitness, the smaller the relative improvement in VO_{2max} for the same volume of training, and vice-versa (KENNEY *et al.*, 2015). For individuals after stroke, baseline cardiorespiratory fitness can also influence improvement of cardiorespiratory fitness with aerobic training (TANG *et al.*, 2013). Lower baseline VO_{2peak} is associated with a larger VO_{2peak} increase (TANG *et al.*, 2013).

However, other individual characteristics, such as time post-stroke, do not seem to have an influence on changes in VO_{2peak} after aerobic exercise training. Boyne *et al.* (2017) found that post-stroke phase (classified as subacute [< six months] or chronic [≥ six months]) did not influence improvement of the VO_{2peak} after aerobic training. In addition, Globas *et al.* (2012) reported that the time interval between the stroke and study enrollment was not associated with the aerobic training response.

Another explanation for why VO_{2peak} of individuals after stroke may change or not after aerobic exercise is related to the prescription of the training. According to the American College of Sports Medicine, the components of an exercise prescription are intensity, duration, frequency, and modality (GARBER *et al.*, 2011; PESCATELLO *et al.*, 2014). These components constitute the dose or quantity, and they determine the effect of exercise, thus, there is a dose-response relationship (GARBER *et al.*, 2011; AMMANN *et al.*, 2014; BILLINGER *et al.*, 2014). Nevertheless, the specific quantity for optimal attainment of the

health benefits of exercise, that is, the shape of the dose–response curve, is not yet clear, but it is probably dependent on the outcome measure of interest (i.e., cardiorespiratory fitness) and individuals' baseline characteristics (GARBER *et al.*, 2011). Therefore, differences in aerobic exercise training prescriptions may result in variation of the benefits accomplished. However, the optimal dose for aerobic exercise training for individuals after stroke has yet to be established.

Intensity, a determinant of the response to exercise training, refers to the effort level or demand of the activity, and is usually measured by relative methods such as, percent of heart rate reserve (GARBER *et al.*, 2011; AMMANN *et al.*, 2014; PESCATELLO *et al.*, 2014). The American Heart Association/American Stroke Association guidelines recommends the prescription of moderate to vigorous intensity aerobic exercise for individuals after stroke (BILLINGER *et al.*, 2014). However, although aerobic training performed at both moderate and vigorous intensity is effective in improving cardiorespiratory fitness (MARSDEN *et al.*, 2013; PANG *et al.*, 2013; SAUNDERS *et al.*, 2016), it seems that the magnitude of this improvement might be different. A secondary analysis comparing two trials, that performed aerobic exercise training at different intensities, with individuals with chronic stroke, found that higher training intensity (80% *versus* 60% of heart rate reserve) was the only variable associated with greater VO_{2peak} improvement (LAM *et al.*, 2010). Boyne *et al.* (2017) in a recent meta-analysis involving 598 individuals after stroke, found that aerobic exercise training of vigorous intensity (60% to 84% of heart rate reserve) was significantly correlated with larger VO_{2peak} improvement when compared to moderate intensity (40% to 59% of heart rate reserve). The effect size for high intensity aerobic exercise training was 3.8 $mL.kg^{-1}.min^{-1}$ (95% confidence interval = 2.4 - 5.2 $mL.kg^{-1}.min^{-1}$), while that for moderate intensity was 1.6 $mL.kg^{-1}.min^{-1}$ (95% confidence interval = 0.8 - 2.4 $mL.kg^{-1}.min^{-1}$) (BOYNE *et al.*, 2017). Furthermore, aerobic exercise training of vigorous intensity had a 99.7% probability of being associated with larger effect size when compared to that of moderate intensity in individuals after stroke (BOYNE *et al.*, 2017). These results are consistent with the randomized controlled trial of Ivey *et al.* (2015). In this study, vigorous intensity aerobic training (30 minutes at 80% of heart rate reserve) was compared with that of moderate intensity (50 minutes at 50% of heart rate reserve), performed by individuals in the chronic phase post-stroke (Ivey *et al.*, 2015). Although there was no control for equivalence of volume of energy expenditure

between groups (GARBER *et al.*, 2011), the authors reported significantly greater gains in VO_{2peak} in the vigorous intensity group (15.9 ± 1.7 mL.kg^{-1}.min^{-1} to 21.3 ± 1.6 mL.kg^{-1}.min^{-1}) when compared to the moderate intensity group (16.6 ± 1.1 mL.kg^{-1}.min^{-1} to 17.5 ± 1.2 mL.kg^{-1}.min^{-1}) (IVEY *et al.*, 2015). Furthermore, Globas *et al.* (2012) found that the improvement in VO_{2peak} after aerobic training was significantly correlated with the degree at which training intensity could be progressed in people with chronic stroke. Therefore, aerobic exercise training intensity and progression seems to be important determinants of the efficacy of aerobic training on VO_{2peak} for individuals in the chronic phase post-stroke. Nevertheless, it is still not clear if the better results of vigorous intensity aerobic training are a consequence of a greater volume of energy expenditure, since there is usually also a superior volume of exercise in the vigorous intensity group (GARBER *et al.*, 2011).

The duration of exercise is usually expressed by minutes per day, the frequency by the number of times an activity is performed per week, and the length of the program by weeks or months (AMMANN *et al.*, 2014; PESCATELLO *et al.*, 2014; BILLINGER *et al.*, 2015). The American Heart Association/American Stroke Association guidelines recommends 20-60 minutes per session, and 3-5 days per week of aerobic training for individuals after stroke while there is no recommendation for the length of the intervention (BILLINGER *et al.*, 2014). According to Boyne *et al.* (2017), the overall volume of aerobic exercise (hours per session x sessions per week x total weeks) did not influence the improvement of the VO_{2peak}. To add to this finding, a systematic review by Pang et al (2013) highlighted that the only study that did not find a significant effect of aerobic training on cardiorespiratory fitness (VO_{2peak}) performed the training during four weeks, while the trials that showed a positive effect on VO_{2peak} in individuals with chronic stroke completed at least eight weeks of aerobic exercise (MOORE *et al.*, 2010; PANG *et al.*, 2013). Thus, it was hypothesized that a 4-week training might not be enough to induce change in people in the chronic phase post-stroke, thus a minimum of eight weeks may be required to achieve an improvement in VO_{2peak} (PANG *et al.*, 2013). Nevertheless, no study specifically investigated the possible effect of the different length of aerobic intervention or frequency of training on gains in VO_{2peak} post-stroke.

There are different modalities for the performance of aerobic exercise, such as, overground, treadmill (with or without body weight support), cycling, swimming, and recumbent stepping (BILLINGER *et al.*, 2015). For individuals after stroke, despite what

could be expected considering the principle of specificity of training, the modality of the aerobic exercise (classified as seated or walking) was not significantly associated with the VO_{2peak} effect size, although it was for gait speed and endurance (higher effect size associated with walking modalities) (BOYNE *et al.*, 2017). Nevertheless, the modalities of aerobic training frequently prescribed for individuals after stroke are treadmill and cycle ergometer (PANG *et al.*, 2013; SAUNDERS *et al.*, 2016).

To summarize, different impairments to the cardiovascular, respiratory, and musculoskeletal systems are seen in individuals after stroke when compared to healthy individuals, and any of these could have an impact on cardiorespiratory fitness following a stroke. Additionally, the low physical activity levels and sedentary behavior commonly observed post-stroke may contribute to reduced cardiorespiratory fitness. Also, the various comorbidities associated with stroke, and the cardiorespiratory fitness level of individuals previous to stroke onset may be contributors to the lower values of VO_{2peak} post-stroke. The reduced cardiorespiratory fitness post-stroke may lead to limitations in activities and restriction in participation. Therefore, improving cardiorespiratory fitness post-stroke is an important outcome. However, the individual VO_{2peak} response to aerobic exercise training of both healthy individuals and individuals after stroke is highly variable. Possible explanations for a change or not, after aerobic exercise training, in VO_{2peak} of individuals with chronic stroke are genetics, baseline value of the VO_{2peak}, and the dose of exercise training prescribed. Nevertheless, chronicity of stroke does not seem to be a reason for the variation in response to aerobic training. Although, the prescription of exercise is a recognizable factor that affects improvement in VO_{2peak}, more studies are required to investigate the optimal aerobic exercise dose for individuals after stroke.

2.3 Knowledge translation

The use of research evidence to inform clinical decision making is important. It has been shown that adherence to clinical guidelines is associated with better functional recovery of individuals after stroke (DUNCAN *et al.*, 2002; HUBBARD *et al.*, 2012). In addition, guideline compliance is related to individuals' satisfaction post-stroke (REKER *et al.*, 2002). Considering the importance of ensuring that health care is based on evidence, there is a

prominence of Evidence-Based-Practice in rehabilitation (DIJKERS *et al.*, 2012). Evidence-Based-Practice might be defined as the use of the best available evidence, along with professional experience, and with ethical principles, including patient values, to make clinical decisions (VERAS *et al.*, 2016).

Nevertheless, the gap between knowledge and its use still exists (STRAUS *et al.*, 2013; WALKER *et al.*, 2013). Thus, there is a growing interest and effort to reduce this gap, and to understand the success and challenges of the complex process of translating knowledge into health care practice (MENON *et al.*, 2010; WALKER *et al.*, 2013; ZIDAROV *et al.*, 2013). As a result of considering new methods to effectively disseminate and implement knowledge into practice, Knowledge Translation has emerged as a strategy for improvement (GRAHAM *et al.*, 2006; STRAUS *et al.*, 2013; ZIDAROV *et al.*, 2013). A comprehensive definition of Knowledge Translation frequently used is the one from the Canadian Institutes of Health Research (CIHR) agency, which is: "*a dynamic and iterative process that includes the synthesis, dissemination, exchange and ethically sound application of knowledge to improve health, provide more effective health services and products, and strengthen the healthcare system*"(THE CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR); MACDERMID; GRAHAM, 2009). Thus, Knowledge Translation comprises the process of turning knowledge into action, into actual use of knowledge by various stakeholders, or the methods for covering the knowledge-to-action gaps (GRAHAM *et al.*, 2006; SALBACH, 2010; STRAUS *et al.*, 2013).

The Knowledge-to-Action model, developed by Graham *et al.* (2006), provides a description of the important aspects or phases that should be considered in the process of creation and implementation of knowledge. According to this model, the knowledge-to-action process includes knowledge creation and application (or action cycle), which are iterative, dynamic, and complex (Figure 2-1) (GRAHAM *et al.*, 2006; STRAUS *et al.*, 2013). Knowledge creation includes three phases: 1) Knowledge inquiry; 2) Knowledge synthesis; and 3) Knowledge tools and/or products. The action cycle can be defined as the phases that lead to implementation of knowledge. These phases are as follow: 1) Identify a problem, and identify, review, and select the knowledge relevant to the problem; 2) Adapt the identified knowledge to the local context; 3) Assess barriers to knowledge use; 4) Select, tailor and

implement interventions; 5) Monitor knowledge use; 6) Evaluate the outcomes of using the knowledge; 7) Sustain ongoing knowledge use. The phases might occur sequentially or simultaneously and can be influenced by the knowledge creation part (GRAHAM *et al.*, 2006).
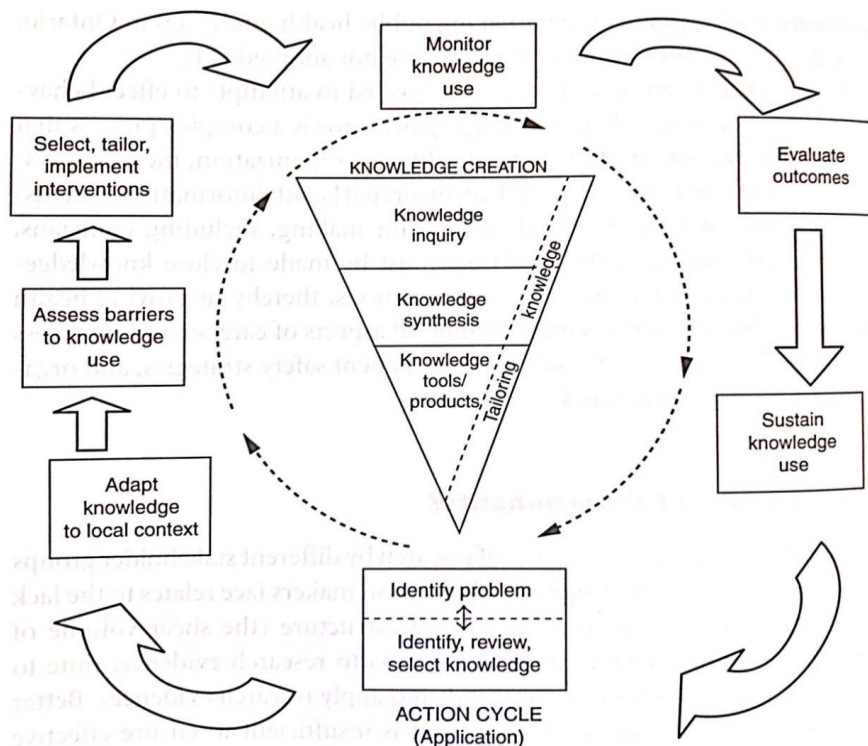
Figure 2-1. The knowledge-to-action framework. (From: GRAHAM *et al.* 2006)

Knowledge inquiry comprises the primary studies (GRAHAM *et al.*, 2006). One of the major interests of both rehabilitation researchers and clinicians is on the efficacy of interventions to improve different outcomes. Randomized controlled trials are primary studies that are considered as the most adequate to provide evidence on the efficacy of interventions (PORTNEY; WATKINS, 2015). However, there is a multitude of randomized controlled trials, and according to the results of different studies investigating barriers/facilitators of the use of evidence in clinical practice by physical therapists and occupational therapists providing services to individuals post-stroke, one of the most reported barriers is lack of time

to search and appraise the literature (SALBACH *et al.*, 2007; KORNER-BITENSKY *et al.*, 2008; SALBACH *et al.*, 2011; DEMERS *et al.*, 2018). In addition, an also commonly cited barrier by physical therapists providing services to people after stroke is lack of research skills related to appraising the literature (SALBACH *et al.*, 2007). Therefore, to facilitate time-efficient access, understanding, and application of the research evidence, knowledge synthesis is important. Knowledge synthesis represent the aggregation of existing knowledge and includes the interpretation of the results of individual studies within the context of global evidence (GRAHAM *et al.*, 2006). Systematic review is a type of knowledge synthesis (GRAHAM *et al.*, 2006). The process of development of a systematic review involves the application of explicit and reproducible methods to the selection, appraisal and synthesis of primary studies relevant to answer specific questions (GRAHAM *et al.*, 2006). Knowledge tools and/or products refer to a concise presentation of knowledge (i.e., guidelines) (GRAHAM *et al.*, 2006). The aim of this phase is to provide clear recommendations in order to facilitate understanding, to influence stakeholders' decisions and optimize patient care (GRAHAM *et al.*, 2006). Clinical guidelines usually based on systematic reviews, point out gaps in the literature and thus, indicate future research directions. Although guidelines have the advantage of including a comprehensive synthesis of knowledge with many clinical recommendations, they require a long time to be developed, thus, they are not always as updated as systematic reviews.

Although the phases of knowledge creation are described in order, it does not mean that they necessarily must occur in this specific sequence. For example, the definition of the studies that comprise this thesis began with the reading of the guideline "Physical Activity and Exercise Recommendations for Stroke Survivors: A Statement for Healthcare Professionals from the American Heart Association/American Stroke Association" (BILLINGER *et al.*, 2014). According to this clinical guideline, the effectiveness of exercise interventions in improving physical activity levels of individuals after stroke was not known (BILLINGER *et al.*, 2014). Therefore, it was suggested that future studies should investigate physical activity changes, as primary outcome, after exercise interventions for individuals after stroke (BILLINGER *et al.*, 2014). In order to have an updated synthesis of the literature regarding interventions with the aim to improve physical activity levels after stroke a systematic review

was conducted. Then, after knowing the gaps and study limitations identified by the systematic review, a primary study (randomized controlled trial) was developed.

If the intervention is found to be effective, one of the important follow-up steps to increase the success of its clinical implementation is to evaluate the various barriers and facilitators of this intervention, in the specific context in which it is intended to be used (GRAHAM *et al.*, 2006). Therefore, after investigating the efficacy of aerobic training to improve physical activity levels in individuals after stroke, if the intervention is found to be effective, efforts will be made to implement it in clinical practice.

2.4 General hypotheses and objectives

This thesis includes four manuscripts that allowed to formulate specific objectives. The general hypothesis was that individuals after stroke would have increased physical activity levels and time spent in low-energy expenditure activities after aerobic training.

Objectives of each paper:

Describe a protocol for the development of a systematic review with the aim to investigate the efficacy of any intervention with the objective to improve physical activity levels of individuals after stroke (**Paper #1**).

To present the results of the systematic review with the aim to investigate which interventions have been employed, and which are effective for increasing physical activity levels after stroke, identify the gaps in the literature and discuss the results (**Paper #2**).

To describe the protocol for a randomized controlled trial with the aim to investigate if aerobic training is an effective intervention to improve physical activity levels and time spent in low-energy expenditure activities of individuals after stroke (**Paper #3**).

To present the full paper with the results of the randomized controlled trial with the primary aim to investigate if aerobic training is effective for improving physical activity levels and time spent in low-energy expenditure activities of individuals after stroke (**Paper #4**).

Chapter 3. Paper #1: Efficacy of interventions to improve physical activity levels in individuals with stroke: a systematic review protocol

3.1 Preamble

Physical activity is defined as voluntary bodily movement using skeletal muscle that requires energy expenditure beyond resting levels (CASPERSEN; POWELL; CHRISTENSON, 1985). Individuals after stroke presents low physical activity, and since physical inactivity is linked with various comorbidities, interventions to improve this outcome after stroke are necessary (ASHE *et al.*, 2009; BILLINGER *et al.*, 2014). Physical activity levels increase might improve function and health in individuals after stroke (BILLINGER *et al.*, 2014). However, to date, there is no broad systematic review about the effects of any interventions on physical activity levels after stroke. Therefore, the aim of this paper is to describe a protocol for the development of a systematic review aimed at investigating the effects of any intervention on physical activity levels of individuals after stroke. The protocol is published in BMJ Journal: Aguiar LT, Martins JC, Nadeau S, Britto RR, Teixeira-Salmela LF, Faria CD. Efficacy of interventions to improve physical activity levels in individuals with stroke: a systematic review protocol. BMJ Open. 7(1): e012479, 2017.

3.2 Paper #1

Title: Efficacy of interventions to improve physical activity levels in individuals with stroke: a systematic review protocol

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3.2.1 Abstract

Introduction: Stroke is a leading health problem worldwide and an important cause of disability. Stroke survivors show low levels of physical activity and increases in physical activity levels may improve function and health status. Therefore, the aims are to identify which interventions that have been employed
to increase physical activity levels with stroke survivors, to verify their efficacy and to identify the gaps in the literature.

Methods: A systematic review of randomized controlled trials that investigated the efficacy of interventions aiming at increasing physical activity levels of stroke survivors will be conducted. Electronic searches will be performed in the MEDLINE, Physiotherapy Evidence Database (PEDro), Excerpta Medica (EMBASE), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) and Scientific Electronic Library Online (SCIELO) databases. Hand searches of the reference lists of the included studies or relevant reviews will also be employed. Two independent reviewers will screen all the retrieved titles, abstracts and full texts. A third reviewer will be referred to solve any disagreements. The quality of the included studies will be assessed by the PEDro Rating Scale. This systematic review will also include a qualitative synthesis. Meta-analyses will be

performed, if the studies are sufficiently homogeneous. This review will follow the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement. The quality of the evidence regarding physical activity will be assessed, according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

Discussion: This systematic review will provide information on which interventions are effective for increasing physical activity levels of stroke survivors. This evidence may be important for clinical decision-making and will allow the identification of gaps in the literature that may be useful for the definition of future research goals and the planning of new trials.

Trial registration number: CRD42016037750.

Keywords: Stroke; physical activity; randomized controlled trial; systematic review, health.

Strengths and limitations of this study

- This systematic review protocol will be reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement

- The three most complete databases for reports of randomized controlled trials (RCT) will be searched.

- The quality of the included studies will be assessed by the PEDro Rating Scale.

- The quality of the evidence will be assessed, based upon the Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

- This systematic review will not include interventions based on invasive procedures, drug, and nutrition therapies, neither other neurological populations besides stroke.

3.2.2 Introduction

Stroke is a leading health problem worldwide and an important cause of long-term disabilities.[1,2] Although stroke mortality rate has decreased, the majority of the growth of the global stroke burden is coming from developing countries and it is expected to increase as a result of demographic changes, such the increases in the ageing population.[1,2] Stroke survivors are more likely to require help with activities and to have restrictions in participation than matched controls.[3] In addition, stroke survivors are at higher risks of having other cardiovascular diseases (CVDs).[2] Therefore, it is essential to develop interventions to recover and promote health and function, as well as to prevent secondary diseases in poststroke survivors.

Physical activity is defined as any bodily movement produced by skeletal muscles that result in energy expenditure, such as those performed during activities of daily living, at work, at home, during leisure activities or transport.[4] Stroke survivors have low levels of physical activity at hospital and community settings.[5,6] The quantity, duration and intensity of physical activities are reduced, even in high functioning community-dwelling stroke survivors, when matched with a healthy elderly.[7] According to a population-based study, community dwelling stroke survivors have the highest proportion of physical inactivity, when compared with older adults with diabetes, musculoskeletal, cardiovascular, respiratory or other neurological chronic diseases.[8]

One of the major consequences of the disabilities after stroke is a chronic sedentary lifestyle.[9] Common disabilities observed after stroke, including muscular weakness,[10] reduced cardiorespiratory fitness,[11] fatigue,[12] physical mobility limitations,[13,14] low perceptions of quality of life[15] and restrictions in social participation,[3] may lead to low physical activity lifestyles.[9] Low levels of physical activity, in turn, have a negative impact on these disabilities and are related to health problems and, therefore, create a vicious cycle.[9]

Increase in physical activity levels can improve function and health in individuals after stroke.[9] Furthermore, increases in physical activity levels could reduce the recurrence of stroke and other CVDs.[16] Recently, the American Heart Association and the American Stroke Association published a scientific statement with recommendations of physical activity for stroke survivors,[9] and there is a consensus that increases in physical activity levels are

important for public health systems worldwide.[9,17] However, according to the best of our knowledge, no broad systematic reviews on this topic have been conducted. There was found only two specific systematic reviews that investigated the efficacy of interventions on physical activity levels in stroke survivors: one targeted behavioral change[18] and the other self-management programmes.[19] The results of both reviews showed, in general, improvements in physical activity levels after tailored counselling[18] and self-management programmes.[19] Nevertheless, the risk of bias in the included studies was high in both reviews.[18,19] Therefore, the overall efficacy of those interventions to improve physical activity levels in stroke survivors remains uncertain. In addition, these reviews had strict eligibility criteria, which may have prevented the inclusion of other relevant studies.[18,19] For instance, they included studies that had follow-up measures at 3 months or longer[18] and that only included community-dwelling participants.[19] Therefore, the aims of the present systematic review are to identify which interventions have been employed to increase physical activity levels and to verify the efficacy of these interventions in individuals with stroke. The ultimate goal is to identify the gaps in the literature to allow for the planning and development of new clinical trials.

3.2.3 Methods

3.2.3.1 Study design

This systematic review protocol will be reported in accordance with the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) (see Research Checklist),[20,21] and the results will be reported following the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.[22,23]

3.2.3.2 Study registration

On the basis of the PRISMA-P guidelines, this systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 14 April 2016 (registration number: CRD42016037750; http://www.crd.york.ac.uk/PROSPERO/).

3.2.3.3 Eligibility criteria

3.2.3.3.1 Types of study

All randomized controlled trials (RCTs) that investigated the efficacy of interventions aiming at increasing physical activity levels in stroke survivors will be included in this systematic review. Quasi-RCTs, controlled clinical trials, cross-sectional studies, case series and case reports will be excluded.

3.2.3.3.2 Participants

All RCTs, in which participants were adults (≥18 years of age) and survived a stroke, will be included, without further restrictions. The authors of the studies that included mixed groups will be contacted for specific data related to the stroke survivors. When specific data are not available, the study will be excluded. Studies with participants with transient ischaemic attack will also not be included.

3.2.3.3.3 Types of interventions

All RCT that employed any type and mode of delivery, including, but not limited to, aerobic, strength exercises, counselling, self-management or behavioral interventions, in isolation or in combination, aimed at increasing physical activity levels, will be included. Trials will be excluded if the experimental interventions were invasive procedures, drug and nutrition therapies.

3.2.3.3.4 Comparisons or control

No restrictions will be made on the comparisons and/or the control group.

3.2.3.3.5 Outcome measures

Studies that quantified physical activity levels by any method, such as self-report assessment tools (eg, selfreport questionnaires, diaries/logs or recall interviews)[24] or by direct measures (eg, accelerometers, pedometers, doubly labeled water, multisensor tools or direct observations) will be included.[24,25] Physical activity levels could be reported as energy expenditure, steps per day, time of physical activity per day, number of transitions, time spent upright or others. Trials reporting walking or exercise capacity, gait patterns or ability to

perform activities of daily living (eg, Barthel or Functional Independence Measure scores), which are not measurements of physical activity levels, will be excluded. Studies reporting only sedentary time will also be excluded.

3.2.3.4 Search strategy for the identification of relevant studies

Electronic searches will be conducted in the MEDLINE (via PubMed), Physiotherapy Evidence Database (PEDro), Excerpta Medica (EMBASE), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) and Scientific Electronic Library Online (SCIELO) databases, from their inception to February 2016, without any language restrictions. The MEDLINE, PEDro and EMBASE databases were chosen because they are the most complete databases for reports of RCT.[26] The LILACS and SCIELO databases were chosen because they contain articles published in the Portuguese or Spanish languages. Hand searches of the reference lists of the included studies or identified relevant reviews will be employed. The search strategy will include terms related to stroke, RCT and physical activity levels. The search strategy related to stroke and RCT, which will be employed at the MEDLINE database, will follow that of a recent Cochrane Systematic Review[27] and the Cochrane Handbook for Systematic Reviews of Interventions,[28] respectively. The search strategy related to physical activity levels will be a combination of terms employed on three previously published systematic reviews.[24,29,30] See online supplementary file 1 for the MEDLINE full-search strategy. The search strategy for the MEDLINE will be adapted to suit the other databases.

3.2.3.5 Screening of the studies

Duplicate studies will be removed. The main author (LTA) will search all databases and extract the titles and abstracts. Two independent reviewers (LTA, JCM) will screen all the retrieved titles and abstracts from the electronic search, according to the previously described inclusion criteria. Full texts will be screened by the same reviewers (LTA, JCM), independently. A third reviewer (CDCMF) will be referred to solve any disagreements. All the reasons for exclusion of ineligible studies will be recorded. The results of the screening process will be provided in details using the PRISMA information flow.[21]

3.2.3.6 Data extraction

The two independent reviewers (LTA, JCM) will extract the data, following recommended guidelines. Data extraction will include: (1) study details: authors and year of publication; (2) study characteristics: inclusion/exclusion criteria and setting; (3) sample characteristics: number of participants, age, sex, type and time since the onset of the stroke; (4) methods: design and allocation, blinding, sampling, time points when data were collected, loss to follow-up, recruitment and retention rates, comparison/control group; (5) interventions: description of intervention, duration, frequency, intensity, length and supervision and (6) outcomes: description, measurement instruments, unit of measurement and intervention effects on the outcome. Any additional information that may express conflict of interest or bias will also be extracted. The corresponding author of the studies with missing or incomplete data will be contacted for further information. Disagreements will be discussed with the third reviewer (CDCMF).

3.2.3.7 Risk of bias

The quality of the included RCT will be assessed by extracting the PEDro scores from the PEDro database (http://www.pedro.org.au). The PEDro Rating Scale is an 11-item checklist, which gives scores that range from 0 to 10, designed for rating the methodological quality of trials. The RCTs, which have not been assessed by the PEDro rating scale, will be scored by the reviewers (LTA, JCM). Once again, disagreements will be discussed with the third reviewer (CDCMF). The scores on the individual items of the PEDro scale of all included trial will be reported in a table. In an attempt to determine if reporting bias is present in the included trials, the trial register's 'ClinicalTrials.gov', 'http://www.anzctr.org.au' and 'http://www.clinicaltrialsregister.eu/ctr-search/search' will be screened to assess whether selective reporting is present.

3.2.3.8 Quality of evidence

The quality of the evidence of the studies will be assessed based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE).[31] The quality of the studies will be judged as high (further research is very unlikely to change the confidence in the effect estimates), moderate (further research is likely to have an important impact on the

confidence in the effect and may change the estimate), low (further research is very likely to have an important impact on the confidence in the effect and is likely to change the estimate) and very low (any estimate of the effect is very uncertain).[31]

3.2.3.9 Strategy for data synthesis

This systematic review will also include a qualitative synthesis, which will provide information, in text and tables, to summarize the results of the included studies. A narrative synthesis will be performed to explore the results and associations within and between the included trials. Forest-plots and meta-analyses will be conducted if the studies are sufficiently homogeneous regarding the interventions and outcomes and if sufficient data are available, to synthesise the direction, size and consistency of the possible effects, using the Review Manager software (RevMan) (Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

3.2.3.10 Analyses of subgroups or subsets

If sufficient data are available, subgroups analyses will be carried out. These analyses will assess differences between the stroke phases (eg, acute, subacute or chronic), physical activity measurements (eg, subjective vs objective instruments), type, duration and delivery of the intervention, group comparisons, quality and risk of bias.

3.2.4 Discussion

According to the best of our knowledge, this systematic review is the first to investigate the efficacy of broad types of interventions aimed at increasing physical activity levels in stroke survivors. Previous systematic reviews with the aim to examine the efficacy of interventions on physical activity levels in poststroke survivors have investigated only two specific types of interventions: targeted behavioral change[18] and self-management programmes.[19] However, the efficacy of those interventions to increase physical activity levels in poststroke survivors continue to be unclear, due to the fact that the risk of bias of the included trials was high in both reviews.[18,19] Moreover, important trials might not have been included because of the stringent eligibility criteria of these reviews.[18,19] These factors limit the interpretation of the findings regarding the impacts of interventions on physical activity

levels in poststroke survivors. Considering that physical inactivity is a major risk for recurrence of stroke and other CVDs and may affect health and function,[2,9,16] it is important to investigate the impact of different types of interventions on physical activity levels in poststroke survivors.

The results of this systematic review will provide comprehensive and rigorous evidence regarding which types of interventions, and/or specific protocols have been investigated and are effective for increasing physical activity levels of stroke survivors. The information from the qualitative synthesis, which will be developed to explore the results and relations within and between the included studies, will be important for clinical decision-making aiming at improving function and health status of stroke survivors. Moreover, if sufficiently homogeneous data to conduct meta-analyses are available, clinicians will have information regarding the expected effect size associated with a given intervention.

Furthermore, this systematic review may allow the identification of gaps in the literature, regarding the types and specific intervention protocols, group comparisons, measurement instruments, short-term and long-term effects and different stroke phases (eg, acute, subacute or chronic). This information will be useful for the definition of future research goals and the planning of new research trials. The results from this systematic review will be spread by scientific publication and presentations in scientific events.

3.2.5 Conflict of interest

The authors report no conflicts of interest.

3.2.6 Funding

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3.2.8 Supplementary file 1

MEDLINE (PubMed) search strategy

[Target population: stroke]

1. cerebrovascular disorders [mh] OR brain injuries [mh] OR hemiplegia [mh] OR paresis [mh] OR dystonia [mh]

2. stroke [tw] OR poststroke [tw] OR post-stroke [tw] OR cerebrovasc* [tw] OR brain vasc* [tw] OR cerebral vasc* [tw] OR cva [tw] OR apoplex* [tw]

3. brain [tw] OR cerebro* [tw] OR cerebra* [tw] OR cerebell* [tw] OR intracran* [tw] OR intracerebral [tw] OR vertebrobasilar [tw]

4. ischemi* [tw] OR ischaemi* [tw] OR infarct*[tw] OR thromboa* [tw] OR thrombob* [tw] OR thromboc* [tw] OR thromboe* [tw] OR thrombof* [tw] OR thrombog* [tw] OR thromboh* [tw] OR thromboi* [tw] OR thrombok* [tw] OR thrombol* [tw] OR thrombom* [tw] OR thrombon* [tw] OR thromboo* [tw] OR thrombop* [tw] OR thromboq* [tw] OR thrombor* [tw] OR thrombos* [tw] OR thrombot* [tw] OR thrombou* [tw] OR thrombov* [tw] OR thrombox* [tw] OR thromboy* [tw] OR thromboz* [tw] OR emboli* [tw] OR occlus* [tw]

5. #3 AND #4

6. brain [tw] OR cerebro* [tw] OR cerebra* [tw] OR cerebell* [tw] OR intracerebral [tw] OR intracranial [tw] OR subarachnoid [tw]

7. haemorrhag* [tw] OR hemorrhag* [tw] OR haematoma* [tw] OR hematoma* [tw] OR bleed* [tw]

8. #6 AND #7

9. brain injury [tw] OR brain injuries [tw] OR brain injured [tw]

10. hemipleg* [tw] OR hemipar* [tw] OR paresis [tw] OR paretic [tw] OR dystoni* [tw]

11. #1 OR #2 OR #5 OR #8 OR #9 OR #10

[Type of study: randomized controlled trial]

12. randomized controlled trial [pt]

13. controlled clinical trial [pt]

14. randomized [tiab]

15. placebo [tiab]

16. clinical trials as topic [mesh: noexp]

17. randomly [tiab]

18. trial [ti]

19. #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

20. animals [mh] NOT humans [mh]

21. #19 NOT #20

[Outcome measure: physical activity]

22. "Physical activity" [tw]

23. Activit* [tw]

24. "Physical mobility" [tw]

25. "Physical function" [tw]

26. Exercise [tw]

27. "Physical exertion" [tw]

28. "Physical endurance" [tw]

29. "Motor Activity" [tw]

30. "Energy Expenditure" [tw]

31. "Energy Metabolism"[Mesh]

32. "Physical fitness" [tw]

33. #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32

34. #11 AND #21 AND #33

Chapter 4. Paper #2: Efficacy of interventions aimed at improving physical activity in individuals with stroke: a systematic review

4.1 Preamble

No broad systematic reviews regarding the efficacy of any intervention to improve physical activity levels of individuals after stroke were found. Therefore, after registering the systematic review and publishing the protocol, the aim of this paper is to present the results of the systematic review with the aim to investigate which interventions have been employed, and which are effective for increasing physical activity levels after stroke, identify the gaps in the literature and discuss the results. This manuscript is published: Aguiar LT, Nadeau S, Martins JC, Teixeira-Salmela LF, Britto RR, Faria CDCM. Efficacy of interventions aimed at improving physical activity in individuals with stroke: a systematic review. Disabil Rehabil. 19:1-16, 2018.

4.2 Paper #2

Title: Efficacy of Interventions aimed at Improving Physical Activity in Individuals with Stroke: A Systematic Review

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4.2.1 Abstract

Purpose: To identify interventions employed to increase post-stroke physical activity, evaluate their efficacy, and identify gaps in literature.

Methods: Randomized controlled trials published until March 2018 were searched in MEDLINE, PEDro, EMBASE, LILACS, and SCIELO databases. The quality of each study and overall quality of evidence were assessed using the PEDro and the GRADE scales.

Results: Eighteen studies were included (good PEDro and very low GRADE-scores). In seven, the experimental groups showed significant increases in physical activity (aerobics, resistance, and home-based training; counseling, aerobics, resistance, and home-based training; electrical stimulation during walking; functional-task training; robot-assisted arm therapy; accelerometer-based feedback, and physical activity encouragement). In seven, there were no significant between-group differences (physical activity plan; stretching, use of toe-spreaders, standard treatment; counselling; circuit video-game; functional-task; counselling and cognitive training). The combined experimental and control groups showed significant declines in physical activity in one study (aerobic training or stretching) and increases in 3 others (aerobic, resistance or sham resistance training; stroke-with advice or only stroke-counselling; aerobic training, educational

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sessions, standard treatment, and coaching, or mobilization and standard treatment). A meta-analysis could not be performed, due to heterogeneity.

Conclusions: Some interventions improved physical activity after stroke. However, the interpretability is limited.

Systematic review registration

PROSPERO 2016: CRD42016037750.

Keywords: Stroke; physical activity; randomized controlled trial; systematic review, health

Implications for Rehabilitation

- Individuals with stroke show low physical activity, which may compromise function and health.
- The use of interventions aimed at improving and maintaining physical activity of individuals with stroke are recommended.
- Some interventions, such as aerobic, resistance, and combined home-based training, electrical stimulation during walking, functional task training, and arm robot-assisted therapy, could improve physical activity after stroke.

4.2.2 Introduction

Stroke is a leading health problem and its burden is increasing worldwide [1]. In 2013, more than 100 million Disability-Adjusted Life-Years were lost, due to ischemic or hemorrhagic stroke [1]. However, more than 90% of the stroke-burden is attributable to modifiable risk factors, such as low physical activity [2].

Physical activity is defined as any bodily movements produced by the contractions of the skeletal muscles, that increase energy expenditure, such as those executed during leisure activities, at work, at home, or while traveling [3]. Physical activity represents a different concept from exercise [3]. Exercise is a sub-set of physical activity, which is repeatedly performed, in a planned and structured way, with the aim to improve or maintain one or more attributes of physical fitness [3]. Physical fitness also represents a different concept from physical activity [3]. Physical fitness is a group of characteristics, such as cardiorespiratory fitness, muscular strength and balance, which are related to the capacity of doing physical activity [3]. The results of a systematic review, which aimed at investigating physical activity of community-dwelling individuals with stroke showed that, their physical activities were low in amount, duration, and intensity [4]. Low physical activities have been reported even in people who have mild physical impairments [4,5]. In addition, individuals with stroke spend significantly less time in standing, walking, and involving in light, moderate, or vigorous physical activity, than age-matched retired healthy controls [6].

Physical inactivity after stroke is associated with reduced mobility, aerobic fitness, and balance [4], higher levels of self-perceived fatigue [7], and worse perception of quality of life [8]. These associations create a vicious cycle of reduced physical activity, which leads to further declines in bodily functions and health status [4]. Therefore, interventions aimed at improving and maintaining physical activity in individuals with stroke are necessary [9].

An extensive Cochrane systematic review, published in 2016, reported the effects of exercise interventions on selected outcomes after stroke [10]. Their primary and secondary outcomes differ from those of the Aguiar *et al.*'s systematic review protocol [15] (see Table 4-1). They are not purely related to physical activity, which is the primary outcome of the present systematic review. In addition, the Cochrane review limited the search to interventions related to cardiorespiratory, resistance, or mixed training (cardiorespiratory plus resistance

training) [10] that differ from the present systematic review that includes studies of the effectiveness of any type of intervention increasing physical activity.

Nevertheless, no systematic reviews have focused on the efficacy of any type of interventions aiming at improving physical activity of individuals with stroke. Only 2 systematic reviews on this subject were found. However, the interventions were specific: one study targeted methods such as counseling, advice, or behavioral change, with or without exercises, while focusing on increasing physical activity [11]; whereas the other focused on problem-solving, goal-setting, decision-making, self-monitoring, coping strategies, or other interventions to facilitate behavioral change, aiming at improving physical activity [12]. The strengths of these 2 reviews were that, they followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines [13,14], and included various types of study designs. However, both reviews had strict inclusion criteria, such as follow-ups for above 3 months [11] and included community-dwelling individuals for the research [12], which might have prevented the inclusion of important trials. Among these reviews, 5 of the 11 studies (in the first review) [11], while 3 of the 5 studies (in the second review) [12], reported significant improvements in physical activity after tailored counseling [11] and self-management programs [12]. However, because of the high risk of bias involved with the included studies that potentially impacted the strength of the conclusions; the authors of both the reviews stated that, the interpretation of the efficacy of the investigated interventions investigated is limited [11,12]. In addition, since the interventions were specific, other strategies, such as aerobic training, were not considered. Hence, the overall efficacy of different interventions aimed at improving physical activity in individuals with stroke remained uncertain. Therefore, the objective of this systematic review was to identify which interventions have been employed for increasing physical activity of individuals with stroke and to evaluate their efficacy. Furthermore, the ultimate goal was to identify the gaps in the literature so far, to facilitate the planning and development of future studies.

4.2.3 Methods

This systematic review was conducted and reported, following the PRISMA statement [13,14]. The protocol of this systematic review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on April 14, 2016 (registration

number: CRD42016037750; http://www.crd.york.ac.uk/PROSPERO/) and has been previously published [15].

4.2.3.1 Data sources and searches

A comprehensive search for the literatures was conducted in the Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, Physiotherapy Evidence Database (PEDro), Excerpta Medica (EMBASE), Latin American and Caribbean Literature in Health Sciences (LILACS), and Scientific Electronic Library Online (SCIELO) databases, from their inception to March 2018, without any language restrictions. The MEDLINE, PEDro, and EMBASE were selected, because they are the most complete databases for the reports on randomized controlled trials [16]. The LILACS and SCIELO electronic databases were selected, because they contain trials published in Portuguese and Spanish languages. The reference list of the included studies was screened, to identify the further ones. The MEDLINE search strategy included words related to stroke (based upon the Cochrane Systematic Review) [17], randomized controlled trials (following the Cochrane Handbook for Systematic Reviews of Interventions) [18], and physical activity (combination of terms, which were previously employed in 3 systematic reviews) [19-21]. Supplementary File 1 shows the published protocol for the MEDLINE full-search strategy. This search strategy was then modified to match with the differences across the other databases.

4.2.3.2 Study selection

The eligibility criteria were pre-determined. The inclusion criteria are outlined in Box 1. Any randomized controlled trial, which investigated the efficacy of any intervention aimed at increasing physical activity (measured as a primary or secondary outcome) of individuals with stroke, was included in this systematic review. Quasi-randomized controlled trials, controlled clinical trials, cross-sectional studies, case series, and case reports were excluded, to ensure internal validity of the included studies. The authors of the studies, which included mixed groups, were contacted for the specific data related to individuals with stroke. However, since none of them provided stroke-specific data, these studies were excluded. Studies considering individuals with transient ischemic attack were also excluded. Trials in which the experimental interventions consisted of invasive procedures, drugs and nutritional therapies;

and those that reported walking or exercise capacity, gait patterns, ability to perform activities of daily living or sedentary time, which are not direct measures of physical activity, were excluded.

To identify relevant studies, 2 authors independently reviewed all the titles and abstracts, which were retrieved from the electronic search. Full-paper copies were independently retrieved and screened by the same reviewers, following the pre-defined criteria (Box 1). Both reviewers were blinded to the authors, journals and results. A third reviewer was referred to solve any disagreements.

4.2.3.3 Data extraction and quality assessment

Two independent reviewers extracted the data from the included studies, using a standardized data-extraction form. Data were extracted for all available time points, as pre-determined in the protocol [15].

The risk of bias involved with the included trials was assessed using the PEDro Rating Scale, which is a checklist designed for rating the methodological quality of trials (www.pedro.org.au). The scores were classified as excellent (9-10), good (6-8), fair (4-5), or poor (0-3) [22]. Various trial registers such as, "clinicaltrials.gov", "www.anzctr.org.au" and "www.clinicaltrialsregister.eu/ctr-search/search" were screened, to evaluate whether the selective reporting bias was present in the included trials.

The overall quality of the evidence of the studies was evaluated based upon the system of Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) [23]. GRADE specifies four categories for the quality of a body of evidence (high, moderate, low, and very low) [23]. The quality (or certainty) of the evidence is defined as high (the true effect lies close to that of the estimate of the effect), moderate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) further research is likely to have an important impact on the confidence on the effects and may change the estimates), low (the true effect may be substantially different from the estimate of the effect) or very low (the true effect is likely to be substantially different from the estimate of effect) [23]. The lower the quality of the evidence, more likely further research would change the confidence in the estimates, and the estimates themselves [23]. According to the GRADE, to assess quality of evidence, all randomized controlled trials are initially considered of high

quality. They are, then, assessed in relation to 5 factors (study limitations, inconsistency of results, indirectness of evidence, imprecision, and publication bias), which can reduce the quality of the evidence [23].

4.2.3.4 Data synthesis and analysis

A meta-analysis could not be performed, due to the heterogeneity of the outcome measures across the trials. However, a detailed summary of the results of all included trials are provided in the table-and-text formats.

4.2.4 Results

4.2.4.1 Flow of trials through the review

The electronic search strategy resulted in 10,608 references, however, 400 were duplicates. After screening the titles, abstracts, and reference lists, 245 potentially relevant full-text articles were retrieved, but 227 trials failed to meet the eligibility criteria and, therefore, 18 trials were included in this systematic review [24–41]. Figure 4-1 shows the flow of trials through this review, including the reasons for exclusion.

4.2.4.2 Characteristics of the included trials

4.2.4.2.1 Quality

The PEDro scores ranged from 3-8, i.e., from poor to good quality. Thirteen trials [24-27, 29, 30,35–41] had scores of 6-8 (Table 4-2) and five studies [28,31–34] had PEDro scores of 3-5 (Table 4-2). All trials randomly allocated participants and reported between-group differences, point estimates and variability. Sixteen of the 18 studies had similar groups at baseline [24–29, 31–33,35–41], 2 studies [30, 34] had dissimilar groups at baseline. Twelve of the 18 studies reported follow-up losses at ≤15% [23–31,35–37,39,41]. Thirteen of the 18 studies had blinded assessors [24–27,29,30,35-41]. However, none of the trials blinded individuals or therapists, which is difficult during the delivery of complex interventions [42]. Of the 18 included studies, only eight [22,35–41] were registered. However, one trial registration could not be found, due to wrong registration number [37]. There was no selective

reporting bias. The overall quality of the evidence, according to the GRADE approach, was considered very low (Table 4-2).

4.2.4.2.2 Overall characteristics of the included trials

The 18 included trials [24–41] involved 1314 participants and 12 of the 18 trials had the sample size <65 [26-34,39,41]; however, only one trial included 314 participants [24]. The interventions employed in the trials and the outcome measures were varied. In only 8 studies, physical activity was evaluated as a primary outcome [24,29,30,34,36,38,39,41]; in 6, it was evaluated as a secondary outcome [26,27,31,35,37,40]; and in other 4 trials [25,28,32,33], there was no clear distinction between primary and secondary outcomes. Details of the overall characteristics of the included studies are provided in Tables 4-3 and 4-4.

4.2.4.2.3 Participants

The mean/median age of the participants ranged from 48 to 76 years, whereas the mean/median time post-stroke ranged from 3.6 days to 9 years in the included studies. The characteristics of the participants are outlined in Table 4-3.

4.2.4.2.4 Employed measurement instruments

Eight of the 18 studies [24, 30, 31,32, 34, 36-38] assessed physical activity using the following measures: Physical Activity for the elderly [24,37], Physical Activity & Disability [30], Physical Activity [31], Yale Physical Activity [32], Human Activity Profile [34], Physical activity subscale of the Health Promoting Lifestyle Profile [36]; The Baecke Inventory and a physical activity diary [38]; The overall hours spent per week with regular physical activity and the types of activities obtained by interview[40].

Six of the 18 studies [26,27,29,33,35,41] considered the measurement of different aspects of physical activity with accelerometers, which included: mean number of steps per day and time spent in physical activity of low, moderate and high-intensity over 7 days [35]; time spent in physical activity of at least moderate intensity over 7 days [26]; number of steps per day over 3 days [27]; amount and intensity of physical activity, but no time element was reported [33]; arm activity ratio (ratio of mean activity) between the paretic and non-paretic

arms over 3 days [29]; mean number of steps, energy expenditure, and time spent in physical activity of low, moderate and high-intensity until discharge [41].

Physical activity was assessed in terms of number of steps, measured with a pedometer in one of the 18 studies [25], and by the Physiological Cost Index (beats/m) in another one [28]. One of the 18 studies assessed physical activity using multiple measures: number of steps with a pedometer, energy expenditure with a multisensor tool, duration at different activity intensities with a coded activity diary, The Physical Activity Scale for Individuals with Physical Disabilities, and The Baecke Questionnaire of Habitual Physical Activity (sport and leisure scores) [39].

4.2.4.2.5 Interventions

The employed interventions were varied, however, 5 of the 18 studies included aerobic training [31,32,34;35,39]; 4 included lower-limb resistance training [30,31,34,35]; and 4 included functional task training [27,29,33,37] (Table 4-3).

Aerobic training. In all the studies, aerobic training was performed at least 3 times per week, but the duration, intensity, and mode of delivery varied [31,32,34,35,39].

Lower-limb resistance training. The target intensity of lower-limb resistance training was set at 80% of one maximum repetition in 2 studies [31,34], and at 60-70% in the other [35]. Two studies reported 3 sets of each exercise [31,34]; however, one study reported 2 or 3 sets [35]. The number of repetitions varied from eight to 12 repetitions [31,34,35]. The total training duration was reported in 2 studies (20/30 min) [34,35]; however, rest intervals were described in only one trial [34]. One study did not report any training parameters [30].

Functional task-training. Functional task training in 2 studies focused only on the upper limb [29, 33]; whereas that in one study focused only on the lower-limb [35], but one trial used whole body functional task-training, such as picking up and transferring objects from one side of the room to the other. However, only the control group performed this whole body functional task-training [27]. Therefore, none of the trials investigated the effects of functional task-training that focused on both upper and lower-limbs while improving physical activity of individuals with stroke.

4.2.4.2.6 Effects of intervention

In 7 of the 18 studies [28,29,33,34,35,38,41], the experimental group showed increases in physical activity, compared to the control group (Table 4-4). The interventions employed in these studies were: aerobic training along with lower-limb resistance training, and home-based exercises [34]; advice and counseling regarding lifestyle changes including, aerobic training, lower-limb resistance training, and home-based exercises [35]; lower-limb electrical stimulation during walking [28]; bilateral arm functional task training [33]; robot-assisted arm therapy [29]; instruction on accelerometer-based feedback, discussion on physical activity targets and encouragement to walk more until discharge and standard treatment [41]; and health information and self-regulation behavior change strategy lessons [38] (Table 4-3).

In 7 of the 18 studies [24–27,30,37,40], no significant differences in physical activities were found between any of the groups (Table 4-4). The employed interventions were: physical activity plan, according to the participants' resources and preferences [24]; lower-limb stretching exercises, in addition to the use of a toe-spreader during walking and standard treatment [25]; circuit functional task training [30,37]; counseling sessions [26]; circuit video-game [27]; and dietary and physical exercise counselling's, cognitive training, and phone calls for adverse events and compliance to medication [40] (Table 4-3).

Between-group comparisons of 4 of the 18 studies [31,32,36,39] showed no significant interaction differences (Table 4-4). However, considerable time effects were revealed, indicating significant differences between baseline and post-intervention evaluation, regardless of the intervention group, that is, no superiority of the experimental group (Table 4-4). In one randomized controlled trial, all participants showed declines in physical activity after aerobic training or stretching [31]; whereas in the other 3 trials, all participants showed increases in physical activity [31,36,39] (Table 4-4). In one study that included 3 groups, the interventions were: aerobic training; lower-limb resistance training; or sham resistance training of the arm [31] (Table 4-3). In the other study with 2 groups, the intervention was usual stroke education along with telephonic sessions with goal-setting advice, or only usual stroke education [36] (Table 4-3). In the other study with 2 groups, the intervention was aerobic training, educational sessions, standard treatment, and coaching, or passive mobilization and standard treatment [39] (Table 4-3).

4.2.5 Discussion

The purpose of this systematic review was to identify and verify the efficacy of interventions aimed at increasing physical activity of individuals following a stroke. The aim was to identify gaps in the literature and to enable the planning and development of new studies. The results of this systematic review showed that some types of exercise interventions are effective at improving physical activity in individuals following stroke. In 7 of the 18 studies [28,29,33,34,35,38,41], the experimental group showed increases in physical activity. The interventions employed in 4 of these studies comprised aerobic training [34,35], lower-limb resistance training [34,35], or functional task-training [29,33] at least as a part of the treatment. Aerobic training [34,35], lower-limb resistance training [34,35], or functional task-training [29,33] were interventions employed at least as a part of the treatment in more than one trial. The quality of thirteen of the 18 trials [24-27, 29, 30, 35–41] was good (scores of 6-8), according to the PEDro scores. The trials were heterogeneous with respect to measurement tools, employed interventions and results; therefore, a meta-analysis was not undertaken. The overall quality of the evidence of the studies based upon the GRADE scale was found to be very low; thus, it may be early to draw definitive conclusions regarding the effects of interventions on physical activity after stroke. An important gap in the literature regarding the assessment of effects of interventions on physical activity in individuals with stroke is the lack of the investigation of the effects of potential intervention strategies, such as whole-body functional task-training.

The number of trials retrieved by searching the databases was 10,608; however, only 18 trials were included in this systematic review. The main reason for their exclusion was that 196 trials did not report physical activity as an outcome. Several trials did not assess this outcome while some reported only the instruments used to measure physical activity instead of reporting the measurement of physical activity and were, thus, excluded from this review. As mentioned before, Caspersen *et al.* [3] provided a clear definition of physical activity, as follows: any bodily movements produced by the skeletal muscles that result in increased energy expenditure (i.e., leisure, work, home, or transportation activities) [3]. However, clear identification and assessment of this outcome are lacking in clinical trials. Since a clear

statement of the assessed outcomes is required for the correct interpretation of the results [13], future studies should report their outcomes correctly.

It was not possible to assess selective reporting biases for 11 included trials [25–34,37], as trial registration was not available, except for 7 studies [24, 35, 36,38-41]. Trial registration has been required since 2005 [43] to increase the transparency in the planning, execution, and reporting of clinical trials; and thus, avoiding selective reporting bias [43]. Although all included studies were published from 2009 to 2018 [24–33,35–37], except one that was published in 1999 [34], 11 of 18 studies were not registered [25–35,37]. Thus, the possibility of selective reporting bias cannot be excluded. Contrary to the favorable scores on the PEDro scale for 13 of the 18 included trials [24–27,29,30,35–41], the quality of the evidence, based upon the GRADE approach, was very low. This result was due to lack of blinding and description of the 95% confidence intervals for the results, heterogeneity of the employed interventions, and small samples in some of the included trials. The very low GRADE-score indicates that it is still too early to draw definitive conclusions regarding the effects of interventions on physical activity after stroke. Therefore, studies investigating the efficacy of interventions on physical activity of individuals with stroke are necessary.

The variety in interventions employed in the included studies may be explained by the complex vicious cycle that involves physical inactivity and common post-stroke disabilities [4]. Since one of the perceived barriers to physical activity after stroke is low motivation, interventions which included an element of verbal encouragement might be effective at improving physical activity after stroke [44]. Ten of the 18 included studies [24,26,31,35-41] had some type of verbal encouragement in their interventions. However, only in three of these 10 studies the experimental group showed increases in physical activity, compared to the control group. Although the interventions were varied, 5 of the 18 trials included aerobic training [31,32,34,35,39]; 4 included lower-limb resistance training [30,31,34,35], and 4 included functional task-training [27,29,33,37]. The use of these types of interventions in more than one trial may be due to the fact that, cardiorespiratory fitness and mobility have already been identified as significant predictors of physical activity in individuals with stroke [45]. The differences between the modes of delivery of the aerobic interventions may explain the different results. The trials in which the experimental group showed increases in physical activity when compared to the control group included walking on the ground as a part of the

aerobic training [34,35], while 3 studies used only instruments to provide aerobic training, such as cycle ergometer [31;39] or treadmill [32]. Given the importance of a more task-specific mode (walking vs. seating) of aerobic training for the improvement of walking speed and endurance in individuals with stroke [46], it may be necessary to employ a task-specific aerobic training to improve physical activity after stroke. Therefore, future studies should investigate the effects of aerobic training performed with a walking modality, which is considered a task-specific approach [47], to improve physical activity in individuals with stroke.

The various instruments, which have been employed to measure physical activity, vary in terms of accuracy, simplicity, and provided information [48]. These instruments are commonly classified into 2 broad categories: objective or subjective methods [21,48]. Objective methods are those that directly measure at least one biological signal, such as body segment acceleration [21], and are performed at the same time when the physical activity occurs [21]. Examples of objective methods used to assess physical activity include accelerometers, pedometers, and multisensor tools [21]. In the present review, 9 of the 18 studies measured physical activity using objective methods: 6 using an accelerometer [26,27,29,33,35,41], two studies [24,39] used a pedometer, one used the Physiological Cost Index (beats/m) [28], while another used a multisensor tool [39].

On the other hand, subjective methods to measure physical activity are based upon the respondents' perceptions and depend upon the persons' precisions in recording the physical activities when they are happening, or on their abilities to remember the previously assessed ones [21,48]. Types of subjective methods used to evaluate physical activity are questionnaires and diaries [21]. Nine of the 18 studies included in this systematic review assessed physical activity using questionnaires [24,30,31,32,34,36-39]. Two of the 18 studies assessed physical activity using diaries [38,39], and one by interviews [40]. Although subjective methods, such as questionnaires, have the advantages of being low-cost and easily administered, recall or social desirability biases may occur [4]. The results of the studies that investigated associations between measures of physical activity, as assessed using questionnaires and objective methods, such as the SenseWear Armband multisensor tool, showed no significant [49] or very-low to moderate correlations [50]. Thus, questionnaires may have some

limitations in their accuracy in measuring physical activity, and the results of the included trials need to be interpreted with caution.

Only 2 of the 18 studies [30,34] included in the present systematic review were also included in the previous broad review of Cochrane [10]. Therefore, it is clear that these two reviews had different aims, and thus, the present systematic review does add knowledge to the current state of rehabilitation research.

Two previous reviews which investigated the efficacy of interventions aiming at improving physical activity of individuals with stroke also found that some interventions (tailored counseling [11] or self-management [12]) improved physical activity after stroke. They reported that the effects of exercise programs provided without counseling on physical activity were fewer [11]. However, the results of the present systematic review showed that, some types of exercise interventions are likely to be effective at improving physical activity of individuals with stroke. Eligibility criteria of the present review was different from those of the 2 previous ones [11,12]. Thus, only 2 of the 18 studies [24,30] included in our review were also included in one of the 2 previous reviews [11], and none was found in common with the other review [12]. The limited number of included studies and the heterogeneity in the interventions, outcome measures, and results of the trials, limited the conclusions of the present study, and the same limitation could be relevant to both the previous reviews [11,12]. Nevertheless, combinedly, these reviews show that physical activity may be enhanced in individuals with stroke.

4.2.5.1 Study limitations

This systematic review has both strengths and limitations. The main strength is that publication bias was avoided, since the most complete electronic databases for reports on randomized controlled trials were screened, and publication language was not restricted to English. Furthermore, the quality of the included studies was evaluated by the PEDro Rating Scale and the quality of the evidence was assessed based upon the GRADE approach. The main limitation is that a meta-analysis could not be performed, and thus the definitive conclusions regarding the effects of interventions on physical activity in individuals with stroke cannot be drawn, due to the limited number of trials. In addition, another possible limitation is that studies that evaluated only aspects of physical activity, such as, gait patterns

or ability to perform activities of daily living, timed walking, muscle strength, were not included.

4.2.6 Conclusions

In conclusion, only few randomized controlled trials evaluated the effects of interventions on physical activity in individuals with stroke. The present review provides evidence that, some types of interventions may improve post-stroke physical activity. However, the limited number of studies and the heterogeneity in the interventions, measurement instruments, and results, limit the overall conclusions. Therefore, more randomized controlled trials are necessary to verify and draw definitive conclusions regarding the effects of interventions on physical activity of individuals with stroke.

4.2.7 Conflict of interest

The authors report no conflicts of interest.

4.2.8 Funding

4.2.9 References

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Table **4-1.** Comparison of the outcome measures of Saunders *et al.*'s Cochrane systematic review [10] and the Aguiar *et al.*'s systematic review protocol [15].

	Saunders *et al.* [10]	**Aguiar *et al.* [15]**
Period	Until February 2015	Until March 2018
Theme	Effects of exercise interventions on selected outcomes after stroke	Effects of physical activity interventions on selected outcomes after stroke
Number of included studies	58	18
Number of common included studies	2	
Outcomes	Death	Physical activity
	Dependence	Subjective measures: Physical Activity for
	Disability: Functional Independence Measure,	the elderly, Physical Activity & Disability,
	Barthel Index, Rivermead Mobility Index,	Physical Activity, Yale Human Activity
	Functional Ambulation Category, Nottingham	Profile, Physical activity subscale of the
	Extended Activities of Daily Living Scale,	Health Promoting Lifestyle Profile, The
	Lawton Index of Activities of Daily Living, and	Baecke Inventory, physical activity diary.
	the Stroke Impact Scale	Objective measures: accelerometers,
	Adverse effects	pedometers, multisensor tools
	Vascular risk factors	
	Mobility	
	Health status and quality of life	
	Mood	
	Cognitive function	
	Physical function: balance, stair climbing, weight bearing, 'timed up and go' test	
	Physical fitness: exercise heart rate and maximum or peak oxygen uptake (peak VO2), muscle strength and power output.	

Table 4-2. Physiotherapy Evidence Database (PEDro) and Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria and scores for the included studies (n = 18).

	Physiotherapy Evidence Database (PEDro) criteria and scores											
Study	Eligibility criteria	Random allocation	Concealed allocation	Baseline comparability	Blinded subjects	Blinded therapists	Blinded assessors	Adequate follow-upᵃ	Intention to-treat analysis	Between-group comparisons	Point estimate and variability	Total (0 to 10)
Teixeira-Salmela, 1999 [34]	Y	Y	N	N	N	N	N	N	N	Y	Y	3
Mudge, 2009 [30]	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	7
Boysen, 2009 [24]	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	7
Kojovic, 2009 [28]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Shaughness, 2012 [32]	N	Y	N	Y	N	N	N	N	N	Y	Y	4
Liao, 2012 [29]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Kono, 2013 [35]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Chiong, 2013 [25]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Severinsen, 2014 [31]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Shim, 2015 [33]	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Wan, 2016 [36]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
English, 2016 [26]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Givon, 2016 [27]	N	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Vahlberg, 2017 [37]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Marquardt, 2017 [38]	Y	Y	N	Y	N	N	Y	N	Y	Y	Y	6
Vanroy, 2017	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8

Teuschl, 2017 [40]	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	8
Kanai, 2018 [41]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7

Note: Reference [39] appears above Teuschl, 2017.

Grading of Recommendations Assessment, Development, and Evaluation (GRADE) quality assessment

Number of studies (number of participants)	Study limitations	Consistency	Directness	Precision	Publication bias	Quality
18 articles (1314) [24-41]	Serious limitations (-1)	Heterogeneity (-1)	Very serious indirectness (-2)	Imprecision (-1)	Serious risk of bias (-1)	Very low

Y = yes; N= no. Note: The eligibility criteria item does not contribute to the total score. [a]Measures of at least one key outcome were obtained from more than 85% of the subjects, who were initially allocated to groups.

Table 4-3. Summary of the included studies (n = 18).

Study	Participants	Intervention		Control
		Content	Delivery characteristics	
Teixeira-Salmela, 1999 [34]	n = 13; IG: n = 6; CG: n = 7 Age (years) = IG: 66 (10); CG: 69 (9) Time post-stroke (years) = IG: 9 (13); CG: 6 (6) Sex, men = IG: 1; CG: 6.	Session: 5-10 min warm-up (calisthenics, mild stretching, and range of motion exercises); 10-20 min aerobic exercises at 50-70% of the maximal heart rate (graded walking plus stepping or cycling); 30 min lower-limb strength training, (performed concentrically/eccentrically with body weight, sandbag weights, and elastic bands); 5-10 min of cool-down (muscular relaxation/stretching with emphasis on the trunk and lower-limb muscles). A list of home exercises was provided. Aerobic training: intensity/duration was increased from the first 5 weeks to the last 5 weeks. Strength training: 3 sets of 10 repetitions at 50%-80% of 1 maximum repetition, with 1-2 min rest (progressed through the weeks or as tolerated).	Duration: 60-90 min sessions, 3 sessions/week for 10 weeks. Home exercises: 3 sessions/week Provider: a physiologist and a physiotherapist.	No intervention.
Mudge, 2009 [30]	n = 58; IG: n = 31; CG: n = 27 Age (years), median = IG: 76 [39-89]; CG: 71 [44-86] Time post-stroke (years), median = IG: 3 [0.6-13]; CG: 6 [0.5-19] Sex, men = IG: 19; CG: 13	"Group circuit exercises": 15 stations graded to each participant's ability and progressed as tolerated. Each station (2 min) contained either a task-oriented gait or standing balance activity or strengthening of a lower-limb muscle. Plus stretching.	Duration: 50-60 min sessions, 3 sessions/week for 4 weeks. Groups of up to 9 participants. Provider: one investigator and 2 physiotherapy students.	Eight social and educational 90 min sessions (groups of 8), led by an occupational therapist, for 4 weeks.
Boysen, 2009 [24]	n = 314; IG: n = 157; CG: n = 157 Age (years) = IG: 69.7 median, [60-78]; CG: 69.4 median, [60- 76] Time post-stroke = IG/CG: 90 days Sex, men = IG: 89; CG: 88	"Repeated encouragement and verbal instruction on being physically active": First session: 30-60 min getting acquainted with the participant and evaluating the consequences of the stroke. The aim was to make the participant choose the most suitable type of physical activity. The program was individualized per participant's resources/former activities/preferences. Participants were encouraged to use facilities in their local community, to walk several km/day, to go bicycling, to go to public swimming pools, and to exercise in their local center. At each visit the participant filled in a standard agreement form with various choices of physical activity, with one	Duration: 7 sessions (every 3 months during the first year, and thereafter every 6 months) for 2 years. Provider: a physiotherapist or a neurologist.	Clinical visits with the same frequency as the intervention group. Information on the benefits of physical activity, no specific instruction. No telephone calls. Standard treatment.

copy of the completed form for the participant. At the 20-30 min follow-up, the instructor repeated instructions and readjust the physical activity plan. Between visits: telephone call to remind each participant about the physical activity agreement. Participants were asked about their activities and encouraged to increase efforts and to exercise more and were told that to become sweaty and short of breath was desirable.
Standard treatment.

Kojovic, 2009 [28]	n = 13; IG: n = 7; CG: n = 6 Age (years) = IG: 61 (13); CG: 57 (13) Time post-stroke (d) = IG: 23 (8); CG: 23 (5) Sex, men = IG: 3; CG: 3	"Functional Electrical Therapy group": walking sessions with instructions on how to improve walking pattern and with electrical stimulation in 4 muscle groups (quadriceps, hamstrings, soleus, and tibialis anterior). Electrical stimulation parameters: 50 Hz frequency and 400 s pulse duration. The slopes of the trapezoidal forms were preset to 5 pulses (rising time) and 3 pulses (fall time). The intensity of stimulation was adjusted between 12 mA and 38 mA. Standard treatment.	Duration: 45 min sessions, 5 sessions/week for 4 weeks. Provider: therapist.	Walking sessions with instructions on how to improve walking pattern. Standard treatment.
Shaughness s, 2012 [32]	n = 64; Age (year) = 64 (9) Time post-stroke = not reported Sex = 28 men	"Task-oriented treadmill intervention": 40 min of aerobic exercise at 60% heart rate reserve. Starting at the individuals' baseline exercise capacity, the duration/intensity of treadmill training was increased every 2 weeks.	Duration: 3 sessions/week for 6 months. Provider: physiotherapist.	Thirteen supervised stretching movements of the major muscular groups. 3 sessions/week for 6 months.
Liao, 2012 [29]	n = 20; IG: n = 10; CG: n = 10 Age (years) = IG: 56 (11); CG: 55 (8) Time post-stroke (months) = IG: 24 (13); CG: 22 (17) Sex, men = IG: 6; CG: 7	"Robot-assisted therapy": bilateral movement with Bi-Manu-Track robotic arm trainer. Four modes: (1) passive-passive (both arms controlled); (2) passive-active (non-paretic arm driving the paretic arm); (3) active-active (paretic arm actively moving against resistance, then both arms cooperating to achieve movement); (4) active–passive (paretic arm actively executing the training). Session: 300-400 forearm cycles, totaling 600–800 repetitions of mode 1 and 2, and 150–200 repetitions of mode 3. If possible, mode 2 was adjusted to mode 4. Visual feedback received. Functional task training (15 min). Standard treatment.	Duration: 90-105 min sessions, 5 sessions/week for 4 weeks. Provider: occupational therapist.	Paretic arm exercise or gross motor training, muscle strengthening, fine motor or dexterity training. Functional task training (15 min). Standard treatment.
Kono, 2013 [35]	n = 70; IG: n = 35; CG: n = 35 Age (years) = IG: 63.05 (7.0); CG: 63.4 (11.4)	"Lifestyle Intervention": advice and counseling about lifestyle modification (increase in physical activity, smoking cessation, alcohol reduction and dietary modification);	Duration: one single 30-40 min individual advice session. One or 2 60-	Advice to facilitate healthy lifestyle modification at

Study	Participants	Intervention	Duration/Provider	Comparison
	Time post-stroke (months) = IG/CG: not reported Sex, men = IG: 21; CG: 27	"Home exercise program": prescription of walking exercise for 30–60 min at a frequency of 3–5 days/week with a target heart rate of 110 bpm. Exercise duration and intensity was checked for 7 consecutive days once per month using a heart rate monitor. "Center-based exercise training": aerobic and resistance exercise. Aerobic exercise (cycle ergometer): 3–5 min of warm-up at 20 W, followed by 20–30 min of exercise at a target heart rate of 110 bpm (initially started with 15 min). Familiarization period of 2 weeks. Resistance training: trunk, upper and lower limbs exercises. Two or 3 sets of 10–12 repetitions targeted at an intensity of 50-60% of 1 maximum repetition for the upper limb, and 60-70% for the lower-limb (first month: 10–15 repetition maximum). The "salt reduction program": a computer-based self-education program to provide knowledge about salt reduction. Salt intake monitoring was performed every 6 weeks.	min exercise training sessions per week for 24 weeks. Provider: physiotherapist	baseline, 3 months, and 6 months. Usual medical care.
Chiong, 2013 [25]	n = 9; IG: n = 5; CG: n = 4 Age (years), median (IQR) = IG: 48 (21) [34-61]; CG: 48 (17) [39-60] Time post-stroke (months) = IG:19 median, 20.5 IQR [12-41]; CG: 25 median, 19 IQR [9-33] Sex, men = IG: 3; CG: 2	"Toe flexors stretches + toe-spreader": daily self-stretching exercises to the toe flexors, gastrocnemius, soleus and adductor hallucis of the paretic lower-limb; use of a customized toe-spreader during walking for 6 months.	Duration: daily for 6 months. Provider: physiotherapist.	'Toe flexors stretches': daily self-stretching exercises to the toe flexors, gastrocnemius, soleus and adductor hallucis of the paretic lower limb.
Severinsen, 2014 [31]	n = 43; IG1: n = 13; IG2: n = 14; CG: n = 16 Age (years), median = IG1: 69 [50-80]; IG2: 68 [57-78]; CG: 66 [52-80] Time post-stroke (months) = IG1:14 [11-29]; IG2: 19 [8-36]; CG: 16 [9-38] Sex, men = IG1: 9; IG2: 11; CG: 11	IG1= "Aerobic training": 5 min warm-up (cycle ergometer); aerobic training of 15 min (cycle ergometer), at 75% of the heart rate reserve, 3 times per session. IG2= "Resistance training": 5 min warm-up (cycle ergometer); lower-limb exercises, using machines. 3 sets of 8 repetitions targeted at an intensity of 80% of 1 maximum repetition (adjusted every 2 weeks). Post-trial: verbal encouragement to remain physically active.	Duration: 1-hour sessions, 3 sessions/week for 12 weeks. Provider: physiotherapist.	'Sham group': 5 min warm-up (cycle ergometer); upper-limb exercises. 3 sets of 15 repetitions bilaterally. Less than 60% of 1 maximum repetition. Same frequency and duration as the IG.
Shim, 2015 [33]	n = 20; IG: n = 10; CG: n = 10	"Bilateral training group": functional task training with both hands, symmetrically.	Duration: 30 min sessions, 5	Unilateral training group: functional

				sessions/week for 6 weeks.	task training with the paretic hand.
	Age (years) = IG: 54 (19); CG: 58 (10) Time post-stroke (months) = IG: 8 (2); CG: 8 (2) Sex, men = IG: 9; CG: 8			Provider: not specified.	Five 30-min sessions/week for 6 weeks.
Wan 2016 [36]	n = 80; IG: n = 40; CG: n = 40 Age (years) = IG: 59.07 (12.36); CG: 60.24 (2.57) Time post-stroke (months) = IG/CG: within 1 month Sex, men = IG: 30; CG: 27	Usual stroke education, including freely available educational brochures on understanding stroke and reducing stroke risk. "Telephone Follow-up Group": The telephone sessions consisted of goal-setting advice. Patients set behavioral goals and developed action plans. First call: discussion about pre-stroke lifestyle, with indication of which aspects should be improved to decrease recurrence risk, and attain healthy lifestyle. Following calls: encouragement of appropriate behavior, reassurance of the benefits of the behavior, and identification of problems.		Duration: Three 15-20 min telephone calls at one week and at 1 and 3 months after discharge. Provider: nurse	Usual stroke education, including freely available educational brochures on understanding stroke and reducing stroke risk.
English, 2016 [26]	n = 33; IG: n = 19; CG: n = 14 Age (years) = IG: 65 (12); CG: 68 (14) Time post-stroke (months) = IG/CG: at least 6 Sex, men = IG: 13; CG: 9	Four counseling sessions with the message to sit less and move more. Encouragement to regularly break up sitting time with short bursts of light-intensity activity. Key motivational interviewing techniques were used. Action plans, goals, and strategies were elicited from the participants.		Duration: 4 sessions, 1, 3, and 7 weeks after the initial session. First session: face-to-face. Follow-up sessions were delivered by phone. Provider: 2 researchers trained in motivational interviewing techniques.	Same schedule of interviews with a placebo message of increasing calcium for bone health.
Givon, 2016 [27]	n = 47; IG: n = 24; CG: n = 23 Age (years) = IG: 57 (9) [29–69]; CG: 62 (9) [42–78] Time post-stroke (years) = IG: 3 (2); CG: 2.6 (2) Sex, men = IG:11; CG: 17	"Video-game group": 5 min warm up (walking while playing a walking game); played games in pairs in 3 different work stations. Some consoles allowed playmates to play simultaneously, if not, participants took turns. While waiting, participants were encouraged to play "outside", or to respond (sit-to-stand, clap hands) every time their playmate scored. Participants too tired to do so, rested. Physical/verbal guidance was provided, if needed. Participants were encouraged to use their paretic upper limb, but if it was not possible, they were guided to hold their paretic hand to integrate it into function.		Duration: 2 sessions/week of one hour in groups of 6 to 8 for 3 months. Provider: occupational therapists.	Warm up (upper and lower limb movements, stretching, marching and upper limb swings, 5 min walk); functional task training in pairs or triads. Same frequency/duration as the IG.

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Vahlberg, 2017 [37]	n = 67; IG: n = 34; CG: n = 33 Age (years) = IG: 72.6 (5.5); CG: 73.7 (5.3) Time post-stroke (months), median (IQR) = IG: 13 (4); CG: 13 (2) Sex, men = IG: 27; CG: 24	"Progressive resistance and balance training": 10 min warm-up (stationary cycling or walking); 45 min circuit class (functional task training, including static and dynamic-balance exercises in combination with lower-limb strength exercises); 20 min motivational session (discussions about physical activity behavior and risk factor modifications with questions about the barriers/facilitators). Progression: increasing the weights according to the perceived exertion or adjusting the exercise performance (e.g. deeper knee bends) or balance challenge (decreased support base). Daily home exercises.	Duration: 2 sessions/week for 3 months Circuit class exercises: 2 min followed by 1 min of rest. Low (>15 repetitions) to moderate (10–15 repetitions) intensity. Provider: physiotherapist	Encouragement to continue regular activities. Participants were not restricted from participating in ordinary physical activities and rehabilitation programs.
Marquardt, 2017 [38]	n = 183; IG: n = 60; CG1: n = 61; CG2: n = 62 Age (years) = IG: 56.68 (8.43); CG1: 56.74 (11.47); CG2: 57.03 (9.20) Time post-stroke (days) = IG: 36 (38); CG1: 38 (52); CG2: 55 (85) Sex, men = IG: 45; CG1: 41; CG2: 49	IG = Four health information lessons with standardized materials about behavioral risk factors for stroke and recommendations for risk reduction. Two sessions of a self-regulation behavior change strategy.	Duration: three weeks Two separate 1-hour lessons per week Provider: psychologists	CG1: Six unstructured usual stroke education. CG2: Six health information lessons with standardized materials about behavioral risk factors for stroke and recommendations for risk reduction. Duration: three weeks Provider: medical doctors, dieticians, physical therapists, psychologists
Vanroy, 2017 [39]	n = 59; IG: n = 33; CG: n = 26 Age (years) = 65.4 (10.3) Time post-stroke = 3 to 10 weeks Sex, men = not reported	Phase I Aerobic training: 5 min warm-up (passive movement by the cycle ergometer); 30 min aerobic training (cycle ergometer), at 60-75% of the heart rate reserve; 5 min cool-down (passive movement by the cycle ergometer). During the three-month program, four 1-hour educational sessions with different themes. Standard treatment.	Phase I Duration: three sessions per week for three months. Provider: physiotherapist Phase II	Phase I Passive mobilization of the paretic hip and knee in supine position. Three sessions per week for three months.

			Duration: One session per month for nine months. Provider: physiotherapist	Standard treatment.
Teuschl, 2017 [40]	n = 166; IG: n = 79; CG: n = 87 Age (years) = IG: 62.5 (8.2); CG: 60.7 (10.2) Time post-stroke (days), median (IQR) = IG: 19 (24); CG: 19 (6) Sex, men = IG: 59; CG: 63	Phase II IG divided in two subgroups: coaching and a non-coaching group. The coaching group received a monthly visit to stimulate active behavior. During the first 12 months: 6 dietary group counselling's, 5 individual dietary counselling's, 6 physical exercise group meetings, monthly cognitive training (optional), every 8 weeks: phone calls for adverse events and compliance to medication. During the last 12 months: 1 dietary group counselling's, 1 individual dietary counselling's, 2 physical exercise group meetings, monthly cognitive training (optional), every 16 weeks: phone calls for adverse events and compliance to medication.	Duration: 24 months Provider: nutritionists, physiotherapists, occupational therapists, neurologists	Phase II participants were not visited. 9 months. During the first 12 months: every 8 weeks: phone calls for adverse events During the last 12 months: every 16 weeks: phone calls for adverse events
Kanai, 2018 [41]	n = 55; IG: n = 27; CG: n = 28 Age (years) = IG: 66.8 (10.0); CG: 62.9 (9.1) Time post-stroke (days) = IG: 3.6 (1.4); CG: 3.8 (1.5) Sex, men = IG: 15 ; CG: 13	Instruction on accelerometer-based feedback, discussion on physical activity targets and encouragement to walk more until discharge. Standard treatment.	Duration: 5-6 times a week until discharge from the hospital Length of hospital stay (days): IG: 12.2 (2.8); CG: 11.4 (3.9) Provider: physiotherapist	Standard treatment.

Numerical data under participant characteristics are mean (Standard Deviation) [range], unless indicated. IG = intervention group; CG=control group; IQR= interquartile range.

Table 4-4. Summary of the results (n=18)

Study	Measure used	Results
Teixeira-Salmela, 1999 [34]	Human Activity Profile (Adjusted Activity Score)	Raw data: IG = Baseline: 49.50 (16.13); 10 weeks: 69.50 (10.03) CG = Baseline: 57.57 (11.27); 10 weeks: 55.71 (11.46) Significant interaction between the time and group ($p = 0.01$). The IG showed significant increases in physical activity between baseline and post-intervention, when compared to the CG. The treatment group showed significant improvement at post-training, whereas no significant differences were observed between the 2 measures for the CG.
Mudge, 2009 [30]	Physical Activity and Disability Scale	Raw data: Mean (SD) IG= Baseline: 75.2 (57.5); 4 weeks: 77.8 (55.7); Follow-up (3 months): 82.1 (72.8). CG= Baseline: 63.6 (77); 4 weeks: 60.9 (67.2); Follow-up (3 months): 62.2 (72.5). No significant differences in physical activity were found between baseline, post-intervention and follow-ups for any of the groups.
Boysen, 2009 [24]	Physical Activity Scale for the Elderly	Raw data: Median (IQR) IG = Baseline: 76 (50-124); 3 months: 73 (42-120); 6 months: 86 (50-133); 9 months: 83 (41-120); 12 months: 80 (45-130); 18 months: 76 (46-123); 24-months: 69 (33-118); CG = Baseline: 65 (50-126); 3 months:68 (43-94); 6 months: 67 (33-102); 9 months: 64 (41-104); 12 months: 69 (36-111); 18 months: 66 (33-111); 24 months: 68 (32-106). The per protocol analysis of the patients who attended all planned follow-up visits showed a significant ($p = 0.03$) difference in pre-stroke score. There was no significant difference between the 2 groups when adjusted for pre-stroke score. No significant differences in physical activity were found between baseline, post-intervention and follow-ups for any of the groups.
Kojovic, 2009 [28]	Physiological Cost Index (beats per min), defined as "Heart rate after, minus heart rate before walking over 6 meters, divided by mean walking velocity (meter/seconds)''.	Raw data: Mean (SD) IG = Baseline:0.43 (0.09); 4 weeks: 0.18 (0.13). CG = Baseline: 0.34 (0.22); 4 weeks: 0.28 (0.18). Between-group comparison: Significant differences ($p<0.05$) between groups. The IG showed significant increases in physical activity between baseline and post-intervention when compared to the CG. IG had a significant improvement ($p<0.05$), and no significant differences in the CG ($p = 0.29$).
Shaughness, 2012 [32]	Yale Physical Activity Survey	Raw data: - Housework (min/week): IG = Baseline: 2,083 (1714); 6 months: 1,695 (1908) CG = Baseline: 2,159 (280); 6 months: 1,693 (1584) - Recreational Activity (min/week): IG = Baseline: 240 (557); 6 months: 190 (388)

CG = Baseline: 142 (262); 6 months: 200 (345)
- Exercise:
IG = Baseline: 902 (1422); 6 months: 880 (876)
CG = Baseline: 850 (1521); 6 months: 776 (1039)
- Total Activity:
IG = Baseline: 3151 (2840); 6 months: 2669 (1990)
CG= Baseline: 3225.6 (2826); 6 months: 2765.5 (2409)

Between-group comparison: no significant treatment by time interaction effect.

All participants showed declines in physical activity between baseline and post-intervention, regardless of the intervention group (amount of housework, baseline: 2,125 (1908); 6 months: 1,694 (1722); $F = 4.00$, $p = 0.05$, *power* 50%).

Liao, 2012 [29]	Accelerometer: Micro Mini-Motion logger activity monitor (Ambulatory Monitoring, New York, NY, USA). Arm activity ratio (ratio of mean activity between the paretic/non-paretic upper limb). Accelerometer used on both wrists for 3 days.	Raw data: Mean (SD) IG= Baseline: 0.71 (0.99); 4 weeks: 0.76 (0.10). CG= Baseline:0.69 (0.12); 4 weeks: 0.69 (0.11). Between-group comparison: significant difference was found between the 2 groups ($F = 5.91$; Effect size $r = 0.26$; $p = 0.03$). The IG showed significant increases in physical activity between baseline and post-intervention, when compared to the CG.IG handled more daily tasks with the impaired arm than the CG.
Kono, 2013 [35]	Accelerometer (Kenz Lifecorder, Suzuken, Nagoya, Japan) (mean daily step count and the duration of low- [<3 metabolic equivalents], moderate- (3–6 metabolic equivalents) and high-intensity physical activity (>6 metabolic equivalents)). Accelerometer used during 24 hours/day for 7 days.	Raw data: Mean (SD) - Steps/day IG = Baseline: 6,250 (2,234); 6 months: 8,422 (2,360). CG = Baseline: 6,524 (2,349); 6 months: 6,534 (1,366). - Low-intensity activity time, min/day IG = Baseline: 50.5 (21.7); 6 months: 54.4 (19.1). CG = Baseline: 53.5 (22.7); 6 months: 52.5 (6.64). - Moderate-intensity activity time, min/day IG = Baseline: 23.2 (16.7); 6 months 31.5 (17.1). CG = Baseline: 22.5 (20.4); 6 months: 19.8 (14.8). - High-intensity activity time, min/day IG = Baseline: 1.19 (1.98); 6 months: 1.64 (2.89). CG = Baseline: 0.99 (1.42); 6 months: 0.87 (1.09).

Between-group comparison: the IG showed significant increases in physical activity between baseline and post-intervention, when compared to the CG. The IG showed a significant increase in daily step counts ($p = 0.012$), and moderate-intensity physical activity time ($p = 0.033$).

Chiong, 2013 [25]	Pedometer (number of steps)	Raw data: median (IQR) IG = Baseline: 2435 (2786); 6 months: 3279 (5145). CG = Baseline: 3418 (4623); 6 months: 4367 (3012). No significant differences in physical activity were found between baseline and post-intervention for any of the groups.
Severinsen, 2014 [31]	Physical Activity Scale	Raw data: no raw data reported. Between-group comparison: no statistically significant changes. All participants showed increases in physical activity, regardless of intervention group, by 5 metabolic equivalents (median) (-6 to 19; $p<0.05$) between baseline and post-intervention, that remained increased at the end of the follow-up period after 1 year by 2 metabolic equivalents (median) (-14 to 21; $p = 0.05$).
Shim, 2015 [33]	Actisleep (GT3X+, LLT, USA) triaxial accelerometer (amount/intensity of physical activity) Accelerometer used on the wrist, waist, and ankle.	Raw data: Mean (SD) - Amount of activity of the paretic/non-paretic side (counts) IG = Baseline: 1145.2 (533.9)/3,307.5 (1,074.8); 6 weeks: 1837.7 (1097.7)/ 3,135.6 (1,285.6). CG = Baseline: 731.4 (541.0)/2,386.3 (757.5); 6 weeks: 807.7 (566.7)/2,393.5 (677.2). - Light activity intensity of the paretic/non-paretic side (%) IG = Baseline: 23.6 (12.5)/26.4 (9.2); 6 weeks: 24.5 (10.4)/24.8 (6.0) CG = Baseline: 17.3 (9.8)/30.5 (9.0); 6 weeks: 16.1 (7.2)/26.9 (9.4) - Lifestyle activity intensity of the paretic/non-paretic side (%) IG = Baseline: 6.3 (4.6)/33.1 (13.2); 6 weeks: 9.9 (7.6)/25.3 (13.2) CG = Baseline: 4.9 (5.7)/25.0 (10.3); 6 weeks: 4.4 (3.4)/20.3 (11.8) - Moderate activity intensity of the paretic side (%) IG = Baseline: 2.5 (1.8)/9.7 (5.4); 6 weeks: 3.5 (2.2)/7.7 (7.9) CG = Baseline: 0.9 (1.1)/5.0 (4.2); 6 weeks: 1.7 (1.7)/5.7 (3.9) Within group comparison: CG showed significant increase in moderate activity intensity of the paretic side ($p<0.05$). IG showed significant decrease in lifestyle activity intensity of the non-paretic side ($p<0.05$). Between-group comparison: IG showed greater quantitative increases in the amount of activity of the paretic side ($p<0.05$) and an increase in the moderate activity intensity of the paretic side ($p<0.05$) compared to the CG. The IG showed significant increases in physical activity between baseline and post-intervention, when compared to the CG.
Wan 2016 [36]	Physical activity subscale of The Health Promoting Lifestyle Profile II	Raw data: Mean (SD) IG = Baseline: 1.73 (0.74); 3 months: 2.31 (0.76); 6 months: 2.32 (0.72) CG = Baseline: 1.78 (0.65); 3 months: 2.38 (0.71); 6 months: 2.21 (0.74) Between-group comparison: no significant group and time interactions were found ($F = 0.540$; $p = 0.465$). However, a significant main effect of time was revealed, indicating a significant difference between times ($F = 20.957$; $p<0.001$). All participants showed increases in physical activity between baseline and post-intervention, regardless

		of the intervention group.
English, 2016 [26]	Actigraph GT3+ accelerometer (time spent in physical activity of at least moderate intensity (≥1952 counts/min)) Accelerometer used on the non-paretic hip during 24 hours/day for 7 days.	Raw data: IG = Baseline: 8.8 (11.2) min/day; 7 weeks: 7.7 (11.4) min/day. CG = Baseline: 7.2 (6.3) min/day; 7 weeks: 10.9 (11) min/day. Within group comparison: IG: -0.6 (10.9) (95%CI -6.4 to 5.3), p = 0.84. CG = 4.1 (9.7) (95%CI -1.9 to 10.3), p = 0.16. Between-group comparison: -3.8 (95%CI -11.8 to 4.1), p = 0.33. No significant differences in physical activity between baseline and post-intervention were found for any of the groups.
Givon, 2016 [27]	Acticial Minimitter Co. accelerometer (mean number of steps/day) Accelerometer used on the hip for 3 days.	Raw data: IG = Baseline: 3368 (3385.1); 3 months: 3786.8 (4178.2); Follow-up (3 months): 3154 (4781.5). CG = Baseline: 2655.5 (2645.9); 3 months: 2540.2 (2593.5); Follow-up (3 months): 3502 (3086.5). Within group comparison: IG: 8.8% (baseline-post-intervention); −4.8% (baseline-follow-up). CG = −4.3% (baseline-post-intervention); 31.9% (baseline-follow-up). No significant differences in physical activity were found between baseline, post-intervention and follow-ups for any of the groups.
Vahlberg, 2017 [37]	Physical Activity Scale for the Elderly	Raw data: Mean (SD) IG = Baseline: 91 (68); 3 months: 99 (47); follow-up (3 months): 80 (51); follow-up (12 months): 94 (58). CG = Baseline: 70 (54); 3 months: 79 (57); follow-up (3 months): 91 (58); follow-up (12 months): 83 (66). No significant differences in physical activity were found between baseline, post-intervention and follow-ups for any of the groups.
Marquardt, 2017 [38]	The Baecke Inventory Physical activity diary with the following question: "How well did you follow the recommendations for physical activity in the last week?" on a 10-cm line ranging from 0%-100%.	Raw data: Mean (SD), only baseline data reported. - The Baecke Inventory (sports) IG = Baseline: 2.74 (0.06) CG1 and 2 = Baseline: 2.59 (0.04) - The Baecke Inventory (other) IG = Baseline: 2.98 (0.06) CG1 and 2 = Baseline: 2.90 (0.04) - Physical activity diary IG = Baseline: 62.45 (3.10) CG1 and 2 = Baseline: 54.11 (2.06) Between-group comparison: IG showed greater increase in the subscale sports activities during leisure time of The Baecke Inventory, and on the diary measure of physical activity than CG1 and CG2. No significant differences in physical activity in the subscale other physical activity during leisure time of The Baecke Inventory for any of the groups.
Vanroy, 2017 [39]	Pedometer (Yamax Digi-Walker SW-200, Yamasa Tokei Keiki co LTD,	Phase I - Raw data: Mean (SD), or median [IQR] - Pedometer (number of steps)

Japan) (number of steps)
Pedometer used on the non-paretic knee during day hours for 3 days.
 	
Multisensor (SenseWear Pro2 Armband, Health Wear BodyMedia, Pittsburgh, PA) (energy expenditure)
Multisensor used on the non-paretic arm during 24 hours/day for 3 days.
 	
Coded activity diary (duration at different activity intensities)
 	
The Physical Activity Scale for Individuals with Physical Disabilities
 	
The Baecke Questionnaire of Habitual Physical Activity (sport and leisure scores)
	IG = Baseline: 2657 [1146–4910]; 3 months: 5340 [2304–9418].
	CG = Baseline: 3155 [1079–4417]; 3 months: 4789 [1458–7036].
	- Multisensor (energy expenditure)
	IG = Baseline: 1906.58 (394.24); 3 months: 2189.87 ± 667.19.
	CG = Baseline: 1945.43 (426.88); 3 months: 2035.85 (569.63).
	- Coded activity diary (duration at different activity intensities)
	  Sedentary activities
	IG = Baseline: 990 [920–1080]; 3 months: 920 [830–1050].
	CG = Baseline: 1040 [873–1153]; 3 months: 1020 [830–1080].
	  Light activities
	IG = Baseline: 410 [294–586]; 3 months: 517 [373–730].
	CG = Baseline: 379 [294–586]; 3 months: 484 [298–702].
	  Moderate activities
	IG = Baseline: 390 [295–510]; 3 months: 420 [265–588].
	CG = Baseline: 345 [260–524]; 3 months: 370 [270–660].
	- The Physical Activity Scale for Individuals with Physical Disabilities
	IG = Baseline: 7.71 [7.71-9.33]; 3 months: 9.03 [6.74-10.90].
	CG = Baseline: 7.71 [7.02–9.60]; 3 months: 8.15 [4.78–11.01].
	Within group comparison: significant time changes (increases) were found for all assessments, except the Physical Activity Scale for Individuals with Physical Disabilities and the diary/moderate activities.
	Between-group comparison: no statistically significant differences were found between baseline, post-intervention and follow-ups.
	<u>Phase II - Raw data: Mean (SD), or median [IQR]</u>
	- Pedometer (number of steps)
	IG (with coaching) = Baseline: 2570 [1634–3731]; 3 months: 2570 [2184–6065]; follow-up (6 months): 5013 [927–7211]; follow-up (12 months): 5636 [1877–8097].
	IG (without coaching) = Baseline: 2745 [650–5595]; 3 months: 2745 [2328–10572]; follow-up (6 months): 4346 [2520–10044]; follow-up (12 months): 5018 [1183–8170].
	CG = Baseline: 3155 [1079–4417]; 3 months: 4789 [1458–7036]; follow-up (6 months): 5695 [1367–8317]; follow-up (12 months): 3722 [805–6810].
	- Multisensor (energy expenditure)
	IG (with coaching) = Baseline: 1929.49 ± 407.78; 3 months: 2136.11 ± 513.22; follow-up (6 months): 1973.34 ± 487.93; follow-up (12 months): 1955.88 ± 420.70.
	IG (without coaching) = Baseline: 1887.96 ± 395.31; 3 months: 2232.87 ± 784.40; follow-up (6 months): 1851.95 ± 663.02; follow-up (12 months): 2060.69 ± 451.85.
	CG = Baseline: 1945.43 (426.88); 3 months: 2035.85 (569.63); follow-up (6 months): 1939.03 ± 606.98; follow-up (12 months): 2143.44 ± 662.55.

- Coded activity diary (duration at different activity intensities)

 Sedentary activities

IG (with coaching) = Baseline: 1000 [950–1080]; 3 months: 1000 [790–1030]; follow-up (6 months): 885 [800–1088]; follow-up (12 months): 850 [768–1070].

IG (without coaching) = Baseline: 970 [865–1134]; 3 months: 970 [875–1090]; follow-up (6 months): 940 [880–1050]; follow-up (12 months): 910 [815–1035].

CG = Baseline: 1040 [873–1153]; 3 months: 1020 [830–1080]; follow-up (6 months): 910 [810–1050]; follow-up (12 months): 946 [890–1020].

 Light activities

IG (with coaching) = Baseline: 410 [295–525]; 3 months: 410 [430–840]; follow-up (6 months): 679 [473–834]; follow-up (12 months): 752 [538–837].

IG (without coaching) = Baseline: 430 [296–600]; 3 months: 430 [348–576]; follow-up (6 months): 660 [461–789]; follow-up (12 months): 715 [419–869].

CG = Baseline: 379 [294–586]; 3 months: 484 [298–702]; follow-up (6 months): 471 [342–771]; follow-up (12 months): 635 [450–775].

 Moderate activities

IG (with coaching) = Baseline: 400 [305–580]; 3 months: 400 [270–590]; follow-up (6 months): 407 [214–498]; follow-up (12 months): 330 [174–489].

IG (without coaching) = Baseline: 315 [260–508]; 3 months: 315 [246–610]; follow-up (6 months): 348 [203–470]; follow-up (12 months): 246 [160–438].

CG = Baseline: 345 [260–524]; 3 months: 370 [270–660]; follow-up (6 months): 510 [230–810]; follow-up (12 months): 305 [120–515].

- The Physical Activity Scale for Individuals with Physical Disabilities

IG (with coaching) = Baseline: 7.71 [7.71–10.24]; 3 months: 7.71 [4.02–9.82]; follow-up (6 months): 5.15 [2.57–8.17]; follow-up (12 months): 6.17 [2.79–10.81].

IG (without coaching) = Baseline: 8.25 [6.75-9.28]; 3 months: 8.25 [7.83–11.18]; follow-up (6 months): 7.15 [4.14–8.63]; follow-up (12 months): 6.88 [3.85–11.95].

CG = Baseline: 7.71 [7.02–9.60]; 3 months: 8.15 [4.78–11.01]; follow-up (6 months): 3.06 [1.29–9.87]; follow-up (12 months): 3.27 [1.45–6.98].

- The Baecke Questionnaire of Habitual Physical Activity (sport and leisure scores)

 Sport scores

IG (with coaching) = Baseline: 2.45 (0.86); follow-up (12 months): 2.28 (0.73).

IG (without coaching) = Baseline: 2.50 (0.98); follow-up (12 months): 2.31 (1.14).

CG = Baseline: 2.46 (1.24); follow-up (12 months): 1.57 (0.82).

 Leisure scores

IG (with coaching) = Baseline: 2.63 (0.76); follow-up (12 months): 2.57 (0.67).

IG (without coaching) = Baseline: 2.67 (0.65); follow-up (12 months): 2.34 (0.69).

		CG = Baseline: 2.63 (0.75); follow-up (12 months): 2.08 (0.46).
		Within group comparison: significant time changes (increases) were found for all assessments.
		Between-group comparison: no statistically significant differences were found between baseline, post-intervention and follow-ups.
Teuschl, 2017 [40]	The overall hours spent per week with regular physical activity and the types of activities obtained by interview	Raw data: number of participants performing more than 150 min moderate intensity or 75 min vigorous-intensity physical activity/week (%) IG = Baseline: 69 (87.3); 12 months: 71 (89.9); follow-up (24 months): 72 (91.1) CG = 74 (85.1); 12 months: 75 (86.2); follow-up (24 months): 75 (86.2) No significant differences in physical activity were found between baseline, and follow-ups for any of the groups.
Kanai, 2018 [41]	Fitbit One accelerometer (Fitbit, Inc., San Francisco, CA, USA) (average daily number of steps, energy expenditure, duration at different activity intensities) Accelerometer used on the waist belt 24 hours/day until discharge, except when bathing.	Raw data: Mean (SD) - Number of steps IG = Baseline: 2726.8 (1931.3); Discharge: 5180.5 (2314.9). CG = Baseline: 2405.0 (1435.5); Discharge: 3113.6 (1150.9). - Energy expenditure IG = Baseline: 288.8 (212.2); Discharge: 420.0 (268.3). CG = Baseline: 268.0 (135.2); Discharge: 295.7 (109.9). - Duration of activity - Light activity IG = Baseline: 101.0 (59.2); Discharge: 139.5 (52.0). CG = Baseline: 110.2 (51.3); Discharge: 113.7 (35.1). - Duration of activity - Moderate activity IG = Baseline: 1.7 (6.4); Discharge: 7.1 (9.4). CG = Baseline: 0.6 (2.1); Discharge: 2.7 (3.8). - Duration of activity - Vigorous activity IG = Baseline: 1.5 (7.1); Discharge: 3.4 (8.2). CG = Baseline: 0; Discharge: 0.8 (1.5). Between-group comparison: IG showed greater increase in number of steps, energy expenditure, and duration of light activity than CG ($17.49 \geq F \geq 13.85$; $p \leq 0.001$). All participants showed increases in moderate and vigorous activity between baseline and post-intervention, regardless of the intervention group ($p < 0.05$).

Outcome measures listed are those that were analyzed in this systematic review; there may have been other measures in the paper. IG = intervention group; CG = control group; min = minutes; IQR = interquartile range; SD = standard deviation.
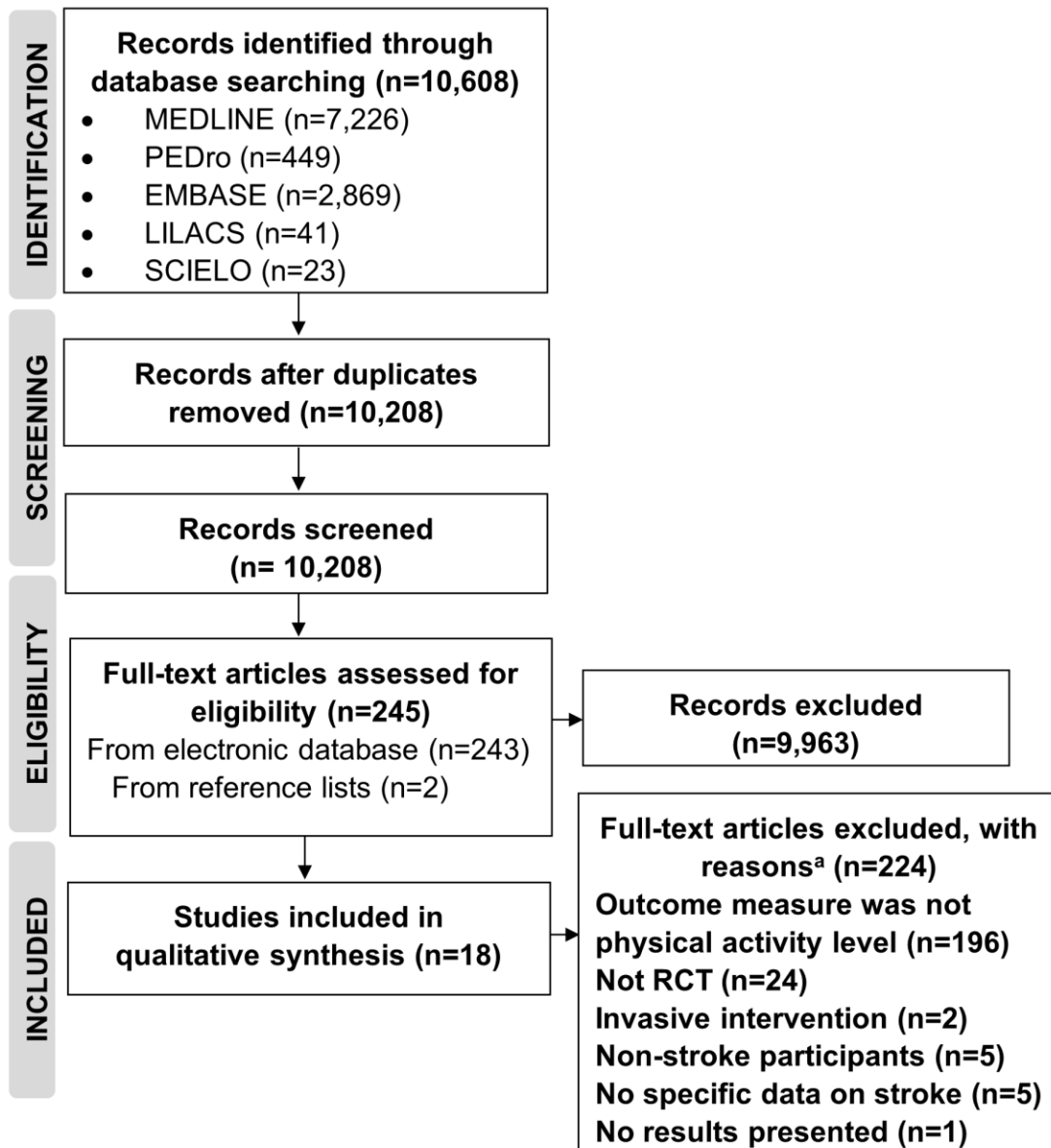
Figure 4-1. Flow of studies through the review

[a]Trials may have been excluded, for failing to meet more than one inclusion criterion.

Box 1. Inclusion criteria:

Study design

- Randomized controlled trials

Participants

- Adults (≥ 18 years)

- Diagnosis of stroke

Intervention

- Any type aimed at increasing physical activity

Comparisons

- No restrictions on the comparisons on the experimental and/or on the control

  group

Outcome measures

- Measures of physical activity by subjective measures such as self-report
  assessment tools, e.g., self-report questionnaires; or by direct measures, e.g.,
  accelerometers, pedometers, multisensor tools, or direct observations.

Chapter 5. Paper #3: Efficacy of aerobic training on physical activity in people with stroke: protocol for a randomized controlled trial

5.1 Preamble

Increasing physical activity level of individuals after stroke is a recognizable aim by different guidelines (BILLINGER *et al.*, 2014; WINSTEIN *et al.*, 2016; BENJAMIN *et al.*, 2018). The results of the systematic review (Paper #2) showed that some types of exercise interventions are effective for improving physical activity after stroke. The intervention of four of the seven studies in which the experimental group had an increase in physical activity levels when compared to the control group comprised aerobic exercise. However, these studies had some limitations, such as the fact that in some studies the control group did no intervention or received an intervention with lower frequency or duration than the experimental group, which could add bias related to the amount of attention. In addition, in some of the studies aerobic training was delivered along with other types of training, which made difficult to understand if aerobic exercise alone was an effective intervention. Furthermore, the overall quality of the evidence, according to the GRADE scale was found to be very low. Therefore, the conclusion of the systematic review is that it is too early to draw definitive conclusions and new randomized controlled trials should be developed. The aim of this paper is to describe the protocol for a randomized controlled trial aimed to investigate if aerobic training is an affective intervention to improve physical activity levels and time spent in low-energy expenditure activities of individuals after stroke. As the randomized controlled trial is the main paper of this thesis, and will be submitted for publication after thesis defense, this chapter will describe in detail the methods related to this paper prior to the presentation of the protocol paper. It has been registered at the www.ClinicalTrials.gov (NCT02798237) and published in Aguiar LT, Nadeau S, Britto RR, Teixeira-Salmela LF, Martins JC, Faria CDCM. Effects of aerobic training on physical activity in people with stroke: protocol for a randomized controlled trial. Trials. 19(1):446, 2018.

5.2 Methods

5.2.1 Design

A randomized controlled trial with blinded assessment and concealed allocation was carried out (Figure 5-1). This study was undertaken between January 2018 and October 2018. Randomization sequence was computer generated and maintained in sealed opaque envelopes, sequentially numbered. The envelopes were prepared prior to commencement of the study by a trained research assistant not involved in the study. A trained examiner, blinded to the group allocation, collected outcome measures immediately before the beginning of the intervention program (week 0), 12 weeks after the beginning of intervention (week 12), and one month following the end of the intervention (week 16) (Figure 5-1). The training therapist opened the envelope and group allocation was revealed. Participants were randomly assigned to one of the two groups: 1) experimental study (high-intensity aerobic treadmill training) (n =11), or 2) control group (low-intensity overground walking) (n =11). This study received approval from the institutional ethical review board (#51454115.6.0000.5149). All participants provided written informed consent (Appendix IV). This trial was prospectively registered at www.clinicaltrials.gov (NCT02798237).

Participants' evaluations were performed at two laboratories from the *Escola de Educação Física, Fisioterapia e Terapia Ocupacional* from the *Universidade Federal de Minas Gerais* (UFMG): *Laboratório de Avaliação e Pesquisa em Desempenho Cardiorrespiratório (LabCare)* and the *Laboratório de Estudos em Reabilitação Neurológica do Adulto (NEUROLAB)*.
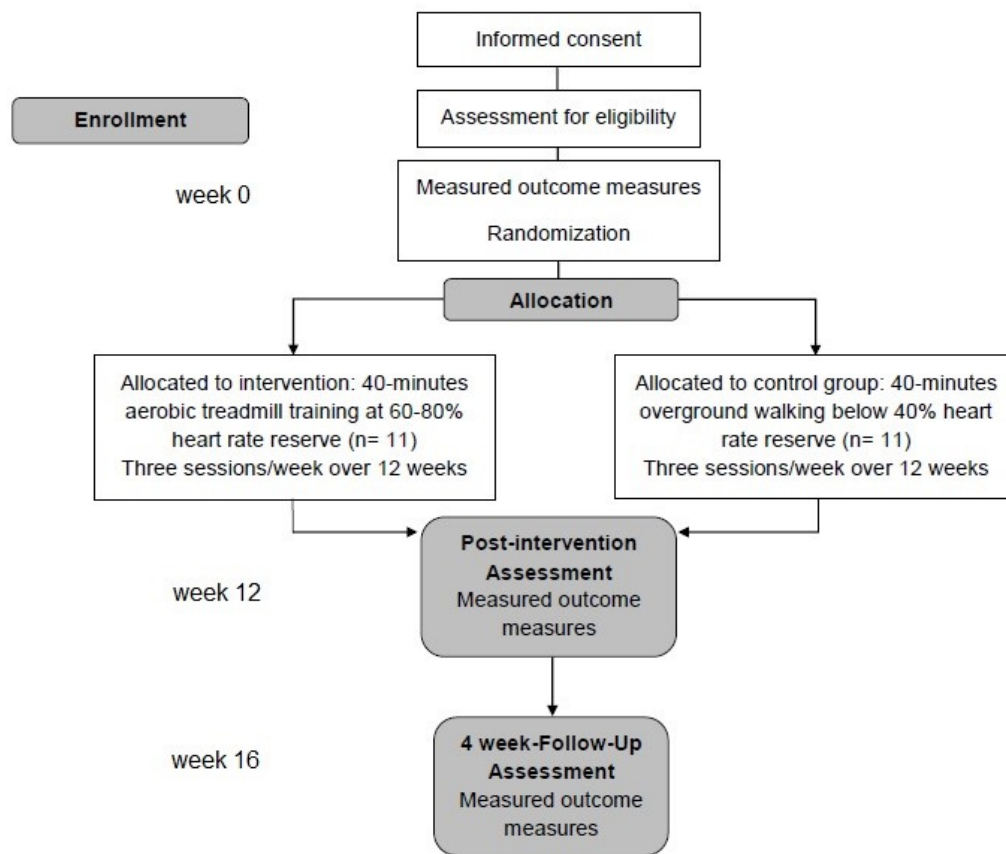
Figure 5-1. Flow of participants through the trial

5.2.3 Sample

Individuals after stroke were recruited from the general community of Belo Horizonte, Minas Gerais, Brazil. Different methods of recruitment were employed: TV and Internet advertisements, posters at various locations (i.e.: pharmacies, churches, university buildings), and by screening out-patient clinics in public hospitals.

Individuals were included in the present study according to the following criteria: ≥20 years of age; diagnosis of chronic stroke (>6months); inactive or insufficiently active (CENTERS FOR DISEASE CONTROL AND PREVENTION, 2001)) and having a written medical release to participate in the trial. Exclusion criteria were: cognitive impairment, as determined by the scores on the Mini-Mental Status Examination (according to educational-specific reference values (BERTOLUCCI, 1994): illiterate < 13 points; elementary and middle school < 18 points; and high-school < 26 points) or the ability to answer to the verbal command "raise your unaffected arm and open your hand" (TEIXEIRA-SALMELA et al.,

2007); inability to walk independently for at least 10 minutes; pain or other disorders precluding participation in aerobic exercise.

5.2.4 Interventions

All participants of the experimental group and the control group received three 40-minute exercise sessions per week over 12 weeks based on the recommendations of previous studies (GLOBAS *et al.*, 2012; PANG *et al.*, 2013; BILLINGER *et al.*, 2014) by trained physiotherapists with more than five years of experience in clinical and research neurological rehabilitation. The sessions were held in groups of two to four participants.

At the beginning of the session, all participants remained at rest for 5 to 15 minutes, and had their blood pressure measured with an aneroid sphygmomanometer Tycos® (Welch Allyn Inc., NY, USA, DS-44 model) and a stethoscope (Litmann Classic II SE 3M®, USA), and their heart rate and peripheral oxygen saturation (SpO_2), with an oximeter (Nonin Medical®, Inc., Plymouth, Minnesota, USA). Blood pressure, SpO_2 and the rate of perceived exertion (Borg Scale) were measured after 15 minutes of exercise Figure 5-2). Heart rate was measured continuously during training (Polar Electro Oy®, Kempele, Finland) (Figure 5-2). After training, all participants remained at rest for 5 to 15 minutes and the same vital signs were measured (heart rate, blood pressure and SpO_2).

Figure 5-2. Vital sign measurements during exercise. A) Blood pressure measurement; B) Rate of perceived exertion measurement; C) Heart rate continuously measured by the heart rate monitor and peripheral oxygen saturation measured by an oximeter.

The **exercise intensity** was determined based on the heart rate reserve (Karvonen method). The training heart rate zone was defined for each participant according to a formula (% (HR_{peak} - HR_{rest}) + HR_{rest}) (PESCATELLO *et al.*, 2014; KENNEY *et al.*, 2015). The HR_{rest} was the heart rate before the beginning of each training session, and the HR_{peak} was the peak heart rate achieved during maximal cardiopulmonary exercise test (Figure 5-3). The maximal cardiopulmonary exercise test with ventilatory expired gas analysis and a 12-lead electrocardiogram (ECG) was performed following the recommendations of the ACSM (PESCATELLO *et al.*, 2014). The treadmill used to perform the exercise test is electronically driven, allow for a wide range of speeds and grades and has an emergency button easily visible. The treadmill has handrails, as recommended by the ACSM, for balance and stability. However, participants were instructed to use the handrails as minimum as possible since its use can have a negative influence on the accuracy of test results (PESCATELLO *et al.*, 2014). The protocol employed for cardiopulmonary exercise test was the progressive ramp protocol adapted for individuals with heart failure (PEREIRA *et al.*, 2012). This type of protocol, which increase work rate in a constant and continuous manner, has been used to improve patient tolerance and test quality (PESCATELLO *et al.*, 2014). The protocol increments in speed and grade were individualized for each participant (PESCATELLO *et al.*, 2014). The increments in work rate were chosen considering a target total duration of exercise test ranging between 8 and 12 minutes (PESCATELLO *et al.*, 2014). All materials and equipment needed to maintain basic and advanced life support were available. A health professional, who has advanced life support training, supervised the exercise test, as recommended by the ACSM (PESCATELLO *et al.*, 2014). Prior to the exercise test, participants received a written detailed instruction about the procedures for exercise testing, as follows (PESCATELLO *et al.*, 2014):

- Refrain from ingesting food, alcohol or caffeine or using tobacco products within three hours of testing;
- Avoid significant exertion or exercise on the day of the assessment;
- Wear clothes that allow freedom of movement and walking shoes;
- Be aware that the exercise test may be fatiguing, and you may wish to have someone accompanying you to the assessment;

- Bring a list of medications including dosage and frequency of administration and report the last actual dose taken;
- Drink ample fluids over 24h period preceding the exercise test to ensure normal hydration before testing.

Figure 5-3. Maximal cardiopulmonary exercise test.

5.2.4.1 Experimental group

For the experimental group, the training sessions occurred at a gym inside a university building, that is open for the public during specific hours (Figure 5-4). Sessions consisted of five minutes of warm-up (walking on treadmill at low intensity), followed by 30 minutes of aerobic training at 60-80% of their heart rate reserve, and five minutes of cool-down (walking on treadmill at low intensity) (GLOBAS *et al.*, 2012; PANG *et al.*, 2013; BILLINGER *et al.*, 2014). Training intensity progression was individualized, depending upon the individual's ability, rate of perceived exertion, heart rate and blood pressure responses (PANG *et al.*, 2013). If a participant required a rest period, it was allowed. However, participants were motivated to come back to training as soon as they felt ready. When participants performed training below their cardiac training range, they were requested to increase speed, until their cardiac training zone was achieved. If participants performed exercise above cardiac training zone, speed was decreased.

Figure 5-4. Experimental group

5.2.4.2 Control group

Participants of the control group performed comfortable overground walking training, at an outdoor walking track inside the university (Figure 5-5). Intensity of the exercise should be maintained below 40% of their heart rate reserve. When participants performed exercise above 40% of their heart rate reserve, they were requested to decrease speed until their heart rate reserve was below 40%.

Figure 5-5. Control group

5.2.5 Outcome measures

Outcome measures were assessed by blinded trained examiners at baseline assessment (week 0), after the intervention (week 12), and one month after the end of the intervention (week 16). Participants were instructed not to comment on the exercise they performed.

5.2.5.1 Primary outcome measures

Physical activity levels and time spent in low-energy expenditure activities were measured with a multisensor activity monitor: SenseWear Armband (BodyMedia, Pittsburgh, PA, USA; software version 8.1) (Figure 5-6). This instrument is portable, non-invasive, light-weighted, provide objective measures and has adequate validity (MOORE *et al.*, 2012; FINI *et al.*, 2015). This equipment uses multiple sensors to measure the heat flux (rate at which heat is dissipated from the body), skin temperature, galvanic skin response (electrical conductivity of skin) and motion and number of steps (triaxial accelerometer) (FINI *et al.*, 2015). Data acquired by these multiple sensors are integrated with clinical characteristics into an algorithm, to provide the estimation of physical activity levels and time spent in low-energy expenditure activities. Average daily energy expenditure, in Kcal, was used to estimate physical activity. Average daily time spent in low-energy expenditure activities (≤ 1.5 metabolic equivalents) was reported in percentage of waking hours. Participants wore this device, attached on the back of their non-paretic arm, for seven days (AINSWORTH *et al.*, 2015; FINI *et al.*, 2015).

Physical activity levels were also measured with the Adjusted Activity Score, in points, of the Brazilian version of the HAP, which is a validated questionnaire (TEIXEIRA-SALMELA *et al.*, 2007). The HAP is a questionnaire, administered in the form of an interview, with 94 activities, each of these hierarchically graded according to the required metabolic equivalent (SOUZA *et al.*, 2006; Teixeira-Salmela *et al.*, 2007). Activities include personal care, transportation, home maintenance, social and leisure activities and exercise. For each item, there are three possible answers: "still doing this activity", "have stopped doing" and "never did" (SOUZA *et al.*, 2006; TEIXEIRA-SALMELA *et al.*, 2007). The Maximum Activity Score indicates the activity with the highest energy expenditure that the individual is still doing (SOUZA *et al.*, 2006; TEIXEIRA-SALMELA *et al.*, 2007). The Adjusted Activity

Score is obtained by subtracting from the Maximum Activity Score the number of activities that the individual stopped doing and indicates the average typical equivalent metabolic level. Based on Adjusted Activity Score the individual can be classified as inactive (< 53 points), moderately active (> 53 and < 74 points) or active (> 74 points) (TEIXEIRA-SALMELA *et al.*, 2007).

Figure 5-6. SenseWear Armband. A) Front view of the equipment; B) SenseWear Armband wore on the back of the arm; C) Back view of the equipment.

5.2.5.2 Secondary outcome measures

Cardiorespiratory fitness (VO$_{2peak}$ and ventilatory threshold) were measured using cardiopulmonary exercise test with gas analyses (CPX Ultima Medical Graphics®, USA) and electrocardiographic records, as described above (Figure 5-3). The test was held on a treadmill, with a progressive ramp protocol and followed the recommendations of the ACSM (PEREIRA *et al.*, 2012; PESCATELLO *et al.*, 2014). The cardiopulmonary exercise test is widely used and considered the gold standard for the evaluation of the peak cardiorespiratory fitness (NEDER, 2002; MENEGHELO, 2010). The cardiopulmonary exercise test is feasible and safe to be performed in individuals after stroke (MARZOLINI *et al.*, 2012; BILLINGER *et al.*, 2014).

Depression was assessed by the Patient Health Questionnaire (PHQ-2 and PHQ-9) (PRISNIE *et al.*, 2016). The PHQ-9 is used to assess the frequency of nine depressive symptoms (depressed mood, anhedonia, trouble sleeping, lack of energy, change of appetite, feeling of guilt or useless, trouble concentrating, feeling slow or agitated and having recurrent thoughts about death) over the last two weeks (DE MAN-VAN GINKEL *et al.*, 2012; PRISNIE *et al.*, 2016). The PHQ-2 includes only two of the nine questions, the ones about depressed mood and anhedonia (DE MAN-VAN GINKEL *et al.*, 2012; PRISNIE *et al.*, 2016). As recommended, the PHQ-9 was applied, by interview, only for the participants who had a positive score on the PHQ-2 (DE MAN-VAN GINKEL *et al.*, 2012; PRISNIE *et al.*, 2016). This instrument is easy to use, quick and had shown adequate measurement properties for evaluating depression in individuals after stroke (DE MAN-VAN GINKEL *et al.*, 2012; SANTOS *et al.*, 2013; PRISNIE *et al.*, 2016).

Endurance was measured by the distance covered, in meters, during the 6MWT and the Shuttle-Walk Test (SWT) (TYSON;CONNELL, 2009; VAN BLOEMENDAAL *et al.*, 2012). For the 6MWT, participants were instructed to walk along a 30-m hallway and cover the maximum possible distance over six minutes (TYSON;CONNELL, 2009; HAMIDZADEH, M.; ZELTZER, 2011). For the SWT, participants were instructed to walk along a 10-m corridor in a speed dictated by an audible signal (Figure 5-7) (VAN BLOEMENDAAL *et al.*, 2012). The SWT is an incremental test, consisting of 12 levels of one minute each, which is held in a corridor of 10 meters (VAN BLOEMENDAAL *et al.*, 2012; PARREIRA *et al.*, 2014). The initial speed is 0.5 m/s, after each level there is a 0.17 m/s increase (VAN BLOEMENDAAL *et al.*, 2012; PARREIRA *et al.*, 2014). The test is stopped when the individual is unable to maintain the required speed (VAN BLOEMENDAAL *et al.*, 2012; PARREIRA *et al.*, 2014). Both tests have adequate measurement properties to measure endurance (TYSON;CONNELL, 2009; VAN BLOEMENDAAL *et al.*, 2012; PARREIRA *et al.*, 2014).

Figure 5-7. Shuttle-Walk Test

Mobility was evaluated by both comfortable and maximum gait speeds during the 10MWT (TYSON; CONNELL, 2009). Gait speed was evaluated while the participants walked, using their assistive devices, usual shoes and orthotics, at their comfortable and maximum speed at a distance of 14 meters (SALBACH *et al.*, 2001). The time spent to complete the central 10 meters was recorded and the speed (m/s) calculated (SALBACH *et al.*, 2001). The instructions were standardized and only one trial was employed (FARIA *et al.*, 2012; NASCIMENTO, 2012). This test has adequate measurement properties and good clinical applicability for evaluation of mobility in individuals after stroke (SALBACH *et al.*, 2001; VOS-VROMANS *et al.*, 2009; FARIA*, et al.*, 2012).

Participation was measured by the participation section of the Stroke Impact Scale 3.0. (SIS) (TSE *et al.*, 2013). The participation section items are evaluated in terms of frequency of self-reported participation restriction over the previous month. The score ranges from 0 to 100 points, with higher scores representing better participation. This instrument has been translated and adapted for Portuguese-Brazil and has adequate measurement properties to

be used in individuals after stroke as well as good clinical applicability (CAROD-ARTAL *et al.*, 2008; TSE *et al.*, 2013).

Quality of life was measured using the Stroke-Specific Quality of Life Scale (SS-QOL), which contains 49 items distributed into 12 domains (energy, family roles, language, mobility, mood, personality, self-care, social roles, thinking, upper extremity function, vision and work/productivity) (FARIA*, et al.*, 2012). The SS-QOL is a simple tool applied in the form of an interview, which can be administered in a short time and which have adequate measurement properties and clinical applicability for evaluating the quality of life of individuals after stroke (LIMA *et al.*, 2008).

5.2.6 Sample size

The sample size was calculated based on the study of Teixeira-Salmela *et al.* (1999). In this study, individuals with chronic stroke were divided in two groups. The experimental group performed aerobic plus lower-limb strengthening training and home exercises, while the control group performed no intervention. The experimental group (*n*=6) showed an average increase in the Adjusted Activity Score of the HAP of 20 ± 6.1 points, whereas the control group (*n*=7) had an average reduction of 1.86 ± 0.19 points (TEIXEIRA-SALMELA *et al.*, 1999). Considering a significance level of 5% and a desired power of 80%, and expected dropout rate of 20%, the number of participants required was eleven participants per group (in total, n = 22).

5.2.7 Statistical analyses

Descriptive statistics were performed and tests for normality (Shapiro-Wilk test) were employed for continuous variables. Independent *t* tests, Mann-Whitney or Fisher's Exact Test were used to compare baseline participant characteristics between groups. Between-group differences over time were evaluated using two-way repeated measures ANOVA and reported as mean differences (95% CI). Data from the last available assessment was considered as the values of sessions lost by dropouts. Statistical analyses were conducted on an intention-to-treat basis. All analyses were performed with the SPSS software (SPSS Inc., Chicago, IL, USA, 25.0 version).

5.3 Paper #3

Title: Effects of aerobic training on physical activity in people with stroke: protocol for a randomized controlled trial

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5.3.1 Abstract

Introduction: Post-stroke physical inactivity is explained by several factors related to the stroke and have been pointed-out as causes and consequences of functional declines and health problems. Therefore, it is important to increase physical activity levels and reduce the time spent in low-energy expenditure activities after stroke. Since the maintenance of cardiorespiratory fitness is a significant predictor of physical activity levels post-stroke, it would be important to investigate whether aerobic training is effective in increasing physical activity levels and reducing the time spent in low-energy expenditure activities in this population. However, this is not well known. The primary objective of this trial will be to investigate the effects of aerobic treadmill training on physical activity levels and on time spent in low-energy expenditure activities in people with stroke. The secondary aim will be to evaluate the effects of the training on cardiorespiratory fitness, endurance, depression, mobility, quality of life, and participation.

Methods: A randomized controlled trial, with blinded assessments, will be performed in a community-based setting. Twenty-two adults with a diagnosis of stroke (>6months), who are sedentary or insufficiently active, will be included. Participants will be randomly assigned to

either: 1) aerobic treadmill training (experimental group, at 60-80% of their heart rate reserve) or 2) overground walking training (control group, below 40% of heart rate reserve). Both groups will receive 40-minute training sessions, three times/week over 12 weeks, in groups of 2 to 4 participants, by a trained physiotherapist. Primary outcomes are physical activity levels and time spent in low-energy expenditure activities (Multisensor SenseWear Armband and Human Activity Profile). Secondary outcomes are cardiorespiratory fitness (peak oxygen uptake (VO_{2peak}) and ventilatory threshold), endurance, depression, mobility, quality of life, and participation. The effects of the training will be analyzed from the collected data and intention-to-treat analysis. Between-group differences will be measured by two-way repeated measures ANOVA, considering the baseline, post-training, and 4-week follow-up.

Discussion: The results of this trial will likely provide valuable new information regarding the effects of aerobic treadmill training on physical activity levels and on time spent in low-energy expenditure activities of individuals with stroke, through changes in cardiorespiratory fitness.

Clinical trial registration number: ClinicalTrials.gov: identifier NCT02798237.

Keywords: stroke; aerobic exercise; physical activity; sedentary lifestyle; walking; health.

5.3.1 Introduction

Stroke has a high prevalence worldwide[1] and people with stroke are more likely to require help with mobility, self-care, and household activities.[2] Furthermore, they are 40% more likely to have limitations in performing activities when compared to matched controls.[2] Furthermore, people with stroke are at high risk of being affected by other cardiovascular diseases or recurrent stroke, which are often associated with the severity of the stroke.[1] Thus, it is important to develop and implement interventions for the prevention and management of the associated post-stroke disabilities, the complications and risk factors associated with recurrent stroke, and for the promotion of functionality.[3]

Physical activity has the potential to influence several functional domains and health status in individuals with stroke.[3] Physical activity is defined as any bodily movements produced by the skeletal muscles, that result in energy expenditure, such as those performed during activities of daily living at home, at work, during leisure, or transport.[4] Exercise is a type of physical activity, that has specific characteristics: it is repeatedly performed, in a planned and structured way, to improve or maintain physical fitness.[4] Sedentary behavior, which is part of the physical activity continuum, but have an independent impact on health, was recently defined as any behavior performed while awake that involves energy expenditure ≤ 1.5 metabolic equivalents (METs) while in a sitting, reclining, or lying posture[5].

People after stroke have low physical activity levels and spend more time in low-energy expenditure activities, when compared with matched individuals without stroke.[6] After a stroke, individuals spend on average 80% of their time in low-energy expenditure activities [7]. Only 15% engage in light and 5% in moderate-to-vigorous intensity physical activity.[7] Post-stroke physical inactivity is explained by several factors, which are directly and indirectly related to the stroke and have been pointed-out as causes and consequences of functional declines and health problems.[1, 3, 6, 7] After a stroke, low physical activity levels are the main consequences of the concomitant presence of cardiovascular diseases and disabilities, such as reduced cardiorespiratory fitness (median of 14 mL.kg^{-1}.min^{-1}, ranging from 8 to 23 mL.kg^{-1}.min^{-1}),[8-10] depression,[3] mobility limitations,[11] as well as low perception of quality of life[12] and restricted social participation.[2] Besides contributing to physically inactive and sedentary lifestyles, these disabilities can also be aggravated by physically inactivity,[3] creating a vicious

cycle, that dramatically impeded post-stroke individuals to adopt healthy life styles. There is evidence that both physical inactivity and time spent in low-energy expenditure activities are risk factors for developing diabetes mellitus and cardiovascular diseases (including stroke), and for overall mortality.[13, 14] For every increase of 25-30 minutes of sedentary time per day, there is a 1% increase in risk of cardiovascular disease for elderly individuals.[13] Therefore, it is important to increase physical activity levels and reduce the time spent in low-energy expenditure activities after stroke.

The investigation of the influence of exercise on physical activity levels and the importance of reducing the time spent in low-energy expenditure activities in people with stroke are pointed-out in the scientific statement from the American Stroke Association, as future research directions.[3] Any exercise would probably increase physical activity level and reduce sedentary duration on the same day that it is performed. However, it is not known which intervention could effectively improve physical activity. In addition, it is also unknown whether these changes occur in individuals with different baseline levels of physical activity and time involved in low-energy expenditure activities, nor if they are maintained after the cessation of the intervention.Since the efficacy of aerobic training in improving cardiorespiratory fitness in people with stroke has been shown[8-10] and that cardiorespiratory fitness is a significant predictor of physical activity after stroke,[15] it would be important to investigate whether aerobic training is effective in increasing physical activity levels and reducing the time spent in low-energy expenditure activities in this population. However, the efficacy of aerobic training on these variables is not well known.[3, 9]

Only four randomized controlled trials investigated the effects of aerobic training on physical activity levels in people with stroke.[16-20] In three trials, no between-group differences were found.[17 18,20] In the other trial, physical activity levels of the experimental group (aerobic training plus lower-limb resistance training and home exercises) improved, when compared to the control group (no intervention).[19] Therefore, it is not known whether aerobic training alone is an effective intervention. In addition, in all four trials,[17-20] physical activity was not the primary outcome and, in three of these trials, physical activity was assessed using self-reported questionnaires.[17-19] Secondary outcomes are not confirmatory, but exploratory, thus, it is not possible to give much credence to it.[21] Although questionnaires are inexpensive and easy to use,[22] their accuracy is questionable, since it can be influenced by recall bias, social

desirability bias, and inability of the participants to estimate the frequency, duration, and intensity of their physical activity.[3, 22] One of the four trials assessed the effects of aerobic training on physical activity levels of people with stroke by the number of steps taken over 48 hours measured by an accelerometer.[20] However, there is some question whether number of steps alone would be an adequate measure of physical activity levels, since it does not provide any information regarding important parameters of physical activity, such as intensity or duration.[15, 23] Furthermore, number of steps does not provide information on upper limb or cycling activities.[4] Although according to a systematic review, there is no gold-standard portable monitor for the assessment of physical activity, the use of a multisensor device, such as the one that will be used in the present study, has the potential to improve accuracy, since the data is estimated from multiple sensors.[22] In addition, a multisensor device is able to provide information on frequency, duration, and intensity of physical activities, including low-intensity and non-ambulatory activities.[22, 23-26] To our knowledge, only one randomized controlled trial investigated the efficacy of an intervention, which was not aerobic training in decreasing the time spent in low energy expenditure activities in individuals with stroke.[24] The experimental group received four counselling sessions with a message of sit less and move more, whereas the control group received the same number of counseling sessions regarding calcium intake for bone health.[24] However, no statistically significant between-group differences were found.[24] Therefore, the measurement of physical activity levels and the time spent in low-energy expenditure activities, as primary outcomes using adequate measures, as planned to be carried-out in the present study, is recognizably important in future trials with people with stroke.[3]

Thus, the primary aim of this trial is to investigate the efficacy of aerobic treadmill training in improving physical activity levels and reducing the time spent in low-energy expenditure activities of people with stroke. The secondary aim is to evaluate the effects of the training on cardiorespiratory fitness, endurance, depression, mobility, quality of life, and participation.

5.3.2 Methods

A superiority parallel-group randomized controlled trial, with concealed allocation and blinded assessments, will be carried-out. A trained researcher, blinded to the group allocation,

will collect the written-consent and the outcome measures at baseline, post-intervention (after the 12-week intervention), and at 16-week follow-up, i.e., 4-weeks after the cessation of the intervention (Figure 5-8). Examiner will be blinded to group allocation, by asking the participants and the treating physiotherapist to not share any information about the intervention with the examiner. Moreover, evaluations will be carried-out in different places. Participants will be randomly assigned to either 1) aerobic treadmill training (experimental group) or 2) overground walking training (control group) (Figure 5-9).

This randomized controlled trial was prospectively registered at www.clinicaltrials.gov (NCT02798237) and received approval (#51454115.6.0000.5149) from the institutional ethical review board. The study commencement date was August/2017 and the estimated completion date is December/2018.

5.3.2.1 Setting

This study will be carried-out in a community-based setting of the city of Belo Horizonte, Brazil.

5.3.2.2 Participants

Individuals will be recruited from the general community, by contacting health centers and research groups. They will be included if they are ≥20 years of age; have diagnosis of stroke(>6months); are inactive or insufficiently active[27]; and have a written medical permission for participation in the study. The classification of the Centers for Disease Control and Prevention will be used to determine if the individual is classified as inactive or insufficiently active.[27] Participants will be asked to inform the exercises they performed most often over the last 4 weeks, including their frequency and duration.[28] Individuals who report not having practiced any exercise over the last month, will be classified as inactive.[27] Those, who report that have performed physical exercise over the last month, ≥ five times per week, for more than 30 minutes, in a moderate intensity, or ≥ three times per week, for at least 20 minutes, in a vigorous intensity, will be classified as moderate or vigorous exercise levels, respectively.[27] The intensity of the exercises reported by the participants will be determined based upon the estimated metabolic expenditure (MET).[27] Exercises performed at vigorous intensity are those with an assigned MET that is greater than 60% of the maximum

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cardiorespiratory capacity of the individual.[27] Sixty percent of the maximum cardiorespiratory capacity is determined by equations for men ([0.6 x (60 - 0.55 x age)]/3.5) and for women ([0.6 x (48 - 0.37 x age)]/3.5).[27] Individuals classified as moderate or vigorous exercise levels will be excluded from the study. Individuals who report performance of some physical exercise over the last month, which is not classified as vigorous or moderate intensity, are classified as insufficient active.[27] Exclusion criteria are cognitive impairments, as determined by the education-adjusted cut-off scores on the Mini-Mental Status Examination depending on education level of each participant (illiterate: 13 points; elementary and middle school: 18 points; and high-school: 26 points),[28] and/or inability to respond to simple verbal commands[29]; inability to walk independently for at least 10 minutes, with or without walking devices; and had pain or other disorders precluding their participation.

5.3.2.3 Participant withdrawal

Participants may withdraw from the trial for any reason at any time. The investigator also may withdraw participants from the study for safety purposes. Interruption to a maximum of 6 consecutive sessions will be allowed.

5.3.2.4 Randomization procedures

Randomization sequence will be computer generated, prior to the commencement of the study by a trained research assistant, who will be not involved in the study, and maintained in randomized blocks in sequentially numbered sealed opaque envelopes. Eligible participants will be randomly allocated to either the experimental or control groups, after the baseline measures. The training therapist will be responsible for revealing the contents of the sealed opaque envelopes, and therefore, for revealing the allocation.

5.3.2.5 Intervention and control

All participants will receive three 40-minute sessions per week over 12 weeks,[3, 9, 30] in groups of 2 to 4. A trained physiotherapist, who has experience with aerobic training, will supervise both groups. The exercise intensity will be determined, based upon the results of the cardiopulmonary exercise test.[3, 9]

Before and after training, the participants will remain at rest for 10-15 minutes, when their heart rate (heart rate monitor), blood pressure (aneroid sphygmomanometer and stethoscope), and peripheral oxygen saturation (oximeter) will be registered. Heart rate will be continuously monitored. Participants will be asked to report any discomfort and not to volunteer to any other exercise program, during their participation in the present study.

5.3.2.6 Experimental group

The participants of the experimental group will perform five minutes of warm-up and cool-down treadmill walking, followed by 30 minutes of aerobic treadmill training at 60-80% of their heart rate reserve.[3, 9] However, for those with poor exercise tolerance, short exercise bouts (minimum of 10 minutes, until completing 30 minutes) may be initially given, with interspersed rest periods.[3, 9] As exercise tolerance improves, longer periods of continuous exercise with shorter rest periods will be implemented.[3, 9] The progression of the treadmill training intensity will be individualized, depending upon the individual's ability, rate of perceived exertion, heart rate, and blood pressure responses.[9] When participants of the experimental group perform treadmill training below their cardiac training range, they will be requested to increase speed, until their cardiac training zone is achieved.

5.3.2.7 Control group

The participants of the control group will perform comfortable overground walking training, at <40% of their heart rate reserve. When participants of the control group perform exercise above 40% of their heart rate reserve, they will be requested to decrease speed, until their training zone reaches ≤ 40%. If the efficacy of the intervention is proved, it will be offered to the participants of the control group at the end of the study.

5.3.2.8 Procedures

A trained researcher, who will be blinded to the group allocation, will collect the sociodemographic data and all outcomes.

5.3.2.9 Primary outcome measures

The primary outcomes will include both physical activity level and time spent in low-energy expenditure activities, as they are part of the physical activity continuum. Both will be

measured by an objective device, the multisensor SenseWear Armband. In addition, physical activity level will be also assessed by a subjective method, the Human Activity Profile (HAP), since objective and subjective methods are complementary and the questionnaire has the advantage of higher clinical applicability.[23, 29]

The multisensor SenseWear Armband (BodyMedia, Pittsburgh, PA, USA; software version 8.1) activity monitor provides objective measures of physical activity levels and time spent in low-energy expenditure activities [23] and it is portable, non-invasive, and lightweight.[23] The data acquired by multiple sensors (heat flux, skin temperature, galvanic skin response, triaxial accelerometer) are integrated with clinical characteristics (age, height, body mass, sex, and smoking habits) into an algorithm, to provide the estimation of physical activity levels and time spent in low-energy expenditure activities.[23] This monitor is capable of measuring the intensity, frequency, and duration of physical activity and is able to detect improvements in physical activity levels in longitudinal studies with people with stroke.[23] Average daily energy expenditure, expressed in kilocalories, will be used to estimate physical activity levels. Average daily sedentary duration, expressed as percentage of total waking time, will be used to estimate the time spent in low-energy expenditure activities (≤ 1.5 METs). The validity of this multisensor monitor has already been established for the measurement of physical activity, compared against indirect calorimetry and double-labeled water.[26, 31, 32] The participants will use this device, attached to the back of their non-paretic arm,[23] for seven days during each assessment time (that is, three times: at baseline, post-intervention (after the 12-week intervention), and at 16-week follow-up), to reduce the possibility of bias related to differences in physical activity levels and time spent in low-energy expenditure activities between the days.[22]

The HAP, which provides subjective measures of physical activity levels,[29] will be administered by interviews.[29] It consists of 94 activities, which are hierarchically graded, according to their required metabolic equivalent.[29] These activities include personal care, transportation, home maintenance, social and leisure activities, and exercise.[29] The HAP Adjusted Activity Score is calculated by subtracting the number of activities that the participant discontinued performing from the number of the last item that they still perform.[29] The Adjusted Activity Score provides better estimative of average energy expenditure spent by an individual.[29] The HAP is commonly used in studies with people with stroke and showed

adequate measurement properties for the assessment of physical activity levels in this population.[29]

5.3.2.10 Secondary outcome measures

Secondary outcomes will be cardiorespiratory fitness (cardiopulmonary exercise test); endurance (Six-Minute Walk Test (6MWT) and Shuttle-Walk Test (SWT); depression (Patient Health Questionnaire (PHQ-2 and PHQ-9); mobility (comfortable and maximum gait speeds); quality of life (Stroke-Specific Quality of Life scale (SS-QOL); and participation (Stroke Impact Scale (SIS). All measures have adequate measurement properties for the evaluation of post-stroke individuals.[33-40]

Cardiorespiratory fitness (peak oxygen uptake (VO_{2peak}) and ventilatory threshold) will be measured using cardiopulmonary exercise test with gas analyses (CPX Ultima Medical Graphics®, USA) and electrocardiographic records. This is an objective, non-invasive, widely used test, and is considered to be the gold standard for the evaluation of cardiorespiratory fitness.[35] The cardiopulmonary exercise test is feasible and safe test to be performed with people with stroke.[3, 41] The test will be held on an electronic treadmill, with a progressive ramp protocol[42] and will follow the recommendations of the American College of Sports Medicine.[35] All tests will be followed by a cardiologist, who has advanced life support training.

Endurance will be measured using the 6MWT and the SWT.[38,39] Although the cardiopulmonary exercise test is the gold standard test for measuring aerobic capacity, its use in clinical practice is limited, due to the need of specialized equipment and trained personnel.[35, 38] Clinical alternatives are sub-maximal exercise tests, such as the 6MWT and the SWT. These tests are simple, inexpensive, and do not require advanced training.[38,39] For the 6MWT, the maximum covered distance will be measured.[39] The SWT is an incremental test, that consists of 12 levels, speed dictated by an audible signal, which is held on a 10-meter corridor.[39]

Depression will be assessed by the PHQ-9 and PHQ-2.[36] The PHQ-9 is used to assess the frequency of nine depressive symptoms over the previous two weeks.[36, 43] The PHQ-2 includes only two of the nine questions.[36, 43] As recommended, the PHQ-9 will be applied, by interview, only for the participants, who have a positive outcome on the PHQ-2.[36, 43]

Mobility will be evaluated by both comfortable and maximum gait speeds during the Ten Meter Walk Test (10MWT).[38] The instructions will be standardized and only one trial will be employed.[44, 45]

Quality of life will be measured using the SS-QOL,[34] which contains 49 items distributed into 12 domains (energy, family roles, language, mobility, mood, personality, self-care, social roles, thinking, upper extremity function, vision, and work/productivity).[34] The SS-QOL is applied by interviews, which can be administered in a short period of time.[34]

Participation will be measured by the social participation section of the SIS 3.0.[37] The participation section items are evaluated in terms of frequency of self-reported participation restriction over the previous month.[37]

5.3.2.11 Data monitoring committee

No data monitoring committee will take part in this study, since aerobic training rarely has adverse effects.[9] However, participants will be monitored during the exercise sessions, to identify any kind of signals or symptoms, such as pain, dizziness, and loss of balance, which would require interruption of the exercise session or their exclusion from the study. In addition, participants will be asked to report any discomfort, and this information will be registered and reported.

5.3.2.12 Sample size calculation

The sample size was based upon the only previous found randomized controlled trial, that measured changes in physical activity levels of people with stroke associated with aerobic exercise training.[16] For this, the effect size has been derived from the study of Teixeira-Salmela et al. 1999,[19] who assessed changes in physical activity levels with the HAP Adjusted Activity Scores, associated with aerobic plus lower-limb strengthening training, and home exercises with people with chronic stroke. The experimental group (n=6) showed an average increase in the Adjusted Activity Score of 20±6.1 after the intervention, whereas the control group (n=7) had an average reduction of 1.86±0.19 points. To be able to detect a between-group difference of 20 points on the HAP Adjusted Activity Score, considering a significance level of 5% and a desired power of 80%, nine participants per group would be required (a total

of 18 participants).[46] Assuming an expected dropout rate of 20%, a target of 22 participants was set (11 participants per group).

5.3.2.13 Statistical analyses

A code will be given to all participants. Two independent examiners, who will be blinded to the group allocation, will perform data entry and verify any missing or apparently wrong values. Original paper forms will be kept in a secure place. Electronic files will be available only to the research team.

An independent examiner, who will be blinded to group allocation, will perform the statistical analysis, using the SPSS software (SPSS Inc., Chicago, IL, USA). Descriptive statistics will be carried-out for all outcomes.

The effects of the interventions will be analyzed from the collected data and intention-to-treat analysis. Data from the last available assessment will be considered as the values of missed sessions. Between-group differences will be evaluated using two-way repeated measures ANOVA, considering the baseline, post-training, and follow-up measures. If baseline differences between the groups exist, analysis of covariance will be used to eliminate the influence of extraneous factors, such as baseline cardiorespiratory fitness, physical activity levels, and time spent in low-energy expenditure activities. The level of significance will be set at 5% and adjusted for multiple comparisons. Data distribution and equality of variance will also be analyzed, to ensure correct use of parametric analysis.

5.3.3 Discussion

Although the efficacy of aerobic training in improving VO_{2peak} in individuals with stroke is well known, it is unknown if this training improves physical activity levels and reduces the time spent in low-energy expenditure activities. In fact, it is still unclear which intervention may improve physical activity levels and reduce post-stroke time spent in low-energy expenditure activities. Therefore, the results of this randomized controlled trial will likely provide valuable new information regarding the effects of aerobic treadmill training on physical activity levels and time spent in low-energy expenditure activities for individuals with stroke. Since low physical activity levels are associated with risk of cardiovascular disease, the investigated intervention has also the potential to improve functionality and health

status and reduce the burden of care on the families of people with stroke. The question of whether exercise improves function and quality of life and prevents secondary diseases, such as stroke, is a top priority research objective that might be answered by this study.[47]

Considering that previous randomized controlled trials have rarely investigated the effects of aerobic training on physical activity levels and that none has investigated these effects on the time spent in low-energy expenditure activities or used a multisensor monitor to measure these outcomes, this study will contribute to increased evidence-based practice in that domain, and, hence, may improve care of people with stroke.

This trial design does have some limitations. It will include a convenience sample, which may limit generalizability. Furthermore, both participants and the physiotherapist, who will provide the interventions, will not be blinded.

5.3.4 Conflict of interest

The authors report no conflicts of interest.

5.3.5 Funding

5.3.6 References

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	STUDY PERIOD				
	Enrolment	Allocation	Post-allocation		Close-out
TIMEPOINT	*-t₁*	**0**	*t₁*	*t₁₂ (12-weeks post-intervention)*	*t₁₆ (follow-up 4 weeks after the cessation of the intervention)*
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
[Experimental group]			●————————●		
[Control group]			●————————●		
ASSESSMENTS:					
[Sociodemographic data]	X				
[Primary and secondary outcome variables]	X			X	X

Figure 5-8. Schedule of enrolment, interventions, and assessments.
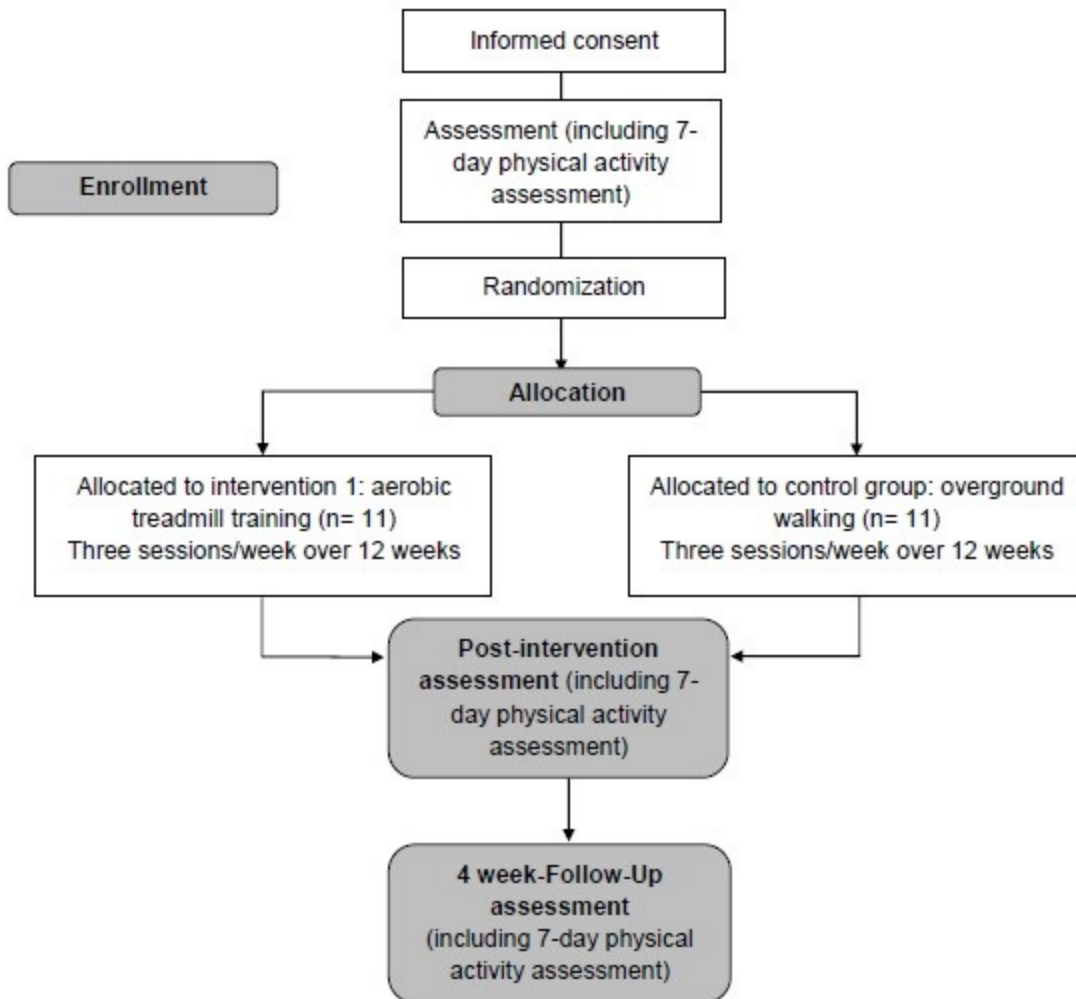
Figure 5-9. Flow diagram through the study

Chapter 6. Paper #4: Effects of vigorous intensity aerobic training on physical activity and time spent in low-energy expenditure activities in people with stroke: a randomized controlled trial

6.1 Preamble

According to the results of the systematic review presented in chapter 3 (Paper #2), aerobic training might be an effective intervention to improve physical activity levels of individuals after stroke. However, more studies are necessary since the studies included at the systematic review had limitations, and the overall quality of the evidence, according to the GRADE scale was found to be very low. Therefore, after registering the randomized controlled trial and publishing the protocol (Paper #3), the primary aim of Paper #4 was to investigate whether aerobic training is effective in improving physical activity levels and time spent in low-energy expenditure activities of individuals after stroke. The secondary objective was to evaluate the effects of the training on cardiorespiratory fitness, endurance, depression, mobility, quality of life, and participation in this population. This randomized controlled trial is the main paper of this thesis and will be submitted for publication after thesis defense in Neurorehabilitation and Neural Repair Journal.

6.2 Paper #4

Title: Effects of vigorous intensity aerobic training on physical activity and time spent in low-energy expenditure activities in people with stroke: a randomized controlled trial

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6.2.1 Abstract

Introduction: Individuals after stroke have low physical activity levels and high amount of time spent in low-energy expenditure activities.

Objective: To investigate whether aerobic training improves physical activity levels and reduces time spent in low-energy expenditure activities, and improves cardiorespiratory fitness, depression, endurance, mobility, participation, and quality of life in people after stroke.

Methods: A randomized controlled trial with blinded assessors was performed. Twenty-two adults with stroke (>6 months) participated. The experimental group received 40-minute aerobic treadmill training at 60-80% of their heart rate reserve three days/week over 12-weeks. The control group performed overground walking below 40% of heart rate reserve with similar frequency/duration. Primary outcomes: physical activity and time spent in low-energy expenditure activities. Secondary outcomes: cardiorespiratory fitness, depression, endurance, mobility, participation, and quality of life. Outcomes were measured at baseline, after intervention, and four weeks beyond intervention. Between-group differences were evaluated

using two-way repeated measures ANOVA. Trial registration: www.ClinicalTrials.gov (NCT02798237).

Results: Compared to the controls, the experimental group improved quality of life (13 points; 95%CI 3.5-23). Both groups improved depression (2.2 points; 95%CI 0.01-4.3), endurance (31-55 m; 95%CI 3.8-107), and mobility (0.12 m/s; 95%CI 0.02-0.2). There were no other significant changes.

Conclusion: Treadmill walking exercise performed at a vigorous intensity improved quality of life and as well as overground walking at a very light to light intensity improved depression, endurance and mobility after stroke. Further studies are needed to clarify the benefits of aerobic training on physical activity and time spent in low-energy expenditure activities.

Key words: Stroke; aerobic exercise; physical activity; sedentary lifestyle; walking.

6.2.2 Introduction

Physical inactivity has a high prevalence worldwide, and it is estimated to be responsible for more deaths than smoking[1]. Physical activity is defined as any bodily movements produced by skeletal muscles, that result in energy expenditure, such as those performed during activities of daily living at home, at work, during leisure, or transport[2]. Sedentary behavior, which is part of the physical activity continuum but has an independent impact on health, is defined as any physical activity performed while awake, that involves energy expenditure $\leq$ 1.5 metabolic equivalents (that is, low-energy expenditure activities), while in a sitting, reclining or lying posture[3]. Therefore, sedentary behavior includes two components (intensity and posture).

Physical inactivity is associated not only with mortality but also with higher risk of cardiovascular diseases, including stroke and heart attacks[1]. Thus, there is important economic consequences of physical inactivity, with an estimated global cost of $54 billion in 2013[1]. Studies have revealed that increases on physical activity levels are associated with reduced incidence of stroke and risk of cardiovascular diseases[1,4]. Therefore, being physically active is an important aspect of overall health, and it is one of the American Heart Association's seven components of ideal cardiovascular health for adults[1].

Individuals after stroke have low physical activity levels and high amount of time spent in low-energy expenditure activities[5]. Those living in the community have higher levels of physical inactivity when compared with older adults with diabetes, musculoskeletal, cardiovascular, respiratory, or other neurological chronic diseases[5,6]. Physical inactivity after stroke can be related to several factors, such as reduced cardiorespiratory fitness[7], depression[8], mobility limitations[9], as well as reduced social participation[10] and low quality of life[11]. These factors are directly and indirectly related to the stroke and can be pointed-out as causes and consequences of low physical activity levels[1,5,8,12]. This create a vicious cycle that dramatically impeded individuals after stroke to adopt a healthy life-style.

Therefore, with the increasing awareness of the relevance of physical activity after stroke, it is important to investigate the effect of exercise interventions on increasing physical activity levels and reducing time spent in low-energy expenditure activities after stroke[5,8,12]. A recent systematic review of randomized controlled trials examined the effects of any intervention on physical activity levels after stroke[13]. Aerobic training was a type of intervention employed at

least as a part of the treatment in five studies included in the review[13]. However, these studies had several limitations including low methodological quality according to the PEDro Rating Scale[14-16], instruments to measure physical activity levels which were not validated for the stroke population (two trials[14,15]) and one used an inadequate heart rate as reference (same absolute value for all participants)[17]. In addition, in some of the studies the control group performed no intervention or received an intervention with lower frequency or duration when compared to the experimental group[16-18], which is an important bias related to the amount of attention. Furthermore, in some of the studies the experimental group received other training besides aerobic exercise (i.e., lower-limb resistance training)[16-18]. Thus, it is unknown whether aerobic training alone was an effective intervention.

The present study, in contrast, was planned to have a good methodological quality according to the PEDro Rating Scale and used instruments to measure physical activity levels with adequate measurement properties for the assessment of the stroke population[19-22]. Furthermore, the prescription of training intensity was planned to be individually tailored and based on the heart rate reserve considering peak heart rate achieved during maximal cardiopulmonary exercise test that was performed according to the recommendations of the American College of Sports Medicine[23]. In addition, the control group performed an intervention with similar frequency and duration when compared to the experimental group and the experimental group received only aerobic exercise training.

Therefore, a randomized controlled trial was conducted with a first objective to investigate whether aerobic training of vigorous intensity was effective in improving physical activity levels and time spent in low-energy expenditure activities of individuals after stroke immediately after the training and four weeks beyond intervention. The secondary objective was to evaluate the effects of the training on cardiorespiratory fitness, depression, endurance, mobility, participation and quality of life immediately after the training and four weeks beyond intervention.

6.2.3 Methods

6.2.3.1 Design

A randomized controlled trial with blinded assessments and concealed allocation was undertaken. A research assistant, not involved in this study, compiled a computer-generated random allocation sequence. The allocation sequence was placed in sequentially numbered, opaque, sealed envelopes, which were held offsite. After baseline assessment, the envelope was opened by the training therapist and group allocation was revealed. Participants were then randomly assigned to either 1) aerobic treadmill training (experimental group) or 2) overground walking (control group) (Figure 6-1). Outcomes were collected within a laboratory setting at baseline (week 0), after training (week 12), and after four-week follow-up (week 16), by trained and blinded assessors (Figure 6-1).

This study report followed the CONSORT statement guidelines[23]. This trial received approval (#51454115.6.0000.5149) from the institutional ethical review board and the protocol was published[24]. The trial was registered at the www.ClinicalTrials.gov (NCT02798237).

6.2.3.2 Participants

Individuals after stroke were recruited from the general community, by means of advertisements and by screening out-patient clinics. Participants were eligible if they were ≥ 20 years of age; had a diagnosis of stroke (> 6 months); were inactive or insufficiently active[25]; and had a writing medical permission for participation in the study.

The classification of the Centers for Disease Control and Prevention was used to determine if an individual was inactive or insufficiently active[25]. Individuals were questioned about the exercises they performed most frequently over the previous month[25]. Those who reported not having practiced any exercise over the last month were classified as inactive[25]. Those who performed exercise at least three times per week for 20 minutes or more at a vigorous intensity were classified as having vigorous exercise level[25]. Exercise intensity of the participants was determined based upon the estimated metabolic equivalent[25]. Exercises performed at vigorous intensity were those with an assigned metabolic equivalent that was at least 60% of the maximum cardiorespiratory capacity of the person[25]. The following equations were employed to establish 60% of the maximum cardiorespiratory capacity: $0.6 \times (48 - 0.37 \times age) / 3.5$ for

women and $0.6 \times (60 – 0.55 \times age) / 3.5$ for men[25]. Those who performed exercise at least five times per week for ≥ 30 minutes were classified as having moderate exercise level[25]. Individuals classified as having vigorous or moderate exercise levels were excluded from the trial. Individuals who reported doing exercise over the last four weeks that was not enough to be classified as vigorous or moderate intensity were classified as insufficiently active[25].

Participants were excluded if they had cognitive impairments, (education-adjusted cut-off scores for the Mini-Mental Status Examination were used[24]. Those having inability to walk independently, with or without assistive devices, for at least 10 minutes; and had pain or other disorders precluding their participation were also excluded.

6.2.3.3 Interventions

The dose of the interventions was three 40-minute sessions per week over 12 weeks[7,8,26]. Interventions were delivered in groups of two to four participants. The exercise intensity was determined based on the heart rate reserve (Karvonen method). The training heart rate zone was defined according to the following formula[22]: $\% (HR_{peak} - HR_{rest}) + HR_{rest}$. The HR_{rest} was the heart rate before the beginning of each training session, and HR_{peak} was the peak heart rate achieved during maximal cardiopulmonary exercise test[8,27]. The maximal cardiopulmonary exercise test with ventilatory expired gas analysis and a 12-lead electrocardiogram were performed on a treadmill, with a progressive ramp protocol[27], following the recommendations of the American College of Sports Medicine[22].

The experimental and control groups were supervised by two trained physiotherapists who had over five years of clinical and research experience in neurological rehabilitation. Physiotherapists kept a record to register compliance of training sessions. Vital signs (heart rate, blood pressure and peripheral oxygen saturation) were monitored before, during and after each intervention session.

6.2.3.3.1 Experimental group

Participants performed five minutes of warm-up, followed by 30 minutes of aerobic treadmill training at 60-80% of their heart rate reserve, and five minutes of cool-down[7,8]. Intensity progression was individually tailored, depending upon the individual's ability and heart

rate responses. When participants performed training below or above their training heart rate zone, they were requested to increase or decrease gait speed, respectively, until their training heart rate zone was achieved. Rest periods were allowed.

6.2.3.3.2 Control group

The participants of the control group performed comfortable overground walking below 40% of their heart rate reserve. When participants performed exercise above 40% of their heart rate reserve, they were requested to decrease their gait speed.

6.2.3.4 Outcome measures

6.2.3.4.1 Primary outcomes

The primary outcomes included both physical activity levels and time spent in low-energy expenditure activities, as they are part of the physical activity continuum. Physical activity levels and time spent in low-energy expenditure activities were measured with a multisensor activity monitor: SenseWear Armband (BodyMedia, Pittsburgh, PA, USA; software version 8.1). This instrument is portable, non-invasive, light-weighted, provide objective measures and has adequate measurement properties to measure physical activity levels[19,20]. In this equipment, data acquired by multiple sensors (heat flux, skin temperature, galvanic skin response, triaxial accelerometer) are integrated with clinical characteristics into an algorithm, to provide the estimation of physical activity levels and time spent in low-energy expenditure activities[25]. Average daily energy expenditure, in Kcal, was used to estimate physical activity. Average daily time spent in low-energy expenditure activities (≤1.5 metabolic equivalents) was reported in percentage of waking hours. Participants used this device, attached on the back of their non-paretic arm for seven days[19,28].

Physical activity levels were also subjectively measured, in points, with the Adjusted Activity Score of the Human Activity Profile (HAP)[21]. The HAP is a questionnaire with adequate measurement properties to measure physical activity levels in individuals after stroke, that was administered by interview[21].

Cardiorespiratory fitness (peak oxygen uptake (VO_{2peak}) and oxygen uptake at ventilatory threshold ($VO_{2ventilatory\ threshold}$)) were measured using cardiopulmonary exercise test, as described above, which is considered the gold standard for the evaluation of cardiorespiratory fitness (CPX Ultima Medical Graphics®, USA)[22]. $VO_{2ventilatory\ threshold}$ was determined using a combination of the V-slope and ventilatory equivalents methods[22]. The cardiopulmonary exercise test is safe to be performed in individuals after stroke[8,29].

Depression was assessed by the Patient Health Questionnaire (PHQ-2 and PHQ-9)[30]. The PHQ-9 is used to assess the frequency of nine depressive symptoms (depressed mood, anhedonia, trouble sleeping, lack of energy, change of appetite, feeling of guilt or useless, trouble concentrating, feeling slow or agitated and having recurrent thoughts about death) over the last two weeks[30,31]. The PHQ-2 includes only two of the nine questions, about depressed mood and anhedonia[30,31]. As recommended, the PHQ-9 was applied, by interview, only for the participants, who had a positive score on the PHQ-2[30,31]. This instrument had shown adequate measurement properties for evaluating depression in individuals after stroke[30,31].

Endurance was measured by the distance covered, in meters, during the Six-Minute Walk Test (6MWT) and the Shuttle-Walk Test (SWT)[32,33]. For the 6MWT, participants were instructed to walk along a 30-m hallway and cover the maximum possible distance over six minutes[32]. For the SWT, participants were instructed to walk along a 10-m corridor in a speed dictated by an audible signal[33]. Both tests have adequate measurement properties to measure endurance in individuals with stroke[32,33].

Mobility was evaluated by both comfortable and maximum gait speeds during the Ten Meter Walk Test (10MWT)[32]. The instructions were standardized and only one trial was performed[34,35]. This test has adequate measurement properties to evaluate mobility in individuals after stroke[34].

Participation was measured by the participation section of the Stroke Impact Scale 3.0. (SIS)[36] The items of the participation section evaluate it in terms of frequency of self-reported participation restriction over the previous month[36]. The SIS has adequate measurement properties to measure participation in individuals after stroke[37].

Quality of life was measured using the Stroke-Specific Quality of Life scale (SS-QOL)[38], which contains 49 items distributed into 12 domains (energy, family roles, language, mobility,

mood, personality, self-care, social roles, thinking, upper extremity function, vision, and work/productivity)[38]. The SS-QOL has adequate measurement properties to evaluate the quality of life of individuals after stroke and was administered by interview[38,39].

6.2.3.5 Sample size calculation

The number of participants was calculated based on the study of Teixeira-Salmela *et al.* 1999[16], in which the experimental group (*n*=6) showed an average increase in the Adjusted Activity Score of the HAP of 20 ± 6.1 points, whereas the control group (*n*=7) had an average reduction of 1.9 ± 0.19 points. Considering a significance level of 5%, a desired power of 80% and expected dropout rate of 20%, the minimum number of participants needed was 11 participants per group. Thus, a total target of at least 22 participants was set.

6.2.3.6 Statistical analyses

Descriptive statistics were performed and tests for normality (Shapiro-Wilk test) and homoscedasticity (Mauchly's sphericity test) were employed for continuous variables. Independent *t* tests, Mann-Whitney, or Fisher's Exact Test were used to compare baseline participant characteristics between groups. Analyses were conducted on an intention-to-treat basis by an independent researcher. Missing data were interpolated, by carrying forward the last known value. Between-group differences over time were evaluated using two-way repeated measures ANOVA and reported as mean differences (95% CI). Post hoc tests (Bonferroni) were also performed. All analyses were performed with the SPSS software (SPSS Inc., Chicago, IL, USA, 25.0 version).

6.2.4 Results

6.2.4.1 Flow of participants

Figure 6-1 provides a flow diagram of participant recruitment and retention. Recruitment of participants were undertaken between December 2017 and April 2018, and follow-ups were performed between June 2018 and October 2018. At the four-week follow-up, three participants in the control group and one in the experimental group had discontinued their participation and did not complete the follow-up assessments.

Baseline characteristics of participants for both groups are reported in Table 6-1. There were no significant between-group differences in any baseline measures ($p>0.12$) (Table 6-1 and Table 6-2). Participants wore the SenseWear Armband on average for six days and 11 hours.

6.2.4.2 Training data

The 10 participants from the experimental group who completed the intervention attended on average 91% (SD 11%) of the offered training sessions. The 8 participants from the control group who completed the intervention attended on average 87% (SD 9.2%) of the offered training sessions. The main reasons for skipping a training session were sickness (number of sessions missed = 16), medical appointments (number of sessions missed = 14) or transport problems (number of sessions missed = 12).

The intensity of the aerobic training performed by the experimental group considering all training sessions was on average 62% (SD 14%) of heart rate reserve. On average the intensity of the exercise on the first week of training was 55% (SD 14%) of heart rate reserve, and 64% (SD 11%) on the last week of training for the experimental group. The intensity of the overground walking performed by the control group considering all exercise sessions was on average 22% (SD 7.8%) of heart rate reserve. On average the intensity of the exercise on the first week was 22% (SD 7.2%) of heart rate reserve, and 20% (SD 4.7%) on the last week of exercise for the control group.

Four participants from the experimental group reported lower-limb pain in one session, and one reported it in nine sessions. One participant from the experimental group had some loss of balance without fall during aerobic training in fourteen sessions. One participant from the control group reported fatigue and some loss of balance without fall in one session. No study-related serious adverse events occurred.

6.2.4.3 Effect of aerobic training

The group means (SD), within-group differences (SD), and between-group differences (95% CI) for all outcomes over time are provided in Table 6-2. The intention-to-treat analysis showed no significant interaction or between-group effects for physical activity levels or time spent in low-energy expenditure activities ($10\% \leq \text{Power} \leq 40\%$). There was a significant interaction effect (time X group) for quality of life (SS-QOL) ($F=4.53$, $p=0.017$). The post-hoc

analysis showed a significant increase of 13 points (95% CI 3.5 to 23 points) on SS-QOL score from baseline to follow-up for the experimental group (p=0.006) while the control group lost 3 points (95% CI -13 to 6 points).

There was a statistically significant time effect, that is, within-group differences for the following outcomes over time: depression (PHQ) (F=4.82, p=0.013), endurance (distance, 6MWT (F=13.3, p<0.001); distance, SWT (F=6.18, p=0.005), and mobility (comfortable gait speed, 10MWT) (F=5.46, p=0.008). There was a significant mean difference of 2.2 points (95% CI 0.01 to 4.3 points) for all participants on the PHQ between baseline and follow-up assessment (p=0.049). There was a significant mean difference of 31 m (95% CI 5.6 to 57 m) for all participants on the 6MWT between baseline and post-intervention assessment (p=0.014), and of 46 m (95% CI 20 to 71 m) between baseline and follow-up (p<0.001). There was a significant mean difference of 55 m (95% CI 3.8 to 107 m) for all participants on the SWT between baseline and post-intervention assessment (p=0.003). There was a significant mean difference of 0.12 m/s (95% CI 0.02 to 0.2 m/s) for all participants on the 10MWT (comfortable gait speed) between baseline and post-intervention assessment (p=0.017).

There were no other significant changes. There was considerable intraindividual variability in the magnitude of change for some outcomes. For example, the change in VO_{2peak} ranged from 29% decline to 37% improvement.

6.2.5 Discussion

This study investigated, as the primary objective, the effects of a vigorous intensity aerobic training on physical activity levels and time spent in low-energy expenditure activities of individuals after stroke when compared to a control group (very light to light intensity overground walking). The secondary objective was to evaluate the effects of the aerobic training on cardiorespiratory fitness, depression, endurance, mobility, participation and quality of life. Participants from the experimental group showed benefit in quality of life (SS-QOL) when compared to the control group. The results of this study demonstrated that all participants had improvements on depression (PHQ), endurance (walking distance on 6MWT and on SWT) and mobility (comfortable gait speed on 10MWT) regardless of the intervention received.

Our hypothesis was that aerobic treadmill training would have a positive impact on physical activity levels and time spent in low-energy expenditure activities of individuals after

stroke through changes in cardiorespiratory fitness (VO_{2peak})[12]. However, no significant differences between groups and over time were observed in the present study in these variables (physical activity levels, time spent in low-energy expenditure activities, nor cardiorespiratory fitness (VO_{2peak})). These results are surprising since an improvement on cardiorespiratory fitness (VO_{2peak}) has been shown by different trials of aerobic training in individuals after stroke[42,43]. The lack of difference between groups in the present study is unlikely to be explained by differences in confounding factors since baseline between-group comparisons demonstrated similarity.

Possible explanations for a lack of change in VO_{2peak} of individuals with chronic stroke after aerobic training might be the genetics of each person, and VO_{2peak} baseline values. The response to aerobic training is, in part, genetically determined, which leads to a high variability of individual responses[44]. Individual changes in VO_{2peak} of participants of a trial about cardiac rehabilitation after stroke ranged from 32% decline to 56% improvement[45]. The high variability of individual responses to aerobic training due to genetics might explain why some individuals from the present study participating in the same aerobic training program showed a 37% improvement and some showed no improvement or even a 29% decline. In addition, baseline values of VO_{2peak} were higher in the present trial than in previous studies. According to a systematic review, mean baseline values of VO_{2peak} across trials about aerobic training after stroke was 15 mL.kg^{-1}.min^{-1} [42]. However, in the present study the mean value of the VO_{2peak} was 22 mL.kg^{-1}.min^{-1} (SD 4.4) for the experimental group and 22 mL.kg^{-1}.min^{-1} (SD 6.7) for the control group. Since lower baseline VO_{2peak} is associated with greater improvements in VO_{2peak}[45], this might be a possible explanation for the lack of change in VO_{2peak} in the present study.

In addition, other possible explanations for why VO_{2peak} of individuals after stroke may not change after aerobic exercise is related to the prescription of the training. The optimal dose for aerobic training for individuals after stroke has yet to be established. Exercise intensity seems to be an important determinant of the efficacy of aerobic training on VO_{2peak} for individuals after stroke. The results of a meta-analysis showed that aerobic training of vigorous intensity (60% to 84% of heart rate reserve) was significantly correlated with larger VO_{2peak} improvement when compared to moderate intensity (40% to 59% of heart rate reserve)[42]. In addition, the results of another study showed that higher training intensity (80% *versus* 60% of heart rate reserve) was

the only variable associated with greater VO_{2peak} improvement of individuals with chronic stroke[46]. Significantly greater VO_{2peak} gains were also reported in a vigorous intensity aerobic training group (30 minutes at 80% of heart rate reserve) than in a moderate intensity group (50 minutes at 50% of heart rate reserve) of individuals in the chronic phase post-stroke[47]. The aim of the present study was to provide a vigorous intensity aerobic exercise (60 to 80% of heart rate reserve), and although participants from the experimental group achieved this target heart rate, they performed exercise, on average, on the lower range of vigorous intensity (62% of heart rate reserve). Future trials should investigate whether treadmill inclination or load addition on the lower limbs might be an alternative to increase training heart rate besides to speed increase.

The control group might have also played a role in this lack of between-group effect. Participants in the control group of the present study received the same number of sessions, with the same weekly frequency and duration by the same physiotherapists whereas in the randomized controlled trial employed in our sample size calculation the control group did not receive any intervention[16]. In addition, in a further attempt to avoid bias, participants were unaware of the intervention of interest, since they were told only that the trial was about walking training, without information on intensity (i.e.: very light to light or vigorous) or modality (i.e.: treadmill or overground) of the intervention.

The benefit of aerobic training on physical activity levels and time spent in low-energy expenditure activities remain unclear. Since no changes in cardiorespiratory fitness were observed, it was not possible to know if aerobic treadmill training has a positive impact on physical activity levels and time spent in low-energy expenditure activities of individuals after stroke through changes in cardiorespiratory fitness. According to the results of systematic reviews, the effects of different interventions (i.e.: aerobics, strengthening, electrical stimulation, functional task training, robot-assisted arm therapy, counseling, activity monitor feedback) on physical activity levels have already been investigated in individuals after stroke[13,48]. However, the high heterogeneity of the measurement instruments and of the results and the very low overall quality of the evidence limit the conclusions[13,48]. Physical activity is a complex construct that can be influenced by multiple factors[2,12]. Therefore, maybe a multifaceted intervention should be necessary to optimized physical activity levels of individuals after stroke[2,12,48]. For example, the experimental group of the randomized controlled trial, used for the sample size calculation of the present study, that showed a significant increase on physical activity levels

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performed a multicomponent intervention: stretching; range of motion exercises; aerobic exercise; lower-limb strength training; and a list of home exercises[16]. Further research with the target to improved various components, including physical function and psychological factors, is warranted.

Individuals from the experimental group showed an increase, on average, of 13 points from baseline to four-week follow-up on quality of life (SS-QOL). Minimal clinically important difference on SS-QOL for individuals after aneurysmal subarachnoid haemorrhage was estimated at 4.7 points[49]. Thus, this improvement was clinically important. Since the improvement was seen only from baseline to follow-up, without a change from baseline to post-intervention, this might be the result of some confusing factor, since we did not have a lot of control about what happen during this period. Although quality of life is an important measure to understand the impact of stroke from individuals' perspective, only few trials with inconsistent results evaluated the efficacy of aerobic exercise intervention on quality of life of individuals after stroke[43]. Therefore, no definitive conclusion can be drawn.

Both groups experienced a significant average reduction of 2.2 points on depression (PHQ). Few previous trials assessed the effects of aerobic training on depression of individuals after stroke, and the combined data from two trials (n = 104) showed no significant effect at the end of intervention[43]. Since minimal clinically important difference for older adults on PHQ was estimated at five points[50], probably, there was no clinically meaningful impact on depression for participants of the present study.

Because both groups experienced a significant average increase of 31-55 m on endurance (6MWT, SWT) and an average increase of 0.12 m/s on mobility (gait speed), walking, independent of intensity, might be beneficial to individuals with chronic stroke. This is consistent with the results of a study investigating factors influencing the efficacy of aerobic training after stroke, in which the meta-regression showed that the modality of the aerobic exercise, seated (i.e.: cycle ergometer) or walking, was the only independent variable significantly associated with gait speed and endurance effect size[42].

Minimal clinically important difference has been estimated at 20-50 m for the 6MWT[51,52] and 0.06-0.18 m/s for gait speed[51,53,54] for individuals after stroke, and 48-70 m for the SWT for individuals after cardiac rehabilitation and with chronic obstructive pulmonary disease[55,56]. Therefore, on average, walking for individuals after stroke may have at least some clinically

meaningful impact on gait speed and endurance. Clinicians targeting to improve gait speed and/or endurance of patients after stroke might prescribe vigorous intensity treadmill aerobic training or very light to light intensity overground walking. The use of vigorous intensity treadmill aerobic training has as advantage the benefit of also improving quality of life. The prescription of very light to light intensity overground walking has as advantage, when compared with vigorous intensity treadmill aerobic training, the fact that no equipment is necessary. In addition, since individuals after stroke do not require a baseline cardiopulmonary exercise test if the exercise is going to be of light intensity and considering that there is limited access to cardiopulmonary exercise test in most clinical and community settings, the use of very light to light intensity overground walking exercise might be an intervention option with good clinical applicability if the aim is to improve gait speed and endurance[8,57]. Since a no-intervention group was not included, this improvement on these outcomes demonstrated by the entire cohort could also be explained by the fact that participants needed to go out of their houses to get the intervention or by natural course of stroke recovery. However, this is unlikely since study participants were in the chronic phase of stroke.

Future studies with the aim to investigate whether aerobic training improve physical activity levels should include a specific baseline VO_{2peak} value as inclusion criteria, since this might impact VO_{2peak} change. In addition, future randomized controlled trials should include energy cost as an outcome measure. Recent studies showed that individuals after stroke present higher energy cost for walking and climbing stairs than healthy matched controls, and that aerobic training can result in a reduction of energy cost[58-60]. This possible reduction of energy cost after aerobic training might have implications for everyday life energy expenditure and it is a possible explanation for the lack of change on energy expenditure measured in the present study.

6.2.5.1 Study limitations

A convenience sample was included in this RCT which may limit generalizability. Furthermore, both participants and the physiotherapists were not blinded to the intervention, however, it is difficult or impossible to blind participants and therapists during the delivery of complex interventions. The loss of four participants for follow-up assessments is also a limitation. Although a sample size calculation was performed, the trial was not powered to detect

statistically significant between-group differences, thus, to investigate the efficacy of aerobic training after stroke a large-scale clinical trial is necessary.

6.2.6 Conclusions

This study revealed that walking exercise performed on a treadmill at a vigorous intensity improved quality of life. In addition, walking exercise performed on a treadmill at a vigorous intensity or overground walking at a very light to light intensity improved depression, endurance and mobility of individuals after stroke. Although walking exercise could be incorporated into clinical practice, further studies are needed to clarify the benefits of aerobic training on physical activity levels and time spent in low-energy expenditure activities.

6.2.7 Conflict of interest

The authors report no conflicts of interest.

6.2.8 Funding

6.2.9 References

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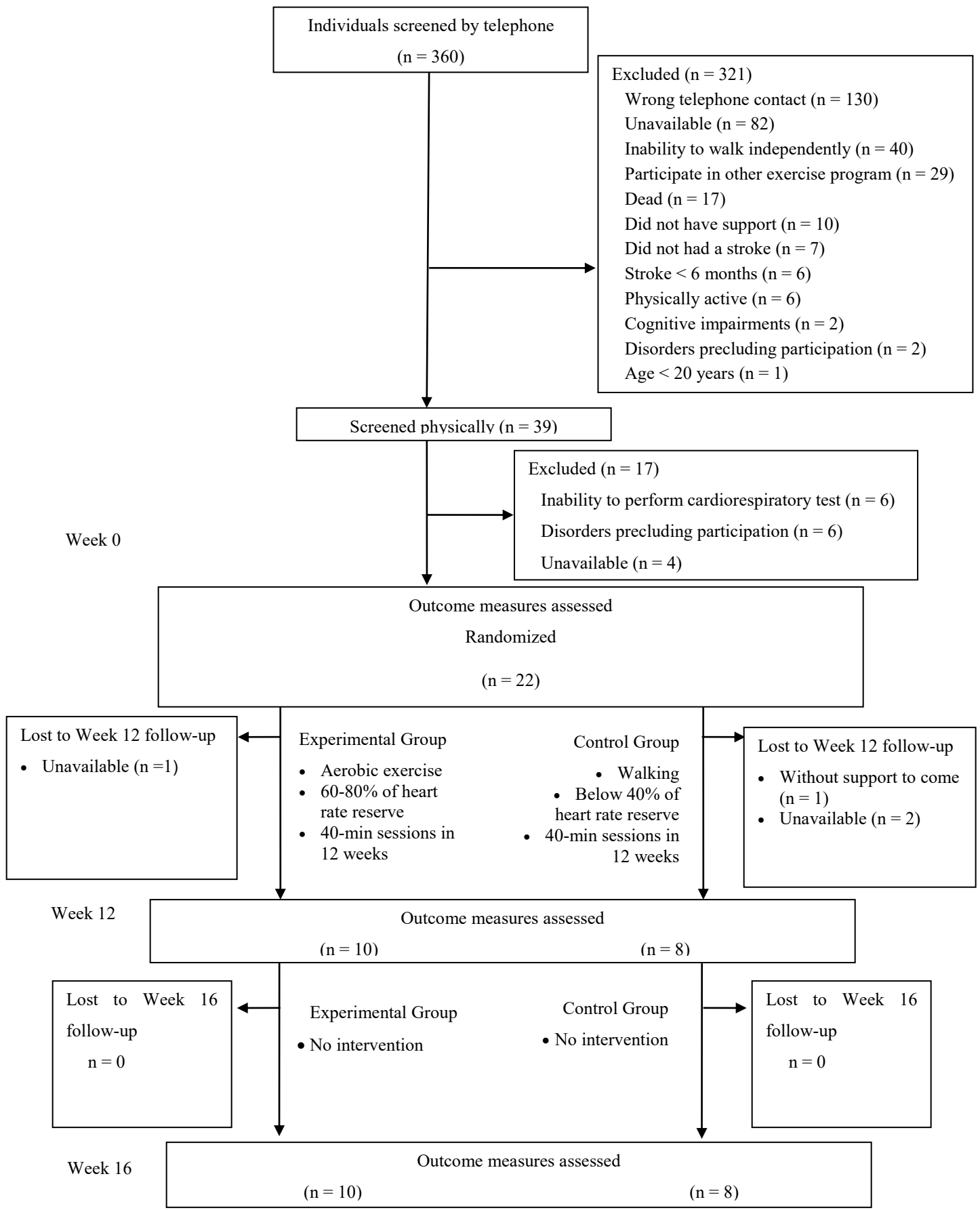
Figure 6-1. Design and flow of participants through the trial.

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Table 6-1. Baseline characteristics of participants.

Characteristic	Randomized (n = 22)		Lost to follow-up (n = 4)	
	Exp (n = 11)	Con (n = 11)	Exp (n = 1)	Con (n = 3)
Age (years), mean (SD)	52 (11)	48 (10)	47	52 (12)
Gender, n males (%)	8 (73)	8 (73)	1 (100)	2 (67)
Body mass index (kg/m^2), mean (SD)	26 (3.3)	29 (2.9)	28	26 (2.2)
Time since onset of stroke (months), mean (SD)	51 (68)	44 (26)	28	35 (37)
Paretic side, n right side (%)	6 (55)	7 (64)	1 (100)	3 (100)
Type of stroke, n (%)				
Ischemic	9 (82)	10 (91)	1 (100)	2 (67)
Hemorrhagic	2 (18)	0 (0)	0 (0)	0 (0)
Ischemic and hemorrhagic	0 (0)	1 (9)	0 (0)	1 (33)
Taking a beta blocker, n (%)	2 (18)	6 (55)	0 (0)	1 (33)
Habitual assistive device, n (%)				
Single point-cane	3 (27)	2 (18)	0 (0)	1 (33)
Ankle foot orthosis	2 (9.1)	0 (0)	0 (0)	0 (0)
Fugl-Meyer Upper Extremity Assessment, score (0–66 points)[40], n (%)				
Mild motor impairments	3 (27)	2 (18)	1 (100)	2 (67)
Moderate motor impairments	1 (9)	0 (0)	0 (0)	0 (0)
Severe motor impairments	7 (64)	9 (82)	0 (0)	1 (33)
Fugl-Meyer Lower Extremity Assessment, score (0–34 points)[41], n (%)				
Mild impairment	6 (55)	7 (64)	1 (100)	3 (100)
Moderate impairment	2 (18)	3 (27)	0 (0)	0 (0)
Moderately severe impairment	2 (18)	0 (0)	0 (0)	0 (0)
Severe impairment	1 (9)	1 (9)	0 (0)	0 (0)
Physical Exercise Classification[21]				
Inactive, n (%)	7 (64)	8 (73)	1 (100)	2 (67)
Insufficiently active, n (%)	4 (36)	3 (27)	0 (0)	1 (33)

Exp = experimental group, Con = control group.

Table 6-2. Mean (SD) of groups, mean (SD) difference within groups, and mean (95% CI) difference between groups.

Outcomes	Groups						Difference within groups				Difference between groups	
	Week 0		Week 12		Week 16		Week 12 minus Week 0		Week 16 minus Week 0		Week 12 minus Week 0	Week 16 minus Week 0
	Exp (n = 11)	Con (n = 11)	Exp (n = 11)	Con (n = 11)	Exp (n = 11)	Con (n = 11)	Exp	Con	Exp	Con	Exp-Con	Exp-Con
Primary												
Physical activity levels (energy expenditure, SenseWear Armband), kcal	2302 (454)	2373 (452)	2277 (482)	2514 (507)	2237 (512)	2466 (486)	-25 (233)	141 (268)	-65 (166)	93 (194)	-166 (-389 to 57)	-158 (-318 to 3.1)
Physical activity levels (Adjusted Activity Score, HAP), points	76 (9.3)	75 (8.1)	77 (9.3)	76 (9.2)	75 (10)	76 (11)	1 (5.8)	1 (3.8)	-1 (7.7)	1 (5.5)	0 (-4.4 to 4.4)	-2 (-8.0 to 4.0)
Time spent in low-energy expenditure activities (SenseWear Armband), %	57 (12)	66 (17)	57 (11)	64 (14)	54 (15)	65 (13)	0 (9.2)	-2 (14)	-3 (13)	-1 (14)	2 (-8.5 to 12.5)	-2 (-14 to 9.7)
Secondary												
Cardiorespiratory fitness (VO$_{2peak,}$), mL.kg.min^{-1}	22.2 (4.4)	22.3 (6.7)	22.7 (4.5)	23.8 (6.9)	23.0 (4.6)	22.7 (7.2)	0.5 (3.7)	1.5 (2.7)	0.8 (3.0)	0.4 (2.5)	-1.0 (-3.9 to 1.9)	0.4 (-2.1 to 2.9)
Cardiorespiratory fitness (VO$_{2ventilatory\ threshold}$, mL.kg.min^{-1})	12.4 (2.0)	13.1 (3.5)	13.0 (2.5)	13.8 (3.9)	12.9 (2.6)	12.2 (3.5)	0.6 (1.8)	0.7 (2.1)	0.5 (2.2)	-0.9 (1.4)	-0.1 (-1.8 to 1.7)	-1.4 (-0.2 to 3.0)
Depression (PHQ), points	4.7 (5.8)	4.9 (6.0)	1.7 (4.0)	3.6 (5.6)	1.8 (3.2)	3.6 (6.4)	-3 (5.0)	-1.3 (2.2)	-2.9 (4.7)	-1.3 (2.7)	-1.7 (-5.1 to 1.7)	-1.6 (-5.0 to 1.8)
Endurance (distance, 6MWT), m	378 (79)	427 (94)	426 (78)	442 (89)	436 (83)	460 (111)	48 (58)	15 (29)	58 (50)	33 (42)	33 (-7.9 to 74)	25 (-16 to 66)
Endurance (distance, SWT), m	285 (132)	327 (156)	334 (118)	389 (171)	322 (120)	375 (144)	49 (31)	62 (127)	37 (45)	48 (101)	-13 (-95 to 69)	-11 (-80 to 58)
Mobility (comfortable gait speed, 10MWT), m/s	1.04 (0.22)	0.97 (0.19)	1.13 (0.22)	1.10 (0.22)	1.09 (0.26)	1.06 (0.18)	0.09 (0.17)	0.14 (0.18)	0.05 (0.19)	0.09 (0.17)	-0.05 (-0.21 to 0.11)	-0.04 (-0.20 to 0.12)
Mobility (maximum gait speed, 10MWT), m/s	1.50 (0.29)	1.54 (0.42)	1.46 (0.27)	1.56 (0.42)	1.52 (0.28)	1.58 (0.41)	-0.05 (0.22)	0.02 (0.16)	0.02 (0.20)	0.05 (0.19)	-0.07 (-0.24 to 0.10)	-0.03 (-0.20 to 0.14)
Participation (SIS), points	33 (6.3)	32 (6.0)	35 (7.7)	32 (7.1)	35 (5.0)	34 (5.7)	2 (7.1)	0 (11)	2 (6.5)	2 (8.7)	2 (-6.2 to 10.2)	0 (-6.8 to 6.8)
Quality of life (SS-QOL), points	190 (19)	191 (29)	193 (20)	194 (28)	203 (25)	188 (27)	3 (16)	3 (16)	**13*** **(14)**	**-3** **(10)**	0 (-14 to 14)	16 (5.2 to 27)

Exp = experimental group, Con = control group, HAP: Human Activity Profile, VO$_{2peak}$: peak oxygen uptake, VO$_{2ventilatory\ threshold}$: oxygen uptake at ventilatory threshold, PHQ: Patient Health Questionnaire, 6MWT: Six-Minute Walk Test, SWT: Shuttle-Walk Test, 10MWT: Ten Meter Walk Test, SIS: Stroke Impact Scale, SS-QOL: Stroke-Specific Quality of Life scale. *A time X group interaction was found ($p<0.05$).

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Chapter 7. Discussion

The general objective of this thesis was to analyze the current level of evidence about different non-invasive interventions to increase physical activity levels after stroke and to develop an experimental study that could provide further evidence on the effects of aerobic training to increase physical activity levels and time spent in low-energy expenditure activities of individuals after stroke. Since the results of each study have already been discussed in each paper, this chapter will have the objective of presenting a more in-depth discussion of the main findings, the limitations of the studies, suggestions for future researches, and the clinical implications of the results.

7.1 Relevance of protocols

The first (Paper #1) and the third paper (Paper #3) are reports of a protocol for the development of a systematic review and for a randomized controlled trial, respectively. Systematic reviews should be developed based on protocols, which describe the justification for the research and the planned methods, because they guarantee a careful planning and documentation of the review process before it begins (MOHER *et al.*, 2015; SHAMSEER *et al.*, 2015). This helps the research team to anticipate and discuss potential problems and it is also important to guide consistent development of the review by researchers (MOHER *et al.*, 2015; SHAMSEER *et al.*, 2015). Furthermore, protocols of systematic reviews enable readers and editors to assess any change made from the planned to the completed review, and thus, it allows the assessment of potential bias, such as selective reporting of outcomes (KIRKHAM *et al.*, 2010; MOHER *et al.*, 2015; SHAMSEER *et al.*, 2015). In addition, protocols of systematic reviews help avoiding duplication of effort by researchers (MOHER *et al.*, 2015; SHAMSEER *et al.*, 2015). Thus, the purpose of the first paper (Paper #1) was to describe the protocol of the systematic review with the aim to investigate the effects of interventions on physical activity levels of individuals after stroke.

All randomized controlled trials also require a protocol with background information describing the justification for the development of the trial, and with the planned methods, including a statistical analysis plan (TETZLAFF *et al.*, 2012). A trial protocol is important

because it enables the assessment of ethical standards and scientific justification before trial beginning (TETZLAFF *et al.*, 2012). Transparent and clearly written trial protocols are also useful to guide trial conduct (TETZLAFF *et al.*, 2012). In addition, trial protocols are important because it may prevent outcome reporting bias (DAL-RE, CAPLAN, 2014; TETZLAFF *et al.*, 2012). Selective reporting of outcomes in clinical trials probably occur because researchers and journal editors are usually more interested on trials that show positive results (large effects of new intervention strategies) or at least equivalence of interventions than trials that show that a new treatment is inferior to usual treatment or inconclusive trials (DE ANGELIS *et al.*, 2004). Outcome reporting bias might misrepresent the body of evidence available for clinical decision-making and thus, need to be avoided (DE ANGELIS *et al.*, 2004). Therefore, the third paper (Paper #3) was published with the purpose to describe the protocol for a randomized controlled trial with the aim to investigate if aerobic training is an effective intervention to improve physical activity levels and time spent in low-energy expenditure activities of individuals after stroke.

7.2 Systematic review

The results of the systematic review (Paper #2) showed that some types of interventions may improve post-stroke physical activity (aerobics, resistance, and home-based training; counselling, aerobics, resistance, and home-based training; electrical stimulation during walking; functional-task training; robot-assisted arm therapy; accelerometer-based feedback, and physical activity encouragement), that is, it is feasible to improve physical activity levels after stroke. However, the limited number of studies and the heterogeneity in the interventions, measurement instruments and results limit the overall conclusions. Therefore, it was concluded that more randomized controlled trials are necessary to verify and draw definitive conclusions regarding the effects of interventions on physical activity of individuals with stroke.

The results of recent published systematic reviews with similar objectives are in accordance with the systematic review of the present thesis (Paper #2). A recent Cochrane systematic review aimed at investigating the effects of the use of activity monitors that provided feedback in increasing physical activity levels of individuals after stroke found that

there is very low quality of evidence that this intervention did not increase physical activity levels (LYNCH *et al.*, 2018). Similar to the systematic review presented in this thesis (Paper #2), studies included in the Cochrane systematic review employed different outcome measures, which also limited pooling of data. Thus, the conclusion of the Cochrane systematic review is that more research is required to determine the efficacy of the use of activity monitors to increase physical activity levels after stroke (LYNCH *et al.*, 2018).

Another recently published systematic review (COULTER *et al.*, 2018) aimed at investigating the effects of any intervention on physical activity levels in people with multiple sclerosis also found that some interventions (behavior change, exercise training, combined exercise and behavior change and health promotion education) appear to improve physical activity levels in this population. Similarly, the authors concluded high heterogeneity in the interventions, measurement instruments employed, physical activity outcomes reported, and results (COULTER *et al.*, 2018). Therefore, more trials investigating the effects of interventions on physical activity levels are still necessary.

Physical activity is a complex outcome, and physical inactivity after stroke is associated with multiple factors, such as cardiorespiratory fitness, depression, fatigue, endurance, mobility and quality of life (CASPERSEN; POWELL; CHRISTENSON, 1985; FARIA *et al.*, 2013; BILLINGER *et al.*, 2014; THILARAJAH *et al.*, 2018). This complexity of physical activity and variety of variables that may explain physical inactivity after stroke might be the reason for the diversity of interventions already employed by clinical trials and can be one of the justification for the lack of a definitive conclusion about the efficacy of interventions to improve physical activity levels reported in Paper #2 and in other systematic reviews (LYNCH *et al.*, 2018; COULTER *et al.*, 2018). Some suggestions for future research with the aim to increase physical activity levels after stroke are discussed in further sections.

7.3 Randomized controlled trial

The results of the randomized controlled trial (Paper #4) showed no change on physical activity levels and time spent in low-energy expenditure activities of individuals in the chronic phase post-stroke after aerobic training. However, baseline average energy expenditure of the participants (experimental group: 2,302 kcal/day, SD 454 kcal/day; control group: 2,373

kcal/day, SD 452 kcal/day) was similar from average energy expenditure reported for healthy individuals (2,041-2,109 kcal/day) and higher than what was previously reported for individuals after stroke (1,257-1,500 kcal/day) (FINI *et al.*, 2017; MENDES *et al.*, 2018). In addition, mean baseline Adjusted Activity Score from the HAP were also higher (experimental group: 76 points, SD 9.3 points; control group: 75 points, SD 8.1 points) than baseline values of a previous trial (experimental group: 50 points, SD 16 points; control group: 58 points, SD 11 points) (TEIXEIRA-SALMELA *et al.*, 1999). Further, baseline average daily time spent in low-energy expenditure activities was lower (experimental group: 57%, SD 12%; control group: 66%, SD 17%) than what has been reported for ambulatory community-dwelling individuals after stroke (mean 80%, SD 11%) (JOSEPH *et al.*, 2017; FINI *et al.*, 2017). Although it is not known whether baseline values affect change on physical activity levels and time spent in low-energy expenditure activities, this might be one explanation for the lack of significant changes on these variables of individuals in the chronic phase post-stroke after the aerobic training proposed on the clinical trial presented in this thesis. One of the eligibility criteria of the trial was related to the physical exercise level of the participants: only inactive or insufficiently active individuals were included (CENTERS FOR DISEASE CONTROL AND PREVENTION, 2001). However, this criterion was not enough to guarantee that participants had a low level of physical activity and high time spent in low-energy expenditure activities. Therefore, future studies related to the topic of this clinical trial should consider physical activity levels as inclusion criteria.

Aerobic treadmill training was effective for improving quality of life (measured with the SS-QOL) of individuals after stroke, and this improvement was both statistically significant and clinically important (Paper #4). Quality of life is a complex and subjective construct that refers to the perception of individuals about the quality of their own life in physical, emotional and social domains (GEYH *et al.*, 2007; FARIA, *et al.*, 2012). Therefore, the improvement of quality of life after aerobic training of individuals after stroke is important. However, only few trials assessed the effects of aerobic training on quality of life of individuals after stroke (PANG *et al.*, 2013; SAUNDERS *et al.*, 2016). Some of these trials showed a significant improvement on quality of life and others not, but all of them used generic instruments, such as the Short-Form Health Survey or the EuroQol (PANG *et al.*,

2013; SAUNDERS *et al.*, 2016). The use of generic instruments of quality of life allows comparisons between different populations, however, meaningful questions specific to a health condition may not be asked and these instruments may not be sensitivity to change (KRANCIUKAITE *et al.*, 2006). On the contrary, specific quality of life instruments, such as the SS-QOL, which is a recommended instrument to measure quality of life after stroke, were developed with the purpose to include relevant and responsive domains commonly affected by a specific health condition (KRANCIUKAITE *et al.*, 2006; ZELTZER *et al.*, 2008).

Paper #4 revealed that walking performed at a vigorous intensity on a treadmill or performed at a very light to light intensity overground significantly improved depression (measure with the PHQ), endurance (measured as distance walked on the 6MWT and on the SWT) and mobility (comfortable gait speed on 10MWT) of individuals after stroke. Few previous trials assessed the effects of aerobic training on depression of individuals after stroke, and the combined data from two trials (n = 104) showed no significant effect at the end of intervention (SAUNDERS *et al.*, 2016). Minimal clinically important difference for older adults on PHQ was estimated at five points (LOWE *et al.*, 2004), and since there was a significant mean difference of only 2.2 points (95% CI 0.01 to 4.3) for experimental and control group on the PHQ between baseline and follow-up assessment in the present trial (Paper #4), probably there was no clinically meaningful impact on depression for participants of the present study.

The magnitude of change of distance walked on the 6MWT of the experimental and control group (mean difference between baseline and post-intervention 31 m, 95% CI: 5.6 to 57 m; mean difference between baseline and follow-up 46 m , 95% CI 20 to 71 m) was similar to the previous one reported in a meta-analysis involving 15 randomized controlled trials with 826 individuals after stroke (mean difference 30 m, 95% CI: 16 to 44 m) (SAUNDERS *et al.*, 2016). It is also interesting to interpret the findings in terms of minimal detectable change. The 90% confidence level ranges from 28 m to 48 m, and the 95% confidence level is 47 m for the 6MWT for individuals after stroke (KUMAR *et al.*, 2008; SALBACH *et al.*, 2017). In addition, minimal clinically important difference has been estimated at 20-50 m for the 6MWT for individuals after stroke (PERERA *et al.*, 2006; TANG *et al.*, 2012). From baseline (week 0) to post-intervention (week 12), seven and four individuals of the experimental and

control group, respectively, had an improvement on 6MWT equal or greater than 20 m. From baseline (week 0) to follow-up (week 16), eight and four individuals of the experimental and control group, respectively, had an improvement on 6MWT of at least 20 m. Thus, it seems that the number of participants who improved significantly might be superior in the experimental group than the control one.

The mean difference between baseline (week 0) and post-intervention (week 12) on comfortable gait speed was slightly higher (mean difference 0.12 m/s, 95% CI: 0.02 to 0.2 m/s) than the value provided by a meta-analysis involving 11 randomized controlled trials with 505 individuals after stroke (mean difference 0.07 m/s, 95% CI: 0.03 to 0.11 m/s) (SAUNDERS *et al.*, 2016). Minimal clinically important difference has been estimated at 0.06-0.18 m/s for gait speed for individuals after stroke (PERERA *et al.*, 2006; TILSON *et al.*, 2010; FULK *et al.*, 2011).

Since the improvement on endurance and gait speed may have at least some clinically meaningful impact, clinicians targeting to improve gait speed and/or endurance of individuals after stroke might prescribe vigorous intensity treadmill aerobic training or very light to light intensity overground walking. The use of vigorous intensity treadmill aerobic training has as advantage the benefit of also improving quality of life, as described previously (Paper #4). The prescription of very light to light intensity overground walking has as advantage, when compared with vigorous intensity treadmill aerobic training, the fact that no equipment is necessary. In addition, a baseline cardiopulmonary exercise test is not required if the exercise to be performed by individuals after stroke is of light intensity, and since there is limited availability to cardiopulmonary exercise testing in most clinical settings, this means greater clinical applicability (BILLINGER *et al.*, 2014; BILLINGER *et al.*, 2015).

Furthermore, it was shown that the effects of aerobic training on endurance of individuals after stroke can be measured with the 6MWT or the SWT. Previous studies that investigated the efficacy of aerobic training to improve endurance after stroke usually employed the 6MWT to measure submaximal walking endurance (PANG *et al.*, 2013; SAUNDERS *et al.*, 2016; BOYNE *et al.*, 2017). However, the SWT is also a simple test, with adequate measurement properties and with the advantage of requiring only a 10-meter corridor to be performed, while the 6MWT requires a 30-m hallway (TYSON; CONNELL, 2009;

HAMIDZADEH; ZELTZER, 2011; VAN BLOEMENDAAL *et al.*, 2012; PARREIRA *et al.*, 2014). Nevertheless, since the speed of the SWT starts at 0.5 m/s and it is increased by 0.17 m/s each minute, to perform the SWT the individual need to be able to walk at least at 0.5 m/s (PARREIRA *et al.*, 2014). Therefore, clinicians might choose the 6MWT or the SWT to measure the effects of aerobic training of individuals after stroke on endurance, according to their preference, space availability and individuals' gait speed.

There were no effects on oxygen uptake at ventilatory threshold ($VO_{2ventilatory\ threshold}$), maximum gait speed or participation of individuals in the chronic phase post-stroke after the aerobic training. Previous trials have not investigated the efficacy of aerobic exercise on $VO_{2ventilatory\ threshold}$ or participation. Therefore, it is difficult to compare the results of the trial presented in this thesis regarding $VO_{2ventilatory\ threshold}$ and participation. However, for maximum gait speed, the result of a meta-analysis of 14 trials with 631 individuals after stroke showed that aerobic exercise training is effective to increase this outcome in individuals after stroke (mean difference 0.11 m/s, 95% CI: 0.05 to 0.2 m/s) (SAUNDERS *et al.*, 2016). Baseline maximum gait speed of participants were lower (experimental group: 1.50 m/s, SD 0.29 m/s; control group: 1.54 m/s, SD 0.48 m/s) than the reference values reported for healthy individuals (1.75 m/s to 2.53 m/s) (SALBACH *et al.*, 2015). However, the the trial was not enough powered to detect statistically significant between-group differences (power = 11%) when it should be, ideally, 80%.

7.4 Strengths and limitations

The studies presented in this thesis have some strengths and limitations that will be detailed below.

7.4.1 Strengths of the studies

7.4.1.1 Systematic Review

The systematic review (Paper #2) was registered with the International Prospective Register of Systematic Reviews (PROSPERO), the protocol was published (Paper #1) and the methods described in the protocol were performed according to what was planned. This

systematic review was reported and completed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement (MOHER *et al.*, 2015). The three most complete databases for reports of randomized controlled trials (RCT) were searched (MICHALEFF *et al.*, 2011). The quality of the included studies was assessed by the PEDro Rating Scale and the quality of the evidence was assessed based upon the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) (GUYATT *et al.*, 2008).

7.4.1.2 Randomized controlled trial

The randomized controlled trial (Paper #4) was prospectively registered at www.clinicaltrials.gov (NCT02798237), the protocol was published (Paper #3) and the methods described in the protocol were performed according to what was planned. In addition, the randomized controlled trial was reported and executed in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement guidelines (SCHULZ *et al.*, 2010).

Furthermore, the randomized controlled trial (Paper #4) had a good methodological quality according to the PEDro Rating Scale (seven over ten). Participants were randomly allocated, the allocation was concealed, there were baseline comparability, assessors were blinded, intention-to-treat analysis was performed, between-group comparisons and point estimates and variability were reported. In addition, the employed instruments to measure physical activity levels (the SenseWear Armband and the HAP) have adequate measurement properties for the assessment of the stroke population (MOORE *et al.*, 2012; MANNS; HAENNEL, 2012; VANROY *et al.*, 2014; MANDIGOUT *et al.*, 2017). Furthermore, the prescription of training intensity was individually tailored and based on the heart rate reserve considering peak heart rate achieved during maximal cardiopulmonary exercise test that was performed according to the recommendations of the American College of Sports Medicine (PESCATELLO *et al.*, 2014). In addition, the control group performed an intervention with similar frequency (three sessions per week) and duration (40-minute sessions during on average 12 weeks) when compared to the experimental group, which avoided amount of

attention bias. The experimental group received only aerobic exercise training, which allowed the investigation of aerobic training alone.

7.4.2 Limitations of the measurement instruments

7.4.2.1 Systematic Review

A limitation is that many different measurement tools (i.e.: accelerometers, pedometer, questionnaires) and outcomes (i.e.: number of steps, energy expenditure, duration at different activity intensities) were used in the studies included in the systematic review (Paper #2). This prevented the development of a meta-analysis and more definitive conclusions. There is a need for a consensus between researchers on the most suitable way of measuring physical activity levels.

Although the best evidences were used, some instruments employed in the trials included in the review (Paper #2) did not have proven measurement properties for the assessment of physical activity levels of individuals after stroke, though they have adequate measurement properties for other population groups (i.e., healthy elderly individuals). This applies to the Physical Activity Scale for the Elderly (PASE), the Yale Physical Activity Survey, the Physical Activity Scale (PAS), the Baecke Questionnaire of Habitual Physical Activity, and the following accelerometers: Micro Mini-Motion logger activity monitor (Ambulatory Monitoring, New York, NY, USA), Kenz Lifecorder (Suzuken, Nagoya, Aichi, Japan), Actisleep (GT3Xþ, LLT, Pensacola, FL, USA), and Acticial (Minimitter, Bend, OR, USA). The value of the results of research depends on the extent that the measurement instruments show adequate measurement properties (PORTNEY; WATKINS, 2015).

7.4.3 Limitations of the Study Protocols

7.4.3.1 Randomized controlled trial

A possible limitation was the lack of an inclusion criteria related to baseline VO_{2peak} value. As mentioned before, low baseline VO_{2peak} values are associated with greater improvements in VO_{2peak} of individuals after stroke (TANG $et\ al.$, 2013). However, VO_{2peak}

average baseline values of the present trial (Paper #4) were higher (22 mL.kg^{-1}.min^{-1}) than that of previous studies (15 mL.kg^{-1}.min^{-1}) (SAUNDERS *et al.*, 2016).

A further possible study limitation is related to the intensity of the training. Vigorous intensity of aerobic training is associated with greater VO_{2peak} improvement of individuals after stroke (LAM *et al.*, 2010; IVEY *et al.*, 2015; SAUNDERS *et al.*, 2016). Although the aim was to provide a vigorous intensity aerobic exercise (60 to 80% of heart rate reserve), participants of the experimental group trained, on average, at the lower limit of the target intensity (62% of heart rate reserve). During training, gait speed was the only variable changed to control intensity. Although, training therapists made an effort to make participants walk as fast as they could tolerate, another way of increasing effort, such as a change in treadmill inclination or load addition, could have been included to help participants to achieve greater exercise intensity.

Energy cost was not directly measured, but values estimated from the prediction equations of Polese *et al.* (2018) seem to indicate a significant time effect with a reduction of energy cost between baseline and post-intervention (mean change 0.03 ml/kg/m, 95% CI: 0.01-0.06 ml/kg/m). Mean predicted values from all 22 participants was 0.16 ml/kg/m at baseline (week 0), 0.13 ml/kg/m post-intervention (week 12) and 0.14 ml/kg/m at follow-up (week 16).

7.4.4 Limitations of the sample

7.4.4.1 Randomized controlled trial

Similar to the majority of the randomized controlled trials, participants from the sample studied presented specific characteristics that might limit generalizability. Participants from the randomized controlled trial (Paper #4) developed in this thesis (n = 22) had a mean time since the onset of stroke of 47 months (SD 50 months), with ages ranging from 27 to 65 years (mean 50 years, SD 11 years), were independently ambulant (mean comfortable gait speed 1.0 m/s, SD 0.21 m/s), and 59% had mild lower-limb impairment. Although these participants seem representative of a relatively large portion of stroke population, some cautious is necessary for generalizing the results.

One of the inclusion criteria was being on the chronic phase post-stroke (> six months). Individuals after stroke exhibit spontaneous recovery, progressing through characteristic phases that are usually defined as acute (zero – seven days), subacute (seven days – six months) and chronic (> six months) (MURPHY *et al.*, 2009; BERNHARDT *et al.*, 2017). Individuals on different phases post-stroke might respond differently to interventions (BERNHARDT *et al.*, 2016; BERNHARDT *et al.*, 2017). The result of studies has shown that aerobic training is effective for improving cardiorespiratory fitness of individuals on different phases after stroke, and that time post-stroke do not seem to have an influence on changes in VO_{2peak} after aerobic exercise training (GLOBAS *et al.*, 2012; PANG *et al.*, 2013; BOYNE *et al.*, 2017). However, there is no information about the influence of stroke phases on the efficacy of aerobic training on other outcome measures, such as, physical activity levels or time spent in low-energy expenditure activities. Therefore, the generalizability of the results of the trial developed in this thesis (Paper #4) might be limited to individuals in the chronic phase post-stroke.

In addition, as with the majority of the trials that investigated the effects of aerobic training post-stroke (SAUNDERS *et al.*, 2016), only ambulatory individuals were included. This was necessary since exercise testing and training involved walking without body weight support. Thus, the results of the randomized controlled trial (Paper #4) might not be generalizable for non-ambulatory individuals.

7.5 For future research

The results of the studies developed in this thesis and the limitations discussed previously lead to implications for future research regarding the measurement instruments, the protocol of experimental studies, and the sample included, that will be discussed below.

7.5.1 Recommendations concerning the measurement instruments

First, as mentioned previously, physical activity levels can be measured with subjective or objective instruments. According to a systematic review with the aim to summarize the measurement properties and the clinical utility of self-report instruments to measure physical activity of individuals after stroke, the instruments that had their measurement properties

already investigated and with the highest clinical utility scores were the FAI and the HAP (MARTINS *et al.*, 2018). Therefore, considering the results of the systematic review, future studies with the aim to assess physical activity levels with a self-report instrument of individuals after stroke might preferentially consider using the FAI or the HAP. Recall, that in the present trial, the mean Adjusted Activity Score from the HAP was used.

Future studies should also consider using the criterion method for objectively measuring physical activity in free-living environment, the doubly labeled water method (WARREN *et al.*, 2010; STRATH *et al.*, 2013; APARICIO-UGARRIZA *et al.*, 2015). Furthermore, if the aim of the study is to measure physical activity levels objectively with a wearable monitor of individuals after stroke, although there is no single gold-standard wearable monitor, the researcher might use the SenseWear Armband (BodyMedia, Pittsburgh, PA, USA) or the Step Activity Monitor (Modus Health LLC, Washington, DC, USA) (FINI *et al.*, 2015). Both instruments have adequate measurement properties for measuring physical activity levels of individuals after stroke and they provide the number of steps (FINI *et al.*, 2015). However, only the SenseWear Armband, used in the present trial, provides other different parameters, such as, energy expenditure, total distance, and physical activity duration per activity intensity (i.e. light, moderate, vigorous, and very vigorous) which are important parameters to include when the aim is to assess physical activity (FINI *et al.*, 2015).

It is true that there is also no consensus on the best parameter for the measurement of physical activity levels. However, as the definition of physical activity indicates an increase in energy expenditure, and since energy expenditure is a result of the frequency, duration, and intensity of the physical activity (CASPERSEN; POWELL; CHRISTENSON, 1985; WOOD; ZHU, 2006), it seems that the measurement of energy expenditure might be the single best parameter to objectively assess physical activity levels. Thus, actually, the SenseWear Armband might be more appropriate than the Step Activity Monitor to measure physical activity.

7.5.2 Recommendations for experimental studies

7.5.2.1 Baseline VO$_{2peak}$

Future randomized controlled trials with the objective to investigate the efficacy of aerobic exercise training to improve physical activity levels and reduce time spent in low-energy expenditure activities should include baseline VO$_{2peak}$ value as an inclusion criterion, since this might impact VO$_{2peak}$ change. However, there is no VO$_{2peak}$ cut-off or threshold values by sex and age groups for defining individuals with low, moderate and high cardiorespiratory fitness, although this has been recommended as an important research direction by the American Heart Association (ROSS *et al.*, 2016).

Individuals with cardiorespiratory fitness below five METs have a high risk for mortality, and because of that they are considered to be unfit (ROSS *et al.*, 2016). Since each MET is about 3.5 mL.kg^{-1}.min^{-1}, five METs would correspond to 17.5 mL.kg^{-1}.min^{-1}. Loss of independence seems to occur below a VO$_{2peak}$ value of 15 mL.kg^{-1}.min^{-1} for elderly women and 18 mL.kg^{-1}.min^{-1} for elderly men (SHEPHARD, 2009). These values might be used by researchers as eligibility criteria in future studies while there are no defined cut-off values for low, moderate and high cardiorespiratory fitness.

In addition, VO$_{2max}$ reference values could also be used for interpretation of the cardiopulmonary test results. Reference values of VO$_{2max}$ were determined for men and women between 20 to 85 years old based on cardiopulmonary tests of 7,059 individuals from Norway (EDVARDSEN *et al.*, 2013). More recently, percentiles of VO$_{2max}$ for men and women were determined for each decade from 20 years of age through 79 years of age based on data from 7,783 individuals from the United States (KAMINSKY *et al.*, 2015), and for six age groups between seven and 84 years based on data from 18,189 individuals from a Brazilian population (ROSSI *et al.*, 2019). As cardiorespiratory fitness varies according to age, sex and population (ROSS *et al.*, 2016), future researchers should choose which reference values to adopt based on the characteristics of their sample.

7.5.2.2 Energy cost

The energy cost of the gait can be measured indirectly by oxygen consumption (VO_2) per unit of distance (RICHARDSON *et al.*, 2015). According to the results of meta-analyses, the energy cost during overground or treadmill walking after stroke range from 0.29 ml/kg/m to 0.69 ml/kg/m (KRAMER *et al.*, 2016). Individual values show a large range of energetic cost of gait at comfortable speed post-stroke (0.18 ml/kg/m to 2.74 ml/kg/m) (COMPAGNAT *et al.*, 2018). Pooled data from meta-analysis showed that individuals after stroke present higher energy cost for overground and for treadmill walking than healthy matched controls (mean difference: 0.47 ml/kg/m, 95%CI: 0.29-0.66 ml/kg/m; mean difference: 0.20 ml/kg/m, 95%CI: 0.12-0.27 ml/kg/m, respectively) (KRAMER *et al.*, 2016). In addition, community walkers (0.51 ml/kg/m, SD 0.09 ml/kg/m) and limited-community walkers (0.64 ml/kg/m, SD 0.15 ml/kg/m) individuals after stroke also presented higher energy cost for climbing stairs than healthy matched controls (0.17 ml/kg/m, SD 0.08 ml/kg/m) (POLESE *et al.*, 2017).

Some adaptations to common disabilities of gait post-stroke may explain the high energy cost (OLNEY; RICHARDS *et al.*, 1996; OLNEY, 2005). For example, lower-limb circumduction or hip hiking, performed to achieve foot clearance and compensate for a decreased hip or knee flexion during the swing phase, might result in higher energy cost (OLNEY; RICHARDS *et al.*, 1996; OLNEY, 2005). This may have implications for physical activity levels, as higher costs may limit daily activities. For individuals after stroke, performing some physical activities may be very hard or even impossible or unsustainable due to the high energetic cost and low cardiorespiratory fitness (VO_{2peak}) (KRAMER *et al.*, 2016; SAUNDERS *et al.*, 2016), and consequently, fatigue.

Energy cost for walking activities seems to be related to gait speed. According to one study, only limited-community walkers (comfortable gait speed < 0.8 m/s) had higher energy cost for walking during the 6MWT when compared to healthy matched controls, but not community walkers (comfortable gait speed ≥ 0.8 m/s) (mean difference: 0.17 ml/kg/m, 95%CI: 0.04-0.29 ml/kg/m; mean difference: 0.02 ml/kg/m, 95%CI: -0.09-0.13 ml/kg/m, respectively) (POLESE *et al.*, 2017). In addition, there is a significant, negative and high association between the energetic cost of gait and comfortable walking speed of individuals after stroke (r = - 0.94) (COMPAGNAT *et al.*, 2018). Furthermore, comfortable gait speed

explained more than 80% of the variance in the energetic cost of gait and 47% of the variance in the energetic cost during stair climbing (POLESE *et al.*, 2015; POLESE *et al.*, 2018). Therefore, it appears that a higher energetic cost is associated to a slower gait speed after stroke.

Aerobic training of individuals after stroke can result in an increase of comfortable gait speed (Paper #4) and in a reduction of energy cost of walking (MUNARI *et al.*, 2018). This possible reduction of energy cost of walking after aerobic training might have implications for everyday life energy expenditure and it is a possible explanation for the lack of change on energy expenditure measured in the randomized controlled trial (Paper #4). Therefore, future randomized controlled trials should quantify energy cost.

7.5.2.3 Aerobic training parameters

Another interesting aspect of aerobic training that could be investigated is whether the increase of participants' effort through changes on treadmill inclination and/or load addition on the lower limbs would lead to a higher intensity than without inclination/load addition, and thus, to greater VO_{2peak} improvement. A randomized controlled trial with the aim to investigate the effects of aerobic treadmill training with a load addition on the non-paretic lower-limb of individuals after stroke on cardiovascular parameters (i.e.: heart rate) was performed (RIBEIRO *et al.*, 2017). There were no differences between the experimental and the control groups, which performed aerobic treadmill training without load addition. However, this study has some important limitations. First, both experimental and control groups performed aerobic training with a target intensity of only 50% of maximum heart rate, which is considered light intensity (PESCATELLO *et al.*, 2014). Furthermore, maximum heart rate was not directly measured, but predicted (formula 220 – age), which is recognized as unprecise estimate of effort (ROBERGS *et al.*, 2012; GORDON *et al.*, 2013; BILLINGER *et al.*, 2015). In addition, only nine sessions of exercise training were provided (RIBEIRO *et al.*, 2017). Therefore, future trials are still necessary to investigate whether treadmill inclination and/or load addition can lead to an increase of aerobic exercise intensity of individuals after stroke.

7.5.2.4 Other interventions

As already mentioned, physical activity is a complex behavior that is related to diverse factors (CASPERSEN; POWELL; CHRISTENSON, 1985; BILLINGER *et al.*, 2014; THILARAJAH *et al.*, 2018). As reported in the systematic review (Paper #2), different interventions showed positive effects on physical activity levels of individuals after stroke. These interventions involved: aerobics, resistance, and home-based training; counselling, aerobics, resistance, and home-based training; electrical stimulation during walking; functional-task training; robot-assisted arm therapy; accelerometer-based feedback, and physical activity encouragement. The randomized controlled trial that showed an improvement on physical activity levels, also measured with the HAP, reported the use of a multicomponent intervention (aerobics, resistance, and home-based training) (TEIXEIRA-SALMELA *et al.*, 1999). Therefore, future studies should consider investigating if a multifaceted intervention is effective for improving physical activity levels of individuals after stroke.

7.5.3 Recommendations concerning the sample

In the randomized controlled trial developed in this thesis (Paper #4) only individuals on the chronic phase post-stroke that could walk independently and with fast gait were included. Future studies with the aim to investigate the effects of aerobic training on physical activity levels of individuals after stroke should include individuals in the acute and subacute phase post-stroke. In addition, in future studies, it will be important to include non-ambulatory participants. Most trials that investigated the effects of aerobic training on different outcomes included only ambulatory individuals in the chronic phase post-stroke (SAUNDERS *et al.*, 2016). Further, a bigger sample size is necessary, since, besides the sample size calculation, the trial was not powered to detect statistically significant between-group differences on physical activity levels or time spent in low-energy expenditure activities. Therefore, there is a need for investigation of the effects of aerobic training on diverse outcomes, including physical activity levels and time spent in low-energy expenditure activities, of a broader population of individuals after stroke, including non-ambulatory individuals in the different phases post-stroke and with lower gait speed.

7.6 Clinical Implications

In the following sections the clinical implications of the results of this doctoral project regarding the effects of aerobic training after stroke will be discussed.

7.6.1 Implications for physical activity outcome

According to the results of the systematic review (Paper #2) and of the randomized controlled trial (Paper #4) no recommendation can be made yet about interventions to improve physical activity levels and reduce time spent in low-energy expenditure activities of individuals after stroke. More research is still necessary.

7.6.2 Implications for quality of life outcome

The results of the randomized controlled trial (Paper #4) showed that aerobic treadmill training, at vigorous intensity, was effective for improving quality of life (SS-QOL) of individuals in the chronic phase post-stroke. Since quality of life is an important outcome, related to the perception of individuals about the quality of their own life, aerobic treadmill training might be used during rehabilitation of individuals in the chronic phase after stroke with the aim to improve quality of life.

7.6.3 Implications for depression, endurance, and mobility outcomes

The randomized controlled trial (Paper #4) revealed that walking exercise performed on a treadmill at a vigorous intensity, as well as overground walking exercise at a very light to light intensity improved depression, mobility and endurance after stroke. Vigorous intensity treadmill aerobic training might also improve quality of life, as described previously (Paper #4), and cardiorespiratory fitness (VO_{2peak}) as reported by other studies (MARSDEN *et al.*, 2013; PANG *et al.*, 2013; SALTYCHEV *et al.*, 2016; SAUNDERS *et al.*, 2016; BOYNE *et al.*, 2017). However, the use of very low to low intensity overground walking exercise might be an intervention option with good clinical applicability if the aim is to improve gait speed and endurance of individuals after stroke, since no equipment or cardiopulmonary exercise testing are necessary for this type of exercise. Furthermore, health professionals can decide,

based on their preference, space availability and individuals' gait speed to measure the effects of aerobic training of individuals after stroke on endurance with the 6MWT or the SWT.

Chapter 8. Conclusion

This doctoral work, developed in a cotutelle between the Program in Rehabilitation Sciences of the Universidade Federal de Minas Gerais (UFMG)/Brazil and the Université de Montréal (UdeM)/Canada, investigated the efficacy of interventions on improving physical activity levels of individuals after stroke.

The results of this thesis showed that the current evidence is insufficient to make a recommendation about interventions to improve physical activity levels and reduce time spent in low-energy expenditure activities of individuals after stroke. The limited evidence currently available indicate that it is feasible to improve physical activity levels after stroke, since in seven trials included in the systematic review aimed at identifying interventions employed to increase post-stroke physical activity, the experimental group showed significant increases in physical activity levels when compared to the control group. The interventions employed in these studies were the following: 1) aerobics, resistance, and home-based training; 2) aerobics, counselling, resistance, and home-based training; 3) electrical stimulation during walking; 4) functional-task training; 5) robot-assisted arm therapy; 6) accelerometer-based feedback; and 7) physical activity encouragement. However, the limited number of studies and the heterogeneity in the interventions and results limit the overall conclusions, and thus, the overall quality of the evidence was considered very low according to the GRADE criteria. Therefore, the best intervention strategy to attain this objective is not clear yet.

Further studies are needed to clarify the benefits of aerobic training on physical activity and time spent in low-energy expenditure activities. The results of this thesis also revealed that walking performed on a treadmill at a vigorous intensity improved quality of life, and, as well as overground walking at a very light to light intensity improved depression, endurance and comfortable gait speed after stroke. And this improvement may have at least some clinically meaningful impact. Thus, the use of very light to light intensity overground walking might be an intervention option with good clinical applicability if the aim is to improve endurance and gait speed after stroke.

Future studies with the aim to investigate whether aerobic training improve physical activity levels should include baseline VO_{2peak} value as inclusion criteria, since this might

impact VO$_{2peak}$ change. In addition, future randomized controlled trials should include energy cost as an outcome measure, since the possible reduction of energy cost after aerobic training might have implications for everyday life energy expenditure and it is a possible explanation for the lack of change on physical activity levels of the present study. Considering the complexity of physical activity, more research investigating different interventions, probably multifaceted interventions with the target to improved various components, including physical function and psychological factors, individually tailored should be necessary to optimized physical activity levels after stroke.

Considering that the heterogeneity in the measurement instruments and outcomes employed limit the overall conclusions, further studies should use consistent outcome measures, in order to allow comparison and pooling of data. Therefore, more randomized controlled trials are necessary to verify and draw definitive conclusions regarding the effects of interventions on improving physical activity levels and reducing time spent in low-energy expenditure activities of individuals with stroke.

Despite some limitations, the work done and presented in this thesis has helped advance knowledge in the field and guide interventions to improve levels of physical activity and time spent on low-energy activities after aerobics training. Given that physical activity is reduced in amount, duration, and intensity after stroke and that physical inactivity is related to various comorbidities such as stroke and heart attacks, it can be concluded that it will be relevant to continue developing evidence on interventions to improve physical activity levels after stroke and to further refine interventions to improve the quality of life of participants after stroke.

Chapter 9. References

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Appendix I Agreement for a joint doctoral program

Université de Montréal

Faculty of Graduate and Postdoctoral Studies

AGREEMENT
FOR A JOINT DOCTORAL PROGRAM
BETWEEN
UNIVERSIDADE FEDERAL DE MINAS
GERAIS (UFMG) AND
UNIVERSITÉ DE MONTRÉAL (UdeM)

SEPTEMBER 2015

AGREEMENT FOR A JOINT DOCTORAL PROGRAM (KNOWN AS COTUTELLE)
BETWEEN UNIVERSITÉ DE MONTRÉAL AND UNIVERSIDADE FEDERAL DE MINAS GERAIS/

Note

The present agreement is being proposed to scientific and administrative authorities in order to permit the establishment of a joint doctoral program and thesis supervision and to ensure its successful functioning.

If necessary, the present may also include additional or complementary provisions, in conformity with the agreement, in order to facilitate the implementation of the Joint Doctoral Program between Université de Montréal and Universidade Federal de Minas Gerais.

A. PREAMBLE

In conformity with the agreement for the Joint Doctoral Program between Université de Montréal and Universidade Federal de Minas Gerais the present agreement is concluded between: /

Université de Montréal, represented by the dean of the Faculty of Graduate and postdoctoral Studies (FGPS): Prof. Michèle Brochu

et,

Universidade Federal de Minas Gerais, represented by the dean Prof. Jaime Arturo Ramírez

Concerning: Tavares Aguiar, Larissa   M :   F : X

███████████████████████████████████████

     Date of birth   *City, country*   *Citizenship*

B. ADMINISTRATIVE PROCEDURES

Article 1 Registration, registration and tuition fees: The candidate shall automatically and compulsorily be registered in the two institutions for the whole duration of his program, [the question of the tuition fees is to be discussed by the institutions]. The precise wording of the diploma should be indicated here.
- Doctoral program: Sciences de la réadaptation
The diploma will be: Philosophiae Doctor (Ph. D.) en Sciences de la réadaptation

At Universidade Federal de Minas Gerais, the candidate will be registered in the doctoral program: Rehabilitation Sciences, since 2015

At Université de Montréal, the candidate will be registered in the doctoral program: Sciences de la réadaptation, since 2015

Article 2 – Studies and thesis

Subject of thesis proposed by the candidate (full title):

EFFICACY OF AEROBIC TRAINING ON PHYSICAL ACTIVITY LEVEL IN INDIVIDUALS AFFECTED BY

STROKE: A RANDOMIZED CONTROLLED TRIAL

Periods of residency proposed in the two institutions:

Université de Montréal	Universidade Federal de Minas Gerais
Fall term: August 1 to December 31/2016	March 2015 to July 2016
Winter term: January 1 to April 30/2017	August 2017 to February 2019
Summer term: May 1 to July 31/2017	

N.B.:

- The anticipated duration of the candidate's course work and research is normally four years, depending on the duration of the required course work. It can be extended by specific agreement between the two institutions on the joint recommendation of the two thesis supervisors by the addition of a provision to the joint doctoral program agreement signed by the supervisors of doctoral studies for each of the institutions. The total time spent in either of the two institutions shall not be less than one year (3 terms) and the full time study with the status of «scolarité» shall not exceed six terms.

- The candidate shall pursue his studies and research alternately in the two institutions, during periods agreed to jointly by the two thesis supervisors and the two institutions, in accordance with the plan described hereinafter. The candidate must spend, on a full-time basis, at least three terms at Université de Montréal in the course of the program.

- Protection of the thesis subject as well as the publication, use and protection of research results and research ethics arising from the candidate's work in the two institutions shall be subject to the regulations in force and applied in conformity with the procedures of each university involved in the joint doctoral program. As required, (i) the provisions concerning the protection of intellectual property rights, especially in particular circumstances such as the potential for commercialization or patent of a research project, will be the object of a specific appendix to this agreement and (ii) the candidate shall conform to the regulations regarding research ethics in force in each of the partner institutions.

Article 3 – Social protection

The candidate shall benefit from social protection to the extent provided for in the legislation of each country and the regulations of each institution.

C. PEDAGOGICAL PROCEDURES

Article 4 – Thesis supervisors

The candidate shall pursue studies and research under the joint supervision of a thesis supervisor at Université de Montréal and a thesis supervisor at Universidade Federal de Minas Gerais (the two supervisors having previously established a close cooperation):

Université de Montréal:

Thesis supervisor for the candidate: Nadeau, Sylvie – Ph.D.

Universidade Federal de Minas Gerais:

Thesis supervisor for the candidate: Coelho de Morais Faria, Christina Danielli – Ph.D.

Participation in the joint doctoral program (the two thesis supervisors should here describe any current or previous collaboration):

Professor Sylvie Nadeau was the co-supervised of Professor Christina Danielli Coelho de Morais Faria during her doctoral course. Professor Christina did part of her Ph.D. at Université de Montréal (doctorate "sandwich") being supervised by Professor Nadeau at the Pathokinesiology and Functional Movement Analysis Laboratory, Institut de réadaptation de Montréal, Université de Montréal (July 1st, 2007 to July 18 2008). During this period, Professor Christina became active in Professor's Sylvie research team, collaborating with graduate students, performing data collection of research projects and participating in the data analysis and interpretation. Professor Christina collaborated on different research projects supervised by Prof. Sylvie during her stay. The most important projects were: "Enhancement of locomotion through external forces applied to the hip flexor in persons with stroke and SCI" and "assessment of the weight bearing distribution during the sit-to-stand task in healthy and stroke subjects". Professor Nadeau co-supervised the Ph.D. project of Professor Christina: "Development and Validation of a Clinical Instrument to Identify Biomechanical Characteristics and Strategies Adopted by Subjects with Hemiparesis following Stroke during the Timed "Up and Go" test". These previous collaboration resulted in many publications (listed below). At Université de Montréal, Professor Faria took several courses in the Ph.D program. Since 2007, Professor Faria and Professor Nadeau participated together in many scientific events. Professor Nadeau has already visited the Post-graduation Program in Rehabilitation Science at Universidade Federal de Minas Gerais two times and these visited were organized in collaboration with Professor Faria. During the time, she visited Universidade Federal de Minas Gerais and she lectured two workshops that were organized by Professor Christina. She also gave conferences and presented the Graduated program in Sciences de la réadaptation at Université de Montréal. Furthermore, Professors Faria and Nadeau planned new research activities together, such as grant writings and student supervision. Since 2014, in addition to share research data and research ideas, Professor Faria is collaborating in the following research project leaded by Professor Nadeau: "Quantification of locomotor asymmetry in various functional tasks after stroke". Finally, Professor Nadeau has already agreed to collaborate with the following research project that will be supervised by Professor Faria: "Efficacy of aerobic training on physical activity level in individuals affected by stroke: a randomized controlled trial". This research project will be developed during the: Tavares Aguiar's doctorate.

Published articles:

- FARIA, C. D. C. M. ; Teixeira-Salmela, Luci Fuscaldi ; Nadeau, Sylvie . Predicting levels of basic functional mobility, as assessed by the Timed "Up and Go" test, for individuals with stroke: discriminant analyses. Disability and Rehabilitation, v. 35, p. 146-152, 2013.
- Faria, C.D.C.M. ; Teixeira-Salmela, L. F. ; NADEAU, S. . Development and validation of an innovative tool for the assessment of the biomechanical strategies: The TUG-ABS for individuals with stroke. Journal of Rehabilitation Medicine, v. 45, p. 1-9, 2013.
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- **FARIA, C. D. C. M.** ; REIS, D. A. ; **NADEAU, S.** . Performance of hemiplegic subjects on the 180 turn: Effects of the turning side and of a training program. In: THe 12th ISSP Congress of Sport Phsychology, 2009, Marrakech. Proceedings of the 12th World Congress of Sport Psychology. Marrakech, 2009.
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The two thesis supervisors will jointly exercise the responsibilities attributed by their respective institutions to a thesis supervisor.

Article 5 – Course of studies (describe the courses, seminars, etc. in each institution)

Candidate's pedagogical activities

Université de Montréal (courses, seminars, etc.)	Universidade Federal de Minas Gerais
REA 7000 - Critique d'approches en réadaptation	Methods for quantitative analysis I - Introduction to SPSS
	Didactics of University Teaching
	Methods for quantitative analysis II - Introduction to SPSS
	Doctoral seminars
	Teaching internship: Neurology clinical teaching; kinesiotherapy; kinesiology; Neurological dysfunctions applied to Physical Therapy.

In addition to the information given in this document, the Faculty of Graduate and Postdoctoral Studies requires at University of Montreal that the candidate fills a detailed Plan for his course of studies. This plan is to be established and approved by both his supervisors on the relevant sections of the FGPS Modular Plan for course of studies (Plan d'études modulaire), or an equivalent document of the partner institution. The FGPS Modular Plan for course of studies is included at the end of this document.

Comprehensive examination: The comprehensive examination is an essential component of some North American Ph.D program. At the School of rehabilitation at Université de Montréal, it is a requisite for the doctoral program. If the partner institution has the equivalent of this examination, the candidate can choose in which university he will pass it. The jury for this examination is formed jointly by both institutions who agree to recognize its result.

The comprehensive examination will take place: Université de Montréal, Canada, Winter term 2017

Article 6 – Thesis defence

The thesis defence will take place: Universidade Federal de Minas Gerais, Brazil, February/2019

Language of text: English
Language of defence: Portuguese with slides in Portuguese and English
Language of summary: English

- The thesis will be subject to only one defence to be recognized by both institutions. However, the candidate will be expected to present during the course of his studies a seminar at the institution in which the defence will not take place.
- The thesis jury will consist of scientists selected on the basis of their competencies and appointed jointly by the two partner institutions. It shall include the two thesis supervisors as well as an external examiner not associated with either of the institutions. The number of examiners will be determined by the two institutions.

N.B.:

At Université de Montréal, theses may be written in English, with prior authorisation of the faculty concerned.

University of Montreal and the Universidade Federal de Minas Gerais agree on terms for the expenses for the defense related to jury members and external examiner. University of Montreal authorizes the participation to a doctoral defence using the most recent developments in the technologies of communication, such as Skype or videoconference.

Article 7 – Granting of degree

In conformity with the applicable regulation in each country and on the basis of the report from the single thesis defence, the degree of doctor of Université de Montréal shall be conferred on Larissa Tavares Aguiar and the degree of doctor of Universidade Federal de Minas Gerais shall be conferred on Larissa Tavares Aguiar

Each institution will deliver its own set of official documents which shall make reference to the collaboration between the partner institutions in the joint doctoral program as well as the degree conferred by each in the student's field of specialization.

Article 8 – Deposit, registration and reproduction of the thesis

In each country, the deposit, the registration and the reproduction of the thesis shall take place in conformity with the applicable regulations. For the procedures of the Faculty of Graduate and Postdoctoral Studies of Université de Montréal, refer to the "*Guide de présentation et d'évaluation des mémoires et des thèses »* (www.fesp.umontreal.ca).

A. OPTIONAL PROVISIONS

(This section is optional; provisions dealing, for example, with financial aid to the candidate or agreement between institutions for defence expenses may be added here)

The division of the fees accrued by each are to gather the members of the examining committee for the thesis defense shall be carried out under the following conditions:

- **Université de Montréal** : the expenses for the videoconference are admissible and the Faculty of Medicine gives 650$ to pay for the expenses of the thesis.
- **Universidade Federal de Minas Gerais**, through the PhD Program Rehabilitation Sciences, shall assume all expenses that are traditionally taken on for the defense of a thesis in Brazil, including travel within the country and hotel expenses.
- In the case of financial difficulties at the time of the defense, the parties signing this agreement undertake to search all possible means to carry out joint defense of the thesis, with communication resources distance as videoconferencing or Skype

B. ASSINATURAS

Afixadas duas cópias originais deste acordo, versão em Português e Inglês (uma cópia para UdeM e outra cópia para UFMG)

Candidata: _____ 09 / 12 / 2015
Larissa Tavares Aguiar   Data

Université de Montréal:

Orientadora: _____ 27-01-2016
Sylvie Nadeau   Data

Diretor do Colégio Doutoral: _____ 27 / 01 / 2016
Debbie Fedman   Data

Reitor da Universidade: _____ 24 / 01 / 2016
Michèle Brochu   Data

Universidade Federal de Minas Gerais:

Orientadora: _____ 09 / 12 / 2015
Christina Danielli Coelho de Morais Faria   Data

Coordenador da Pós-graduação: _____ 09 / 12 / 2015
Aline Alvim Scianni   Data

Profa. Dra. Aline Alvim Scianni
-coordenadora do Colegiado
Pós-graduação em Ciências da Reabilitação
Inscrição UFMG: 24717-0 SIAPE 2287391

Reitor da Universidade: _____
Jaime Arturo Ramírez   Data

Prof Sandra Regina Goulart Almeida
Vice-Reitora

PLAN FOR COURSES OF STUDIES AT UNIVERSIDADE FEDERAL DE MINAS GERAIS

Student: Larissa Tavares Aguiar   **Supervisor:** Christina DCM Faria

Code	Title	Credits
DTO806	Methods for quantitative analysis I - Introduction to SPSS	2
FIT810	Teaching internship: Neurology clinical teaching - Ambulatório Bias Fortes/Hospital das Clínicas	1
FIT822	Neurosciences and rehabilitation	2
DTO815	Doctoral seminars	2
EFI 816	Exercise physiology	3
FAE914	Didactics of University Teaching	2
DTO806	Methods for quantitative analysis II - Introduction to SPSS	2
FIT810	Teaching internship: Neurology clinical teaching - Ambulatório Bias Fortes/Hospital das Clínicas	1
FIT810	Teaching internship: kinesiotherapy	1
FIT810	Teaching internship: kinesiology	1

Appendix II Academic credits – UFMG

Universidade Federal de Minas Gerais
Pós-Graduação *Stricto Sensu*
Histórico Escolar

Nome do Aluno
LARISSA TAVARES AGUIAR

Número de Registro ▓
Forma de Admissão: EXAME SELECAO
Data de Início: 2015/1 02/03/2015

Filiação ▓

Exame de Língua Estrangeira
02/03/2015 INGÊS

CPF ▓

Identidade ▓
Órgão Emissor ▓
UF MG

Doc. Militar ▓
R.M. 00
Circunscrição ▓
Título de Eleitor ▓
Zona ▓
Seção ▓

Curso
3581 - CIÊNCIAS DA REABILITAÇÃO

Data de Nascimento ▓
Cidade de Nascimento ▓
UF

Nível: DOUTORADO
Data Criação: 18/08/2005
Resolução: 0505

País Nascimento ▓
Nacionalidade ▓

Área de Concentração
DESEMPENHO FUNCIONAL HUMANO

Curso de Graduação
GRADUAÇÃO
20002 - FISIOTERAPIA

Linha de Pesquisa
****

Estabelecimento
UFMG
Término 2012/2

Orientador
CHRISTINA DANIELLI COELHO DE MORAIS FARIA

Cidade/País ▓
UF

Coorientador
SYLVIE NADEAU

Atividades Acadêmicas Cursadas

Ano/Sem.	Descrição	TUR	NAT	CR	CH	FR	NOTA	CONC	SF
2015/1	DIP DTO806 - TOPICOS ESPECIAIS: METODOS DA ANLISE QUANTITATIVA- INTRODUÇÃO AO SPSS	U	OP	2	30	S	94.0	A	A
2015/2	DIP DTO815 - SEMINARIOS DE DOUTORADO	U	OB	2	30	S	84.0	B	A
2015/2	DIP EFI816 - FISIOLOGIA DO EXERCICIO	1	EL	03	45	S	95.0	A	A
2015/2	DIP FIT810 - ESTÁGIO EM DOCÊNCIA	U	OP	4	60	S	100.0	A	A
2015/2	DIP FIT834 - NEUROCIÊNCIAS E REABILITAÇÃO	U	OP	2	30	S	95.0	A	A
2016/1	DIG UNI043 - INGLÊS PARA FINS ACADÊMICOS IV	TA	EL	4	60	S	91.0	A	A
2016/1	DIP DTO806 - TOPICOS ESPECIAIS: METODOS DE ANALISES QUANTITATIVA II- DOUTORADO	A	OP	2	30	S	92.0	A	A
2016/2	ETF GER000 - ELABORACAO DE TRABALHO FINAL								
2017/1	EQP CRE005 - EXAME DE QUALIFICAÇÃO	U	OB						A
2017/1	ETF GER000 - ELABORACAO DE TRABALHO FINAL								
2017/2	ETF GER000 - ELABORACAO DE TRABALHO FINAL								
2018/1	ETF GER000 - ELABORACAO DE TRABALHO FINAL								
2018/2	ETF GER000 - ELABORACAO DE TRABALHO FINAL								
2019/1	ETF GER000 - ELABORACAO DE TRABALHO FINAL								

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COLEGIADO DE PÓS-GRADUAÇÃO EM CIÊNCIAS

Belo Horizonte, ~~16 de Janeiro~~ de 19

AV. ANTÔNIO CARLOS, Nº 627 - CAMPUS UNIVERSITÁRIO
PAM ▓

Secretário(a) ▓

Profa. Dr. ▓
Coordenador/do Programa de Pós-Graduação
em Ciências da Reabilitação- EEFFTO-UFMG
Coordenador(a) Inscrição UFMG 22500-2
Siape 1815812

(Este documento é válido somente com carimbo e assinatura do(a) coordenador(a) do curso ou do DRCA, em todas as páginas)

Legenda:

NAT = Natureza (OP=Optativa, OB=Obrigatória, EL=Eletiva, (*)=extracurricular)
CH = Carga Horária   CR = Créditos   TUR = Turma
FR = Frequência (S=Suficiente, I=Insuficiente)   CONC = Conceito
SF = Situação Final (A=Aprovado, R=Reprovado, T=Trancado, D=Dispensado)

Tipo da Origem da Dispensa ou do Aproveitamento de Créditos
AE = Aproveitamento de Estudo
AM = Aproveitamento de Créditos de Pós-Graduação
EQ = Equivalência

(Até 30/07/1990)		(Após 30/07/1990)	
A - Excelente	(90 a 100)	A - Excelente	(90 a 100)
B - Ótimo	(75 a 89)	B - Ótimo	(80 a 89)
C - Regular	(60 a 74)	C - Bom	(70 a 79)
D - Insuficiente	(40 a 59)	D - Regular	(60 a 69)
E - Rendimento Nulo	(0 a 39)	E - Fraco	(40 a 59)
		F - Rendimento Insuficiente	(0 a 39)

Universidade Federal de Minas Gerais

Pós-Graduação *Stricto Sensu*

Histórico Escolar

Emissão
16/01/2019
Página
2 de 3

Aluno	2015701154	LARISSA TAVARES AGUIAR

Atividades Acadêmicas Cursadas

Ano/Sem.	Descrição	TUR	NAT	CR	CH	FR	NOTA	CONC	SF

** Atividades utilizadas como origem de dispensa

Aproveitamento de Créditos

Ano/Sem.	Créditos	Origem (Tipo, Ano/Sem, Ativ. Acadêmica, Turma)	Data de Aprovação
2019/1	18	AE - 2013/1 EST DTO808	08/01/2019
		AE - 2013/1 EST FIT828	
		AE - 2013/1 EST MVP875	
		AE - 2013/2 EST DTO806	
		AE - 2013/2 EST FIT815	
		AE - 2013/2 EST FIT819	
		AE - 2014/2 EST CRE004	
		AE - 2014/2 EST FIT809	
		AE - 2015/1 EST CRE004	

Estudos

Ano/Sem.	Código/Local/Descrição	CH	CR	NOTA
2013/1	DTO808 UFMG/EEFFTO METODOLOGIA DA PESQUISA	60	04	98
2013/1	FIT828 UFMG/EEFFTO PRATICA BASEADA EM EVIDENCIA EM REABILITAÇÃO	45	03	91
2013/1	MVP875 UFMG/EEFFTO BIOESTATISTICA	60	04	90
2013/2	DTO806 UFMG/EEFFTO TOPICOS ESPECIAIS- MENSURAÇÃO EM CIENCIAS DA REABILITAÇÃO	30	02	88
2013/2	FIT815 UFMG/EEFFTO ATUALIZAÇÕES EM DISFUNÇÕES CARDIORRESPIRATORIAS	45	03	81
2013/2	FIT819 UFMG/EEFFTO MEDIDAS E INSTRUMENTOS DE AVALIAÇÃO I	45	03	95
2014/2	CRE004 EEFFTO/UFMG DEFESA DE DISSERTAÇÃO	75	05	100
2014/2	FIT809 UFMG/EEFFTO INSTRUMENTOS DE MEDIDA E AVALIAÇÃO DO INDIVIDUO COM DISFUNÇÃO NEUROLOGICA	30	02	85
2015/1	CRE004 UFMG/EEFFTO SEMINARIOS DE DISSERTAÇÃO	75	05	100

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COLEGIADO DE PÓS-GRADUAÇÃO EM CIÊNCIAS
DA REABILITAÇÃO / EEFFTO

Belo Horizonte, 16 de janeiro de 19

FP 31270-901 - BH / MG

Secretário(a)

Profa.
Coordenadora do Programa de Pós-Graduação
em Ciências da Reabilitação - EEFFTO-UFMG

Coordenador Inscrição UFMG 22500-2
Siape 1815312

(Este documento é válido somente com carimbo e assinatura
do(a) coordenador(a) do curso ou do DRCA, em todas as
páginas)

Legenda:

NAT = Natureza (OP=Optativa, OB=Obrigatória, EL=Eletiva, (*)=extracurricular)
CH = Carga Horária   CR = Créditos   TUR = Turma
FR = Frequência (S=Suficiente, I=Insuficiente)   CONC = Conceito
SF = Situação Final (A=Aprovado, R=Reprovado, T=Trancado, D=Dispensado)

Tipo da Origem da Dispensa ou do Aproveitamento de Créditos
AE = Aproveitamento de Estudo
AM = Aproveitamento de Créditos de Pós-Graduação
EQ = Equivalência

(Até 30/07/1990)		(Após 30/07/1990)	
A - Excelente	(90 a 100)	A - Excelente	(90 a 100)
B - Ótimo	(75 a 89)	B - Ótimo	(80 a 89)
C - Regular	(60 a 74)	C - Bom	(70 a 79)
D - Insuficiente	(40 a 59)	D - Regular	(60 a 69)
E - Rendimento Nulo	(0 a 39)	E - Fraco	(40 a 59)
		F - Rendimento Insuficiente	(0 a 39)

Universidade Federal de Minas Gerais

Pós-Graduação *Stricto Sensu*

Histórico Escolar

Aluno	2015701154	LARISSA TAVARES AGUIAR

Exame de Qualificação

Resultado Final: APROVADO   Data da Realização: 12/05/2017

Integralização

Créditos Exigidos:	36	Créditos Cursados:	19	Créditos aproveitados/dispensados:	18

Créditos Utilizados para a Integralização: 28

Correspondência Carga Horária/Crédito: 15 Horas / 1 Crédito

Pós - Graduado: NÃO

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COLEGIADO DE PÓS-GRADUAÇÃO EM CIÊNCIAS
DA REABILITAÇÃO/ EEFFTO

Belo Horizonte, 16 de janeiro de 19

Secretário(a)

Profa.

Coordenadora do Programa de Pós-Graduação
em Ciências da Reabilitação- EEFFTO-UFMG

Coordenador(a) Inscrição UFMG 22500-2
Siape 1815812

(Este documento é válido somente com carimbo e assinatura
do(a) coordenador(a) do curso ou do DRCA, em todas as
páginas)

Legenda:

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CH = Carga Horária   CR = Créditos   TUR = Turma

FR = Frequência (S=Suficiente, I=Insuficiente)   CONC = Conceito

SF = Situação Final (A=Aprovado, R=Reprovado, T=Trancado, D=Dispensado)

Tipo da Origem da Dispensa ou do Aproveitamento de Créditos

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AM = Aproveitamento de Créditos de Pós-Graduação

EQ = Equivalência

(Até 30/07/1990)		(Após 30/07/1990)	
A - Excelente	(90 a 100)	A - Excelente	(90 a 100)
B - Ótimo	(75 a 89)	B - Ótimo	(80 a 89)
C - Regular	(60 a 74)	C - Bom	(70 a 79)
D - Insuficiente	(40 a 59)	D - Regular	(60 a 69)
E - Rendimento Nulo	(0 a 39)	E - Fraco	(40 a 59)
		F - Rendimento Insuficiente	(0 a 39)

Appendix III Ethics Certification

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COMITÊ DE ÉTICA EM PESQUISA - COEP

Projeto: CAAE – 51454115.6.0000.5149

Interessado(a): Profa. Christina Danielli Coelho de Morais Faria
Departamento de Fisioterapia
EEFFTO- UFMG

DECISÃO

O Comitê de Ética em Pesquisa da UFMG – COEP aprovou, no dia 09 de março de 2016, o projeto de pesquisa intitulado " **Eficácia do treino aeróbio no nível de atividade física de indivíduos acometidos pelo acidente vascular encefálico: um ensaio clínico aleatorizado**" bem como o Termo de Consentimento Livre e Esclarecido.

O relatório final ou parcial deverá ser encaminhado ao COEP um ano após o início do projeto através da Plataforma Brasil.

Profa. Dra. Telma Campos Medeiros Lorentz
Coordenadora do COEP-UFMG

Av. Pres. Antonio Carlos, 6627 – Unidade Administrativa II - 2° andar – Sala 2005 – Cep:31270-901 – BH-MG
Telefax: (031) 3409-4592 - e-mail: coep@prpq.ufmg.br

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Appendix IV Consent Form for Participants

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO   Nº_____

TÍTULO DO PROJETO DE PESQUISA: "Eficácia do treino aeróbico no nível de atividade física de indivíduos acometidos pelo Acidente Vascular Encefálico: um ensaio clínico aleatorizado"

INVESTIGADORAS:
- Prof.ª Christina Danielli Coelho de Morais Faria, fisioterapeuta, Ph.D. Professora do Departamento de Fisioterapia da Universidade Federal de Minas Gerais (UFMG). Telefone: ▮▮▮▮▮▮▮▮▮▮▮▮

- Prof.ª Raquel Rodrigues Britto, fisioterapeuta, Ph.D. Professora do Departamento de Fisioterapia da UFMG. Telefone: ▮▮▮▮▮▮▮▮▮▮
- Prof.ª Paula Luciana Scalzo, fisioterapeuta, Ph.D. Professora do Departamento de Morfologia da UFMG. Telefone: ▮▮▮▮▮▮▮▮▮▮
- Larissa Tavares Aguiar, fisioterapeuta, aluna do Programa de Pós-Graduação em Ciências da Reabilitação da UFMG. Telefone: ▮▮▮▮▮▮▮▮▮▮
- Júlia Caetano Martins, fisioterapeuta, aluna do Programa de Pós-Graduação em Ciências da Reabilitação da UFMG. Telefone: ▮▮▮▮▮▮▮▮▮▮

INFORMAÇÕES
Você está sendo convidado a participar de uma pesquisa a ser desenvolvida no Departamento de Fisioterapia da Escola de Educação Física, Fisioterapia e Terapia Ocupacional da UFMG, que tem como objetivo avaliar os efeitos do treino aeróbio em pessoas que sofreram derrame (acidente vascular cerebral - AVC).

DETALHES DO ESTUDO
Várias estratégias de reabilitação de indivíduos que sofreram AVC demonstram melhora da capacidade funcional. Contudo, não se sabe qual estratégia de tratamento determina melhores resultados relacionados ao nível de atividade física e ao condicionamento cardiorrespiratório. A partir das informações obtidas neste estudo, será possível indicar o melhor tipo de treinamento para melhora do nível de atividade física e do condicionamento cardiorrespiratório.

DESCRIÇÃO DOS TESTES E DAS INTERVENÇÕES A SEREM REALIZADOS

Avaliação inicial
A avaliação para começar o programa de exercícios será uma coleta de dados pessoais e exame físico, a ser realizada por um examinador treinado. Caso você participe, será necessário responder alguns questionários acerca da sua saúde e da sua funcionalidade. Serão realizados alguns testes e medidas, simples e facilmente realizados para se obter informações sobre as estruturas e funções do seu corpo, as atividades que você realiza com e sem dificuldades e aquelas que você não realiza, assim como sobre o seu nível de participação, comumente empregados na prática clínica dos profissionais da área da saúde. Um dos testes a ser realizado é o teste ergoespirométrico, que tem como finalidade principal avaliar as respostas cardiovasculares frente à aplicação de esforço físico progressivo. Existe a possibilidade do aparecimento de sintomas como cansaço, falta de ar e dor no peito, entretanto, são mínimas as chances de ocorrerem complicações de difícil controle clínico. O teste ergoespirométrico será realizado sob acompanhamento médico. Também será realizada uma coleta de 30ml de sangue e um pouco de saliva, por um enfermeiro com capacidade técnica, seguindo os procedimentos recomendados.

Grupos do estudo
Será realizado um sorteio para saber em qual dos grupos do estudo você fará parte. Durante os meses de participação no estudo, nenhum voluntário poderá participar de outros exercícios, como os que envolvem o fortalecimento muscular ou o treino aeróbico (por exemplo, hidroginástica e musculação).

Procedimentos
Inicialmente, será realizada uma avaliação inicial, em que algumas medidas serão realizadas, como o seu peso e altura, você responderá alguns questionários e desempenhará testes que envolvem atividades rotineiras e que comumente são utilizados na prática clínica do fisioterapeuta. Além disso, você realizará um teste ergoespirométrico sobre a esteira, que será acompanhando por um médico. Finalmente, será realizada a coleta de 30 ml de sangue e um pouco de saliva por um enfermeiro. Em seguida você irá realizar as 36 sessões de exercícios, em grupos de três a quatro participantes, supervisionados por um fisioterapeuta. As sessões serão realizadas três vezes por semana por 12 semanas. Os mesmos procedimentos da avaliação inicial, ou seja, todos os testes e medidas empregados, serão realizados novamente após 12 semanas de intervenção e 4, 12 e 24 semanas após o término da intervenção. Todos procedimentos, testes, medidas e intervenções a serem

_____   _____
Rubrica do Participante   Rubrica do Pesquisador
Christina Faria/Raquel Britto/ Paula Scalzo/Larissa Aguiar/Júlia Martins

realizados no presente estudo são padronizados e comumente adotados na prática clínica ou em estudos científicos já realizados anteriormente. Durante todos os procedimentos, serão considerados a sua segurança e o seu conforto.

Riscos

Os riscos associados com estes testes e com o programa de intervenção são mínimos e similares aos que você está exposto no seu dia a dia. Durante as sessões de treinamento você pode vir a sentir-se cansado. Caso isto aconteça, períodos de repouso serão permitidos. Há um risco de você sentir dor, mal-estar, ou apresentar hematoma no local da punção venosa durante a coleta de amostra de sangue por um técnico de Enfermagem, o qual recebeu o devido treinamento para realizar este procedimento. Qualquer tipo de desconforto vivenciado durante os testes ou treinamento deve ser revelado para que os pesquisadores tomem as devidas providências com o objetivo de minimizá-lo. Caso durante os testes ou treinamento você sofra alguma complicação, como queda ou evento cardiovascular, os pesquisadores irão fornecer o auxílio necessário ou o encaminharão para outros profissionais da saúde, caso seja necessário. Alguns voluntários poderão ser fotografados durante a participação no estudo, para fins de apresentações em eventos científicos. Antes de fotografar, será solicitada a permissão individual para o uso da imagem, através da assinatura de um termo de autorização. A identidade dos voluntários não será revelada.

Benefícios

Você e futuros pacientes poderão se beneficiar com os resultados desse estudo, principalmente porque o objetivo principal do mesmo é determinar a melhor abordagem de tratamento fisioterápico para indivíduos após o AVC. Se após a conclusão do estudo for observado maior benefício alcançado em um grupo em relação aos demais, a intervenção de maior benefício será ofertada para os participantes do grupo controle.

Confidencialidade

Você não será reconhecido pelo nome e recebera um código que será utilizado em todos os seus testes para preservar sua identidade. Se as informações originadas deste estudo forem publicadas em revista ou evento científico, você não será reconhecido individualmente, pois será representado pelo número.

Natureza voluntária do estudo e pagamento

Sua participação neste estudo é voluntária e você é livre para concordar ou não em participar. Caso deseje, você pode abandonar o estudo a qualquer momento, sem que isto lhe traga qualquer prejuízo pessoal. Você não receberá nenhuma forma de pagamento pela participação. Caso seja necessário gastos adicionais serão de responsabilidade dos pesquisadores.

Após ter lido as informações acima, se desejar participar, por favor, preencha e assine a declaração abaixo.

DECLARAÇÃO E ASSINATURA

Eu, _____li e entendi toda a informação repassada sobre o estudo, sendo que os objetivos, procedimentos e linguagem técnica foram satisfatoriamente explicados. Tive tempo suficiente para considerar as informações acima e tive a oportunidade de tirar todas as minhas dúvidas. Estou assinando este termo voluntariamente e tenho direito de agora, ou mais tarde, discutir qualquer dúvida ética que venha a ter com relação à pesquisa com:
  - Comitê de Ética em Pesquisa da UFMG: (31) 3409-4592
Av. Antônio Carlos, 6627 Unidade Administrativa II, sala 2005. Campus Pampulha, BH/MG. CEP 31270-901
Tenho direito de agora, ou mais tarde, discutir demais dúvidas que venha a ter com relação à pesquisa com:
  - Prof. Christina Danielli Coelho de Morais Faria: ███████████████████████
  Av. Antônio Carlos, 6627, Escola de Educação Física, Fisioterapia e Terapia Ocupacional, Departamento de Fisioterapia, Sala 3109. Campus Pampulha, BH/MG. CEP: 31270-901.
  - Larissa Tavares Aguiar: ████████████████
  - Júlia Caetano Martins: ██████████████

Assinando esse termo de consentimento, estou indicando que concordo em participar deste estudo.

_____   _____
          Assinatura do Participante   Data
RG:_____ CPF:_____
End.: _____

_____   _____
Assinatura da Investigadora Responsável   Data
Christina DCM Faria/ Raquel R Britto/ Paula L Scalzo/Larissa T Aguiar/Júlia C Martins

Appendix V Academic credits – UdeM

RELEVÉ DE NOTES

Date d'émission:
Matricule:
CPER QC:

Université de Montréal

Larissa Tavares Aguiar

Relevé des études de cycles supérieurs

Automne 2016

Programme d'études: 374310 - Sciences de la réadaptation (Doctorat)

Cours	Description	Crédits:	Suivis	Obtenus	Note	Points	Moy.gr.
PLU 6150	Rédaction scientifique-anglais	1.000	1.000		A	0.000	
	3-743-1-0 Cours en surplus						
REA 7000	Critique: approches/réadapt.	3.000	3.000		A-	11.100	
	3-743-1-0 Cours obligatoire						

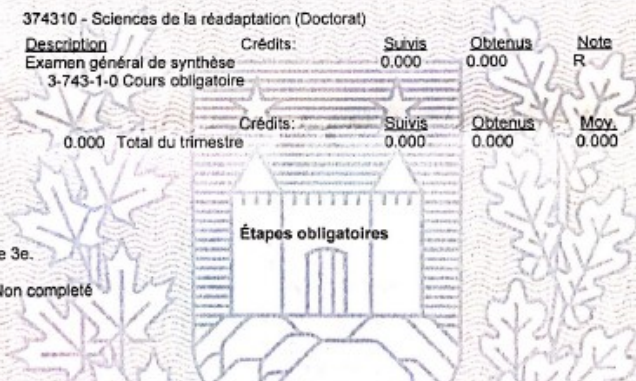|		Crédits:	Suivis	Obtenus	Moy.	Points	
Moyenne générale trimestrielle	3.700	Total du trimestre	4.000	4.000	3.000	11.100	

Hiver 2017

Programme d'études: 374310 - Sciences de la réadaptation (Doctorat)

Cours	Description	Crédits:	Suivis	Obtenus	Note	Points	Moy.gr.
REA 7010	Examen général de synthèse	0.000	0.000		R	0.000	
	3-743-1-0 Cours obligatoire						

		Crédits:	Suivis	Obtenus	Moy.	Points	
Moyenne générale trimestrielle	0.000	Total du trimestre	0.000	0.000	0.000	0.000	

Programme: Mobilité et posture 3e.
Rapport définitif - Thèse
Statut: Non complété

Étapes obligatoires

Sommaire des moyennes et des crédits cumulés par programme d'études

	Trimestre	Moyenne cumulative	Crédits contributoires	Crédits cumulés
374310 - Sciences de la réadaptation (Doctorat)	Hiver 2017	3.700	3.000	4.000

Fin du relevé des études de cycles supérieurs

MARIE-CLAUDE BINETTE
REGISTRAIRE

Pour être officiel, le relevé de notes doit porter le sceau de l'Université et la signature du Registraire. VOIR NOTES AU VERSO   Page 1 de 1

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ÉCHELLE DE NOTATION

CHEMINEMENT AU PREMIER CYCLE	NOTE	VALEUR NUMÉRIQUE	CHEMINEMENT AUX CYCLES SUPÉRIEURS
	A+	4,3	
excellent	A	4,0	excellent
	A-	3,7	
	B+	3,3	
très bon	B	3,0	bon
	B-	2,7	
	C+	2,3	passable
bon	C	2,0	
	C-	1,7	
passable	D+	1,3	
	D	1,0	échec
faible (échec)	E	0,5	
nul (échec)	F	0,0	
échec par absence	F*	0,0	

En vigueur depuis le 1ᵉʳ septembre 1989 (Faculté de droit : septembre 1990)

AUTRES NOTES SANS VALEUR NUMÉRIQUE

AC : accepté	CMP : complet	EXE : exemption	REM : remise
ABA : abandon	(E) : échec	INC : incomplet	(S) : succès
ACC : accompli	EF : évaluation facultative	ND : non déposé	SE : sans évaluation
AJ : ajourné	EPR : en progression	R : réussi	SN : sans notation
ATN : en attente d'une note	EQV : équivalence	REF : refusé	

DÉFINITIONS GENERALES

cheminement	deux cheminements sont possibles : le premier cycle, les études supérieures.
crédit	représente 45 heures consacrées par l'étudiant à une activité de formation, y compris, s'il y a lieu, le nombre d'heures de travail personnel jugé nécessaire par l'Université.
moyenne par programme d'études (moy. cumulative)	consiste en la moyenne pondérée des cours d'un programme d'études. Elle doit être arrondie à la première décimale pour déterminer la progression dans ce programme, tel que le prévoient le Règlement des études de premier cycle et le Règlement pédagogique de la Faculté des études supérieures et postdoctorales.
moyenne trimestrielle	consiste en la moyenne pondérée de tous les cours du trimestre.
trimestres	automne (du 1ᵉʳ septembre au 31 décembre) hiver (du 1ᵉʳ janvier au 30 avril) été (du 1ᵉʳ mai au 31 août)

DÉFINITIONS PROPRES AU RELEVÉ DE NOTES

crédits contributoires	total des crédits qui contribuent au calcul de la moyenne cumulative du programme d'études.
crédits cumulés	total des crédits obtenus associés à ce programme d'études.
date d'octroi	date à laquelle un grade, un diplôme ou un certificat est recommandé par le Conseil de la Faculté et par la suite conféré par le Conseil de l'Université. La date de la tenue du Conseil de l'Université n'apparaît pas au relevé de notes mais uniquement sur le parchemin.
moy.	sous moy. est inscrit le nombre total de crédits qui contribuent au calcul de la moyenne.
points	correspondent à la valeur numérique de la note multipliée par le nombre de crédits du cours. Servent au calcul des moyennes pondérées.

Appendix VI Paper with data collected during the exchange period held at UdeM

Title: Activity monitor placed at the non-paretic ankle is accurate in measuring step counts during community walking in post-stroke individuals: a validation study

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Abstract

Background. Different environmental factors may affect the accuracy of step-count activity monitors (AM). However, the validation conditions for AM accuracy largely differ from ecological environments.

Objectives. To assess and compare the accuracy of AM in counting steps among post-stroke individuals: during different locomotor tasks, with AM placed at the non-paretic ankle or hip, and when walking in a laboratory or inside a mall.

Design. Validation study.

Settings. Laboratory and community settings.

Participants. Twenty persons with chronic hemiparesis, independent walkers.

Methods. 1st session: participants performed level walking (6MWT), ramps and stairs in the laboratory with AM placed at the non-paretic ankle and hip. 2nd session: participants walked a mall circuit, including the three tasks, with AM placed at the non-paretic ankle. The sessions were video-recorded.

Main Outcome Measurements. Absolute difference between the steps counted by AM and the steps viewed on the video-recordings (errors, %); occurrence of errors >10%.

Results. Median errors were similar for the 6MWT (0.86 *(0.22, 7.70)*%), ramps (2.17 *(0.89, 9.61)*%) and stairs (8.33 *(2.65, 19.22)*%) with AM at the ankle. Step-count error was lower when AM was placed at the ankle (8.33 *(2.65, 19.22)*%) than at the hip (9.26 *(3.25, 42.63)*%, *p* =.03). The greatest errors were observed among the slowest participants (≤0.4 m/s) on ramps and stairs, while some faster participants (>1 m/s) experienced the greatest error during the 6MWT. Median error was slightly increased in the mall circuit (2.67 *(0.61, 12.54)*%) compared to the 6MWT (0.50 *(0.24, 6.79)*%, *p* = .04), with more participants showing errors >10% during the circuit (7 vs. 2, *p* = .05).

Conclusions. Step counts are accurately measured with AM placed at the non-paretic ankle in laboratory and community settings. Accuracy can be altered by stairs and ramps among the slowest walkers and by prolonged walking tasks among faster walkers.

Introduction

After a stroke, a low level of physical activity contributes to several secondary physical and psychological disorders, including poor health-related quality of life [1]. Being involved with personally meaningful activities, such as community-based activities [2], is essential for life satisfaction [3]. A person capacity to go into the community is commonly predicted by walking speed [2,4]. After a stroke however, there is often a discrepancy between what a person can do (motor capacity, such as clinical walking speed tests) and what a person actually does (motor performance) during the day [5,6]. The number of steps individuals take during the day is a good indicator of community-based activities and walking performance [7,8], and thus informs clinicians about the related physical and psychological components of health [1,9]. Healthcare professionals and researchers need precise devices, evaluated by well-defined protocols, to assess and inquire on walking performance in the community. Ideally, the devices should be precise regardless

of the individuals' sensorimotor and functional levels of deficit, which are heterogeneous among post-stroke individuals [10].

Previous studies have revealed that consumer-based activity trackers are inaccurate in monitoring walking activity in slow walkers (<0.8 m/s) [11,12]. In this context, one activity monitor has received particular attention. When the evaluated device is placed at the hip (as recommended by the manufacturer) in older healthy subjects walking slower than 0.8 m/s, its step error rate is higher than 10% [13] (i.e. arbitrary threshold used previously and considered acceptable [14]). The inaccuracy of the monitor when placed at the hip while walking slowly is a significant limitation considering that many individuals with disabilities, including those with post-stroke hemiparesis, have a self-selected gait speed under 0.8 m/s [15]. The error rate of the evaluated monitor tested with short distances (15 m) and in a straight-ahead direction became acceptable (<10%) for speeds as slow as 0.4 m/s when the device was placed at the right ankle in older healthy adults [13] or at the non-paretic ankle in post-stroke individuals [16]. This observation was recently replicated in a clinical context. During post-stroke rehabilitation physical therapy sessions, with at least 30 minutes of gait retraining, the mean difference (standard deviation *(SD)*) between the actual number of steps and the count provided by the monitor was 10.9 *(5.3)*% for the slowest participants (walking speed <0.4 m/s, n = 12 participants) and 6.8 *(3.0)*% for participants with a walking speed between 0.4 and 0.8 m/s (n = 7) [17]. Placing the evaluated monitor at the non-paretic ankle was thus considered as appropriate for monitoring walking activities in post-stroke individuals in a rehabilitation setting.

It must be noted that the validation conditions proposed in the literature largely differ from daily ambulatory activities in the community. Ambulatory factors that individuals encounter when out in the community such as ramps and stairs [18] are known to affect the accuracy of consumer-based monitors [19,20]. Most activity monitors fail to count steps properly on stairs, ranging in error from 10% to 41% in healthy adults [14]. A more distal placement of the monitor, rather than it being on the hip, has also been suggested to improve step-count accuracy on stairs [20], but this has yet to be tested. Another issue is that most studies report having tested monitors accuracy over a short distance (15 m) with the monitor placed at the ankle while walking on level ground. Only one study investigated the validity of monitors in measuring step counts during the 6-

minute walk test (6MWT), among inpatients including some post-stroke individuals [21]. This may indeed represent the minimal distance required for outings in the community after discharge [6,22]. However, an even better strategy would be to test the accuracy of the monitor in real-life situations where different aspects of locomotion are encountered such as walking with abrupt changes in speed and direction (to avoid other pedestrians, for example), as well as ramps and stairs. These factors might affect the activity monitor accuracy compared to walking straight ahead over a long distance such as during the 6MWT [23]. Thus, the accuracy of the monitor should be tested in a real-life setting to adequately portray what post-stroke individuals have to deal with as they go about their daily activities.

The aim of this study was thus to assess and compare the accuracy of an activity monitor in counting steps among post-stroke individuals: during different locomotor tasks (walking for a long period of time (6MWT), going up and down a ramp and going up and down stairs), with the evaluated activity monitor placed at the non-paretic ankle or hip (first part of the study), and when walking in a laboratory or inside a shopping mall (second part of the study). The hypotheses were that the accuracy of the monitor placed at the ankle would be 1) similar between tasks, 2) better compared to the hip placement. In addition, step count would be less accurate in the ecological situation compared to the controlled clinical situation. The relationship between ecological and clinical accuracy was tested as well.

Method

Participants and settings

This cross-sectional study was conducted from August 2016 to August 2017. Recruitment of a convenience sample of participants (n = 20) was conducted via: 1) the consultation of a list of hemiparetic persons who previously participated to other projects and agreed to be contacted again, 2) the diffusion of the presentation pamphlet of the study among a local exercise group for people with hemiparesis. Eligibility criteria were: at least 6 months post stroke, ability to walk independently and safely in the community (with or without a walking aid), and presence of residual sensorimotor deficits at the paretic lower

limb. Individuals with additional disorders (orthopedic, musculoskeletal, etc.) that could affect their locomotor abilities were excluded. Participation included two sessions (separate from 7 to 10 days), at two different locations. The first session took place inside our gait analysis laboratory. The second session took place inside a shopping center *(#1 - affiliation suppressed – blinded peer-review)*. Residual lower-limb motor function was assessed with the Chedoke-McMaster Stroke Assessment during the first session (**Table 1**). Ethics approval was obtained from the Ethics Committee of the *(#2 - affiliation suppressed – blinded peer-review)*, and written informed consent was obtained from all participants.

Device

The monitor used in this study (Fitbit® One) is a small (4.8 × 1.9 × 1.0 cm), commercially available device containing a tri-axial accelerometer that converts inertial characteristics of movement into step counts based on proprietary algorithms. This low-cost piece of equipment is easy to use and provides immediate feedback about the number of steps.

Procedure

For the laboratory session, two monitors were attached by a clip (on the back of the device) to the participant's sock (ankle placement) and to the front pocket (or waist) of the participant's pants (hip placement) on the non-paretic side. Participants were asked (randomly) to go up and down an access ramp (four times) and up and down a set of four steps (four times) in our laboratory. Each participant also completed the 6MWT (back and forth over a 30-m path) in a quiet corridor.

For the session at the shopping center, the monitor was attached by its clip to the participant's sock on the non-paretic side. A circuit inside the shopping mall was chosen. It involved going up and down an access ramp (twice), going up and down eight steps (twice), walking on level ground on two different floors (transition by elevator) to reach a grocery store, and then going back through the circuit encountering all the same obstacles (**Appendix 1**). The total distance of the circuit was 615 m. Participants were asked to walk at their self-selected walking speed, "as if they were alone and out shopping." They were told that they could rest as often and as long as necessary.

Data collection

Step counts displayed on the monitors were observed and recorded before and after the 6MWT, ramp and stair tasks in the laboratory and before and after the circuit inside the mall. The tasks were video-recorded (Samsung, HMX-QF20) by a research assistant who followed the participant with a camera.

Data analysis

For each task, the step count was the difference in the number of steps displayed on the monitor between the beginning and end of the task (Steps$_{Fitbit}$). The number of steps counted on the video-recordings (Steps$_{Video}$) was used as a reference. A step was counted when the heel or toes (having left the ground) struck the ground again [14]. Two independent reviewers counted the steps taken by the non-paretic leg (i.e. the one wearing the monitor) based on the video-recordings for the circuit and 6MWT tasks. For each participant, if the difference between the two reviewers' counts was greater than one step for the mall circuit or the 6MWT, a consensus was reached following a second viewing of the video recording and a discussion with a third viewer. When no further discussion was needed, one of the reviewers then counted the steps from the videos for the ramp and stair tasks. To obtain the total number of steps, the number counted on the video (i.e. non-paretic steps) was doubled and then compared with the step count recorded on the monitors.

Walking speed was also calculated during level walking. The 6MWT walking speed was obtained by dividing the distance covered during the test by 360 seconds. In addition, the circuit walking speed was measured based on the video-recordings by using the average time it took participants to walk along two, marked 10-m sections during the first part of the circuit.

Gait pattern was assessed subjectively by a physical therapist researcher (N.C.D.) with 8-years experience. She viewed the video recordings of the participants walking along the two, marked 10-m sections of the circuit, categorized their gait as "normal" or "abnormal" [24] and described the main disturbances [25] (**Table 1**). In addition, the walking aid and strategy used by the participants to go up and down the stairs (step-over-step (SOS) or step-by-step (SBS)) was noted (**Table 1**).

Statistical analysis

The accuracy of the monitor was assessed for each task using an error value calculated as: (absolute value $|Steps_{Fitbit} – Steps_{Video}|$) / $Steps_{Video} \times 100$. A positive value for the difference between $Steps_{Fitbit}$ and $Steps_{Video}$ indicated over-counting, with extra steps being detected by the Fitbit® One monitor. A negative value indicated under-counting by the monitor (missed steps). Both over- and under-counting were errors. We thus chose to consider absolute difference values in order to calculate the error rate (%) in the analysis. An error rate lower than 10% was interpreted as acceptable [14,16]. Normality of the distribution of errors was checked for all tasks with a Shapiro-Wilk test, revealing that non-parametric statistics were indeed required.

Descriptive statistics were used for each task (i.e. median, first quartile (Q1) and third quartile (Q3)). The interquartile range (IQR) was defined by Q3 - Q1. Any error that fell more than 1.5 times the IQR below Q1 or above Q3 was considered as an outlier value. For boxplot representations, the adjacent values were defined as the highest value above Q3 which was not an outlier, and the smallest value below Q1 which was not an outlier.

In the first part of the study, a Friedman ANOVA was used to assess whether the errors varied with the ambulatory tasks. Spearman rank-order correlation coefficients were used to estimate whether errors during the 6MWT, ramp and stair tasks were correlated. A Wilcoxon signed-rank test was used to compare errors between ankle monitor placement and hip monitor placement, during the 6MWT, ramp and stair tasks. For the Wilcoxon test, participants were excluded of the analysis in case of missing data in at least one condition. To determine the influence of gait pattern and stair strategy on the error, we also assessed whether gait pattern influenced accuracy of the device using a visual analysis.

In the second part of the study, a Wilcoxon signed-rank test allowed for the comparison of errors during the circuit at the mall and the 6MWT. A Spearman rank-order correlation coefficient was calculated to estimate their relationships. In addition, the number of "unacceptable" errors (>10%, [14]) in the group was compared between the 6MWT and the circuit with a Chi-squared test. Statistical analyses were performed using IBM SPSS Statistics 24.0 software. Significance was set at an alpha level of < .05. Details

relating to number of steps in each task (**Table SI**) as well as Bland-Altman plots (**Figure SI**) are presented in supplementary data.

Results

Twenty participants were recruited. For data collection of the first seven participants, the monitor placed at the hip was not used. In addition, technical difficulties with the monitor lead to inappropriate data collection in three participants: their data in the ramp and stairs tasks were excluded from the analysis. Among the next thirteen participants, one did not participate in the second session due to his lost of interest in the study (**Table 1**).

With the evaluated monitor placed at the hip (n = 13), the errors (i.e. absolute difference between the steps counted by the monitor and the steps viewed on the video-recordings, %) were lower during the 6MWT than during the ramp and stair tasks ($\chi^2(2) =$ 7.54, $p = .02$; post-hoc analysis: $z = -2.48$ and -2.55, $p = .008$; **Figure 1**). The errors were significantly correlated between the 6MWT and ramp task ($r_s = .61$, $p = .02$) and the ramp task and stair task ($r_s = .61$, $p = .03$). With the monitor placed at the ankle (n = 17), the errors were similar during the 6MWT, ramp and stair tasks ($\chi^2(2) = 5.76$, $p = .06$; **Figure 1**). The errors observed during the different tasks (6MWT, ramp and stairs) were not significantly correlated (p > .33).

Step count errors were significantly decreased with the monitor placed at the ankle (median *(Q1, Q3)*: 8.33 *(2.65, 19.22)* %) compared to it being placed at the hip (9.26 *(3.25, 42.63)* %) when going up and down stairs ($z = -2.13$, $p = .03$; **Figure 1**). Of the 93 *(20)* steps (mean *(SD)*) taken by the participants to go up and down the stairs, 78 *(28)* steps were counted by the monitor placed at the ankle whereas only 61 *(30)* were counted by the monitor placed at the hip (**Table S1**). During the 6MWT and ramp tasks, the placement of the monitor did not significantly affect the error ($z = -0.31$, $p = .75$ and $z = -1.57$, $p = .12$, respectively).

Individual data (**Figure 2**) for ankle and hip placements revealed that for the two slowest participants (1. and 2., walking speed ≤0.4 m/s; each walked with a specific gait pattern: circumduction vs. shuffling; both climbed stairs using a SBS strategy), the monitor underestimated the step count by more than 50% during the ramp and stair tasks. One

participant (5.) climbed stairs using a SBS strategy and had an acceptable error (3.0%) when the monitor was placed at the ankle. All participants walking slower than 0.8 m/s had an acceptable error during the 6MWT with the monitor placed at the ankle whereas some participants with faster walking speeds (>0.8 m/s; 15. and 16.) also experienced an unacceptable error. All participants who walked faster than 0.8 m/s had an acceptable error during the 6MWT with the monitor at the hip.

The errors that occurred during the circuit inside the mall (2.67 *(0.61, 12.54)* %, n = 19) were significantly superior to the errors that occurred during the 6MWT (0.50 *(0.24, 6.79)* %, z = -2.61, p = .04; **Figure 3-A**). The participants took an average of 1532 *(423)* steps during the circuit which were counted as 1441 *(373)* steps by the monitor. For the 6MWT, the number of steps was 617 *(152)* whereas 588 *(144)* steps were counted by the monitor (**Table 2**). The correlation between the errors obtained during the circuit and the 6MWT was significant (r_s = 0.77, p < .01), but a >10% error rate occurred more frequently during the mall circuit (7/19 participants: 1., 3., 14., 13., 8., 15. and 17., 37% of the sample) than during the 6MWT (2/19 participants: 15. and 17., 10.5% of the sample; χ^2 = 3.83, p = .05; **Figure 3-B-C**). When the error was unacceptable during the 6MWT, it was also unacceptable during the circuit (**Table 3**). Except for one participant during the circuit (11., overestimated step count; **Table 2**), errors greater than 10% were always an underestimation of the steps counted by the monitor. These errors were observed for the slowest participants (circuit) and for some of the fastest participants (6MWT and circuit). We did not find any specific gait abnormalities associated with these findings.

Discussion

The main results of this study are: 1) When counting steps on stairs, the evaluated monitor was more accurate when it was placed at the ankle than when it was placed at the hip, on the non-paretic side. However, step counts during other locomotor tasks overall were not influenced by the position of the monitor; 2) For very slow walkers (≤0.4 m/s), the monitor placed at the non-paretic ankle accurately measured the number of steps during level walking, but not during other locomotor tasks; 3) For faster walking participants (>0.8 m/s), step count errors were always considered as acceptable with the device positioned at the hip during level walking, but not when it was placed at the ankle. 4) Step-count errors

observed during the 6MWT and throughout the circuit in the community were significantly correlated but were considered unacceptable (>10%) more frequently during the circuit.

Our group of participants adequately represented the heterogeneity of walking capacity among post-stroke individuals. Their walking speeds in the community ranged from 0.3 m/s to 1.2 m/s, and up to 1.7 m/s during the 6MWT. They generally used various walking aids and had different gait abnormalities when walking on level ground (shuffling, stiff knee, hip hike, etc.) and on stairs (step-over-step, step-by-step or a mix of both). It was relevant to include several walking capacities to support the generalizability of our results since slow walking speeds (<0.8 m/s), walking aids and post-stroke gait abnormalities are known to affect step count accuracy by monitors and pedometers [24,26]. Activity monitors step counting requires an automatic detection of steps in accelerometric signals. It might be possible that step count would be more altered among populations walking with high gait variability, like people older than the recruited sample [27] or with less chronic hemiparesis [28].

Placing the monitor at the ankle improved its accuracy in counting steps on stairs, as shown by the comparison conducted on data obtained when the monitor was located at the hip (position recommended by the manufacturer). When placed at the hip, the evaluated monitor accuracy in counting steps was inconsistent between participants, with a median error of 10% indicating that the monitor miscounted the steps in half of the subjects. As for the slowest participants, the error rate reached 100%, which means that no step was counted by the monitor when the subject went up and down stairs. This is consistent with earlier results observed in healthy subjects [14,20]. The acceleration at the hip might be too low to be detected as a step, and a more distal placement of activity trackers has been suggested to improve performance, given that higher accelerations occur at more distal segments when going up and down stairs [29]. However, in a previous study, the placement of a spring-levered pedometer at knee level in stroke and healthy adults failed to improve the consistency of step counts on stairs. In addition, there was no relationship between the number of steps on the stairs and the number of steps counted, regardless of the hip or knee position of the tracker [30]. It seems that placing the monitor at the ankle, as tested in our study, reduces the errors that occur but no one position provides an acceptable step count on stairs for participants walking under 0.4m/s. The errors were also not acceptable when

participants with a speed under 0.4 m/s walked on a ramp. The ramp slope in the laboratory was set to 11% and may have therefore altered the accuracy of the step count as suggested by Leicht and Crowther[19] with inclinations ≥ 9%. The slope of the ramp may alter the accelerometric pattern of the step during slow walking and contribute to an inaccurate step count. The proprietary algorithms used by the monitor are confidential, but the failures that lead to the errors in ramp and stair tasks might be different, since errors in both tasks were not correlated when the monitor was placed at the ankle. In addition, algorithms are specific to each company and monitor, and the effect of monitor placement and locomotor tasks on step-counting accuracy of other monitors than the one evaluated in this study should be further explored within a larger sample and including a larger proportion of slow walkers.

In contrast with previous studies [13,16], placing the monitor at the ankle did not significantly decrease the step count error while walking on a level ground. However, individual data revealed that for the slowest walkers (<0.8 m/s during the 6MWT), step count errors which were >10% with the monitor at hip level, were lower than 10% with the monitor at the ankle. This result supports placement of activity monitors at the non-paretic ankle to count steps accurately among post-stroke individuals walking slower than 0.4 m/s on level ground for longer periods of time. However, these observations were different among those who walked faster than 0.8 m/s, suggesting that monitors should be placed at the hip among these participants to ensure an accurate step count. A practical recommendation should be to assess gait speed and place the activity monitor on the hip or ankle according to the speed measured. The lack of a significant difference between errors with the monitor placed at the ankle and hip is probably affected by the small sample size and the heterogeneity of the observed errors. However, the difference between the two placements is evident in slow walkers. This suggests that slow and fast walkers should be considered in separate groups in future studies. Further analysis of acceleration time-series data might help to clarify why the ankle position of the evaluated monitor is not the best position for counting steps in faster post-stroke walkers.

Walking in the community is a more complex task than the 6MWT. For example, it included situations where participants turned with successive movements of the non-paretic foot on the floor, slightly rotated without any sagittal acceleration or moved in the elevator with multiple small backward steps. We counted all these foot movements as a step. These

situations probably contributed to the error obtained in the circuit task. Similar difficulties have already been observed during household activities when performed at slow ambulation speeds and with shuffling-like steps. In these cases, lower step count accuracy has been reported with monitors [14]. One limitation of the study is that it is not possible to infer on step counts to determine when exactly the steps were missed, since the monitor display screen was only viewed at the beginning and the end of the circuit. However, the observations made during the ramp and stair tasks in the laboratory suggest that step counts during these locomotor activities might be more problematic than during level walking. Overall, our results highlight the need for improvements in activity monitor algorithms to allow quantification of walking activity in realistic and ecological conditions regardless of walking speed and gait deviations of individuals post stroke.

The errors obtained during the community-based circuit give a realistic indication as to the quantity of steps that might be miscounted by the monitor during a period of monitoring. However, another limitation of this study is that the characteristics of the circuit chosen in the community might have increased the error reported for slow walkers. Indeed, the circuit required participants to go up and down the ramp and stairs four times each, and steps were likely not accurately counted by the monitor, as shown in the first part of the study. In a real-life situation, a person with mobility disabilities would likely have used stairs only once while at a shopping center [31]. Therefore, a fewer number of steps would be missed compared to the proposed circuit. In addition, considering the barrier that stairs represent for physical activity after stroke [18], slow walkers are less likely to climb stairs frequently than the faster walkers. The inability of the monitor to accurately count steps on stairs in very slow walkers might have a minor impact on the value obtained after a monitoring period where stairs and ramps are encountered less frequently. A recent study recommended assessing agreement between the step counts recorded by an activity monitor and the steps counted by a therapist before any activity monitoring [21]. Our results suggest that a 6MWT could be an appropriate test and further studies are needed to confirm if the error observed during the 6MWT is predictive of the actual error in a real-life setting.

In conclusion, placing the monitor at the ankle seems to be the more appropriate position for counting steps during the three tested ambulatory activities (walking for a long period, going up and down a ramp and going up and down a set of stairs). In most of the

participants, the inaccuracy of the step count observed in a real-life setting is small enough to enable health professionals to appropriately infer on walking performance in the community among post-stroke individuals after discharge and long-term follow-up. However, steps can be inaccurately counted during different activities, such as stairs among slow walkers and long periods of walking among faster walkers. The impact of these inaccuracies on monitored walking activity should be considered individually with regard to daily ambulatory activities. In this perspective, proprietary algorithms should be improved for monitoring other activities other than level walking among slow individuals.

Table 1: Individual participant characteristics and missing data (according with the monitor's placement and task performed)

	Age (years)	Gender	Time post stroke (months)	Side of hemiparesis	CMSA (Leg /7 – Foot /7)	Distance covered in 6 minutes (m)	Gait abnormalities (main disturbance)	Walking aid	Stair strategy	Missing data (if any)
1.	40	F	16	R	6 – 2	120	Circumduction	Quad cane	SBS	
2.	60	M	65	L	6 - 4	157	Shuffling	Stick	SBS	
3.	57	M	76	R	3 - 2	162	Knee hyperextension	Stick	SBS	Hip
4.	54	M	38	L	4 - 3	201	Circumduction	Quad cane	SBS	Hip + Ramp/stairs
5.	52	F	55	L	3 - 1	219	Stiff knee	Stick	SBS	
6.	71	F	169	L	6 - 6	219	Shuffling	Stick	SOS and SBS	Hip + Ramp/stairs
7.	47	M	65	R	6 - 7	330	Circumduction	English cane	SOS and SBS	Hip
8.	60	F	389	R	5 - 3	336	External rotation	None	SOS	
9.	62	M	58	R	5 - 1	374	None	None	SOS and SBS	Hip + Ramp/stairs
10.	57	M	17	R	6 - 2	387	None	None	SOS	Mall's circuit
11.	60	M	89	L	6 - 6	387	Circumduction	None	SOS	
12.	68	M	9	L	6 - 5	387	None	None	SOS	
13.	66	F	79	L	6 - 6	459	None	Stick	SOS	
14.	56	M	78	L	6 - 6	474	Asymmetries	None	SOS	
15.	29	F	60	L	4 - 2	480	None	Stick	SOS	
16.	42	M	67	R	6 - 6	510	External rotation	Stick	SOS	Hip
17.	41	F	231	L	4 - 3	510	Hip hiking	None	SOS	
18.	58	M	65	L	7 - 5	546	None	Stick	SOS	
19.	60	M	122	L	7 - 6	594	External rotation	Stick	SOS	Hip
20.	37	M	X	L	6 - 3	622	None	None	SOS	
Group	**53.9** *(10.8)*	**7F / 13M**	**92.0** *(86.6)*	**7R / 13L**	**5.3** *(1.2)* – **3.9** *(1.9)*	**373.7** *(148.9)*	**7 normal / 13 abnormal**	**12 with / 8 without**	**12 SOS / 8 other strategy**	

CMSA: Chedoke McMaster Stroke Assessment; F: Females, M: Males; "X" indicates non-appropriate data (stroke at birth); R: right, L: left; SOS: step-over-step, SBS: step-by-step.

Table 2: Description of walking performance among participants (n = 19) during the 6MWT and through a complex circuit in the community, including the number of steps taken by participants (Steps$_{Video}$), steps counted by the Fitbit® One monitor (Steps$_{Fitbit}$) placed at the ankle on the non-paretic side, the monitor's rate of error (%) and the walking speed of participants. Walking speed was calculated during the 6MWT and on two, level-ground 10-m sections at the beginning of the circuit. Mean *(SD)* and median *[Q1, Q3]* values are reported for the entire group.

	StepsVideo		StepsFitbit		Error (%)		Walking speed (m/s)	
	6MWT	Circuit	6MWT	Circuit	6MWT	Circuit	6MWT	Circuit
1.	314	1920	287	1495	8.60 (-)	22.14 (-)	0.33	0.34
2.	410	2262	409	2068	0.24 (-)	8.58 (-)	0.44	0.37
3.	402	2516	400	2229	0.50 (-)	11.41 (-)	0.45	0.42
4.	430	1866	432	1782	0.47 (+)	4.50 (-)	0.56	0.49
5.	516	1994	515	1969	0.19 (-)	1.25 (-)	0.61	0.54
6.*	440	624*	442	631*	0.45 (-)	1.12 (-)	0.61	0.64
8.	640	1308	641	1304	0.67 (+)	0.00 (-)	0.92	0.95
9.	798	1308	794	1332	0.34 (-)	0.00 (-)	0.93	1.07
10.	596	1640	594	1640	0.16 (+)	0.31 (-)	1.04	0.82
11.	600	1414	604	1414	6.79 (-)	12.90 (+)	1.08	0.80
12.	780	1488	727	1296	1.40 (+)	12.54 (-)	1.08	1.00
13.	642	1734	585	1522	0.00 (-)	0.61 (-)	1.08	1.02
14.	690	1308	690	1300	8.88 (-)	12.23 (-)	1.28	1.02
15.	712	1268	722	1427	0.50 (-)	1.83 (-)	1.32	1.01
16.	860	1326	812	1294	**31.17 (-)	24.96 (-)	1.33	1.14
17.	770	1386	762	1423	5.58 (-)	2.41 (-)	1.42	1.20
18.	710	1242	582	1067	0.15 (-)	0.16 (-)	1.52	1.21
19.	738	1242	508	932	1.04 (-)	2.67 (+)	1.65	1.09
20.	668	1256	667	1254	**18.03 (-)	14.09 (-)	1.73	1.15
Group :	**617**	**1532**	**588**	**1441**	**0.50**	**2.67**	**1.02**	**0.86**
	(152)	*(423)*	*(144)*	*(373)*	*[0.24, 6.79]*	*[0.61, 12.54]*	*(0.41)*	*(0.29)*

*: Steps were counted through half of the circuit only, because of technical difficulties with Fitbit® One; **: Data considered as outliers in the statistical analysis; (-): when the monitor missed some steps; (+): when the monitor over-counted*

Table 3: Occurrence of acceptable and unacceptable errors in step counting with Fitbit® One placed at the ankle (n = 19).

		Circuit		
		< 10%	> 10%	Total
6MWT	< 10%	12	5	17
	> 10%	0	2	2
	Total	12	7	**19**

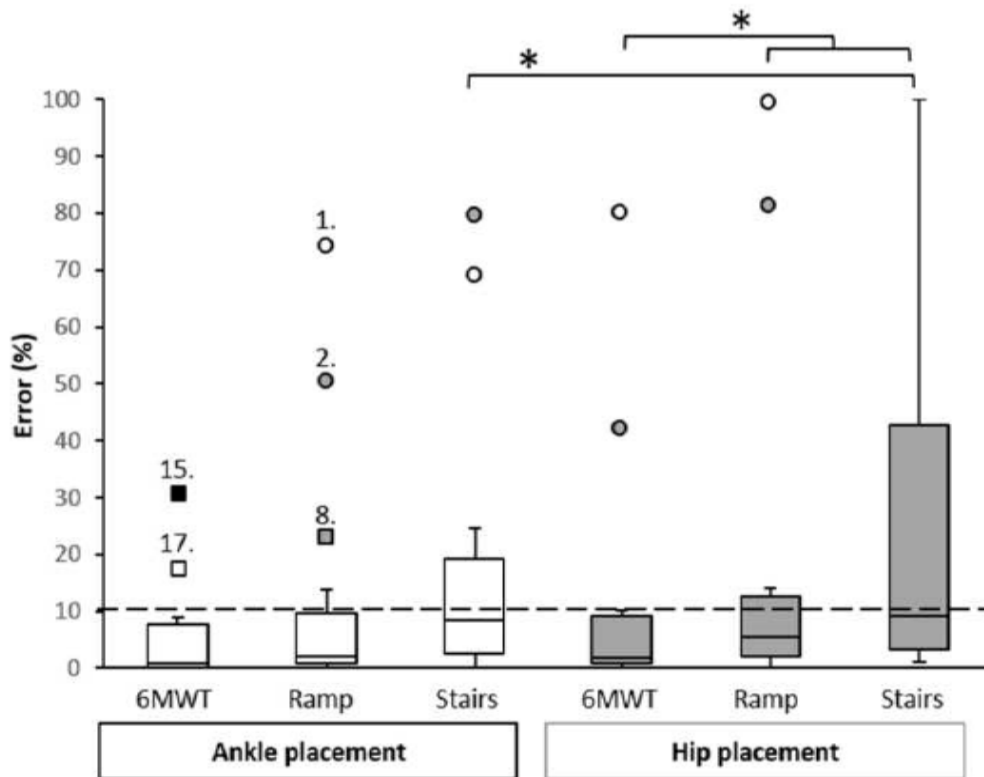6MWT: 6-minute walk test; 10%: acceptable threshold.

Figure 1: Error boxplots (%) (with median, first (Q1) and third (Q3) quartiles, adjacent values and outliers) for steps counted by the monitor, when placed at ankle level (white columns, n = 17) or at hip level (grey columns, n = 13) on the non-paretic side, relative to the number of steps taken by individuals post stroke, during the 6-minute walk test (6MWT), going up and down a ramp and up and down stairs. The 10% dashed line represents the threshold for an acceptable error. * indicates a significant difference between conditions. There were outlier values (i.e. more than Q3 + 1.5*inter-quartile range) among the slowest participants (≤ 0.4 m/s during the 6MWT, circle) and participants with a walking speed > 0.8 m/s during the 6MWT (square), who are each represented by a color and their labels.
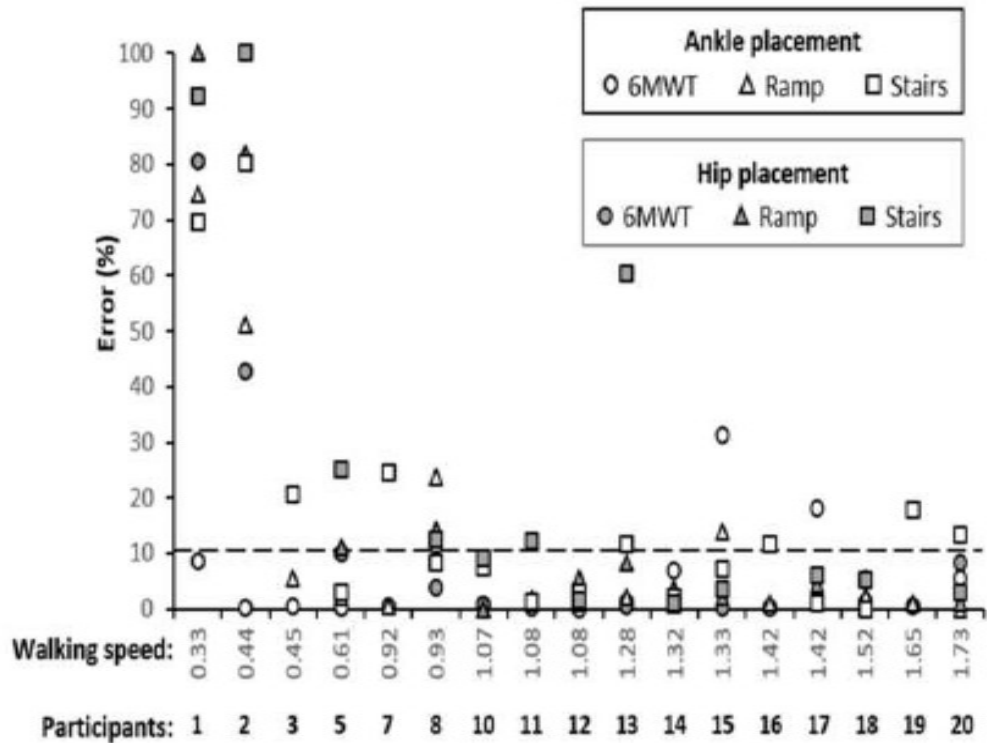
Figure 2: Error (%) made by Fitbit® One when placed at the ankle (white fill, n = 17) and at the hip (grey fill, n = 13) on the non-paretic side of each participant while walking for 6 minutes (6MWT - circles), going up and down a ramp (triangles) and going up and down stairs (squares). The walking speed during the 6MWT is indicated at the bottom, with the label of the participants.
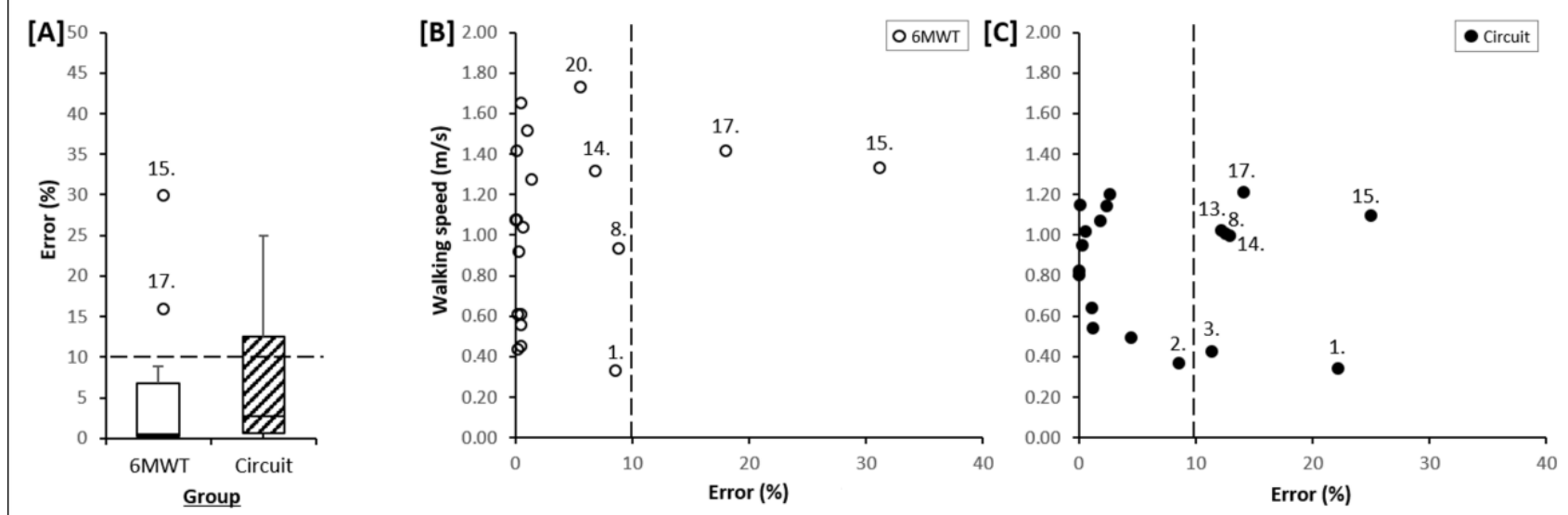
Figure 3: Error (%) for steps counted by the monitor, when placed at the ankle on the non-paretic side of individuals post stroke (n = 19) while walking for 6 minutes in a quiet corridor (6MWT, white) and through a complex circuit in the community (black): [A] For the group with boxplots (with median, first and third quartiles, adjacent values, and outliers); [B] On an individual level with respect to the walking speed during the 6MWT and [C] the circuit. The 10% dashed line represents the threshold for an acceptable error. Participant labels were added for data close to or higher than the 10% threshold.

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Appendix 1:

Total distance of the circuit: 615 m
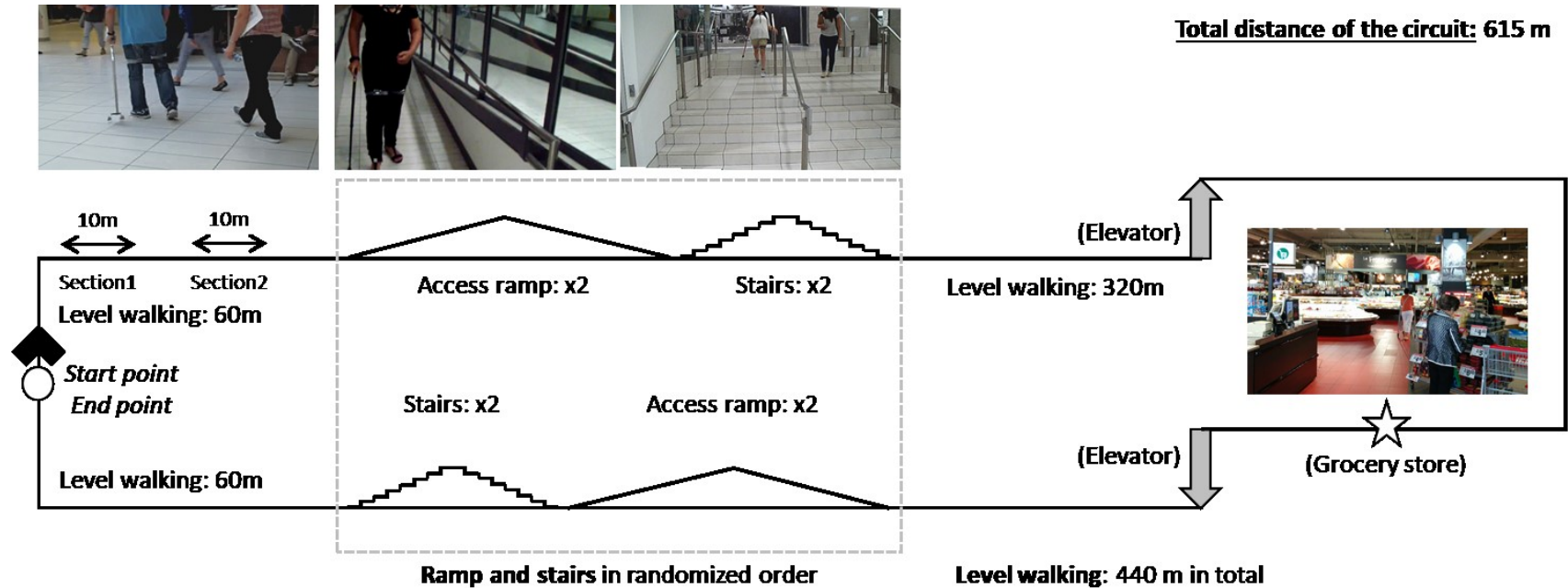
Description and illustration of the circuit with various locomotor activities (level walking, going up and down a ramp and up and down stairs) chosen in the shopping mall *(#3 – affiliation suppressed – blinded peer-review)*. The black arrow indicates the direction of the circuit. The circuit walking speed reported in this study was calculated by using the average time it took participants to walk through two, 10-m sections in the first part of the circuit (measured afterwards using the video-recording).

Supplementary table:

Table SI: Steps counted on the video-recordings (Steps$_{Video}$) and by the monitor (Steps$_{Fitbit}$) placed at the ankle and hip levels, during the clinical 6-minute walk test (6MWT), going up and down a ramp (four times) and four stairs (four times) for the participants that were included in the first part of the study (n = 12).

Participants	6MWT			Ramp			Stairs		
	Steps$_{Video}$	Steps$_{Fitbit}$ Ankle	Steps$_{Fitbit}$ Hip	Steps$_{Video}$	Steps$_{Fitbit}$ Ankle	Steps$_{Fitbit}$ Hip	Steps$_{Video}$	Steps$_{Fitbit}$ Ankle	Steps$_{Fitbit}$ Hip
#1	314	287	61	186	47	0	132	40	10
#2	410	409	235	198	97	36	116	23	0
#5	516	515	464	134	137	119	132	128	99
#8	640	641	634	102	103	100	74	75	83
#9	780	727	768	114	115	118	88	86	87
#10	712	722	715	132	135	121	78	69	31
#11	690	690	677	108	107	102	64	62	65
#12	642	585	618	106	81	91	96	88	84
#14	738	508	737	94	81	92	56	52	54
#15	860	812	789	94	94	93	68	59	66
#17	770	762	759	92	90	87	78	78	74
#18	710	582	696	92	90	88	98	97	92
Mean	**649**	**603**	**596**	**121**	**98**	**87**	**90**	**71**	**62**
SD	*153*	*148*	*220*	*35*	*23*	*34*	*24*	*26*	*31*

Supplementary figure:

Figure S1: Bland-Altman plots with the mean step counted based on video-recordings (Steps$_{Video}$, gold standard) and by the monitor (Fitbit® One, Steps$_{Fitbit}$) on the horizontal axis, and the difference between these counts on the vertical axis, for participants walking for six minutes (6MWT, circle), going up and down a ramp (four times, triangle) and four stairs (four times, square); with the monitor placed at the non-paretic ankle (white) and the hip (grey) level. The steps were also counted during a circuit in the community (black circles) with the monitor placed at the ankle. Dashed lines represent the upper and lower limits of agreement for data collected in each task, with dotted lines when n = 12 (first part of the study, black lines for data collected with the monitor at the ankle level and grey lines for hip level) and stippled lines when n = 18 (second part of the study). Labels of participants were added on data outsides the limits of agreement.

xlviii
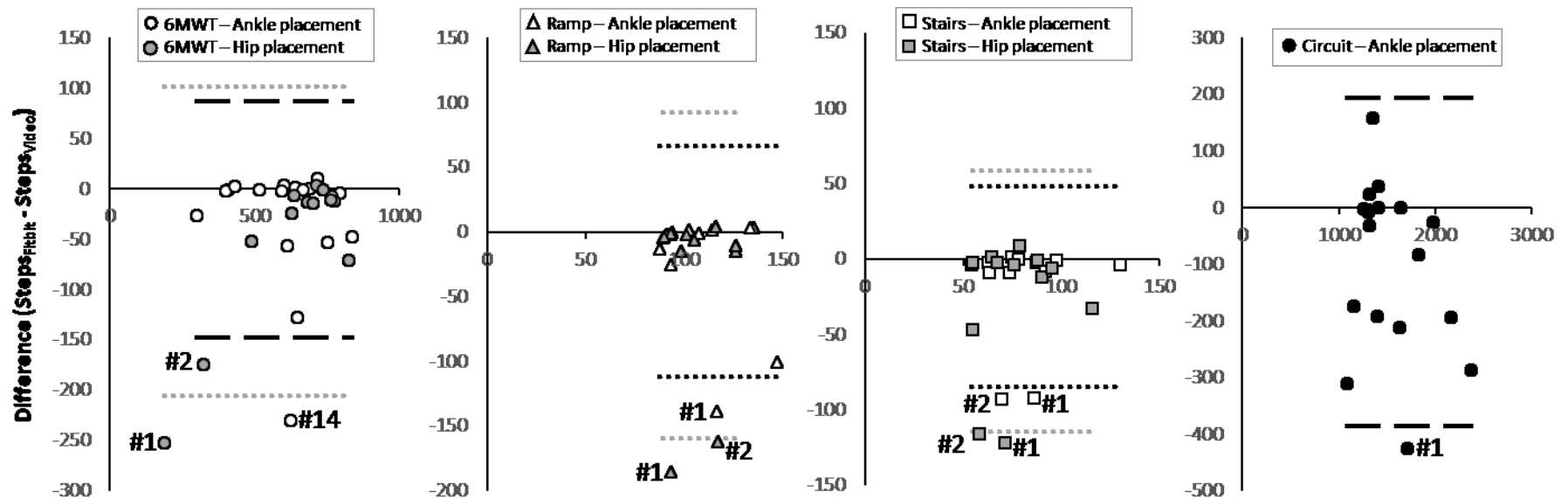
Appendix VII Mini Curriculum Vitae (2015-2019)

PAPERS PUBLISHED IN PEER REVIEWED JOURNALS

1. AGUIAR, L.T.; CAMARGO, L.B.; ESTARLINO, L.D.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Strength of the lower limb and trunk muscles is associated with gait speed in individuals with sub-acute stroke: cross-sectional study. **Brazilian Journal of Physical Therapy,** v.22, n.6, p.459-466, 2018.

2. AGUIAR, L.T.; MARTINS, J.C.;QUINTINO, L.F.; BRITO, S.A.F.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. A single trial may be used for measuring muscle strength with dynamometers in individuals with stroke: A cross-sectional study. **PM&R,** v.S1934-1482, n.18, p.30849-30859, 2018.

3. AGUIAR, L.T.; NADEAU S.; BRITTO, R.R.; TEIXEIRA-SALMELA, L.F.; MARTINS, J.C.; FARIA, C.D.C.M. Effects of aerobic training on physical activity in people with stroke: protocol for a randomized controlled trial. **Trials,** v.19, n.1, p.446, 2018.

4. AGUIAR, L.T.; MARTINS, J.C.; BRITO, S.A.F.; MENDES, C.L.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Knee extensor muscles strength indicates global lower-limb strength in individuals who have suffered a stroke: A cross-sectional study. **Brazilian Journal of Physical Therapy,** v.S1413-3555, n.17, p.30542-7, 2018.

5. AGUIAR, L.T.; MARTINS, J.C.; NADEAU, S.; BRITTO, R.R.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Efficacy of interventions aimed at improving physical activity in individuals with stroke: a systematic review. **Disability and Rehabilitation**, v.19, p.1-16, 2018.

6. OLIVEIRA, D.M.G.; AGUIAR, L.T.; LIMONES, M.V.; GOMES, A.G.; SILVA, L.C.; FARIA, C.D.C.M.; SCALZO, P.L. Aerobic Training Efficacy in Inflammation, Neurotrophins, and Function in Chronic Stroke Persons: Randomized Controlled Trial Protocol. **Journal of Stroke and Cerebrovascular Diseases**, v.28, n.2, p.418-424, 2019.

7. BENFICA, P.A.; AGUIAR, L.T.; BRITO, S.A.F.; BERNADINO, L.H.N.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Reference values for muscle strength: a systematic

review with a descriptive meta-analysis. **Brazilian Journal of Physical Therapy,** v.22, n.5, p.1-8, 2018.

8. MARTINS J.C., AGUIAR L. T., NADEAU S., SCIANNI A. A., TEIXEIRA-SALMELA L. F., FARIA C. D. C. M. Efficacy of task-specific training on physical activity levels of people with stroke: protocol of a randomized controlled trial. **Physical Therapy**, v.97, n.6, p.640-648, 2017.

9. AGUIAR L. T., MARTINS J.C., NADEAU S., BRITTO R. R., TEIXEIRA-SALMELA L. F., FARIA C. D. C. M. Efficacy of interventions to improve physical activity levels in individuals with stroke: a systematic review protocol. **BMJ Open**, v.7, n.1, p.e012479, 2017.

10. MARTINS J.C., AGUIAR L. T., NADEAU S., SCIANNI A. A., TEIXEIRA-SALMELA L. F., FARIA C. D. C. M. Measurement properties of self-report physical activity assessment tools in stroke: a protocol for a systematic review. **BMJ Open**, v.7, n.2, p.e012655, 2017.

11. AGUIAR, L.T.; LARA, E.M.; MARTINS, J.C.; QUINTINO, L.F.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Modified sphygmomanometer test for the assessment of strength of the trunk, upper and lower limbs muscles in subjects with subacute stroke: reliability and validity. **European Journal of Physical Rehabilitation Medicine**, v.52, n.5, p.637-49, 2016.

12. AGUIAR, L.T.; ALBUQUERQUE, J.A.; MARTINS, J.C.; LARA, E.M.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Dynamometry for the assessment of grip, pinch, and trunk strength in subjects with subacute stroke: reliability and various sources of outcome values. **Brazilian Journal of Physical Therapy,** v.20, n.5, p.395-404, 2016.

13. MARTINS, J.C.; AGUIAR, L.T.; LARA, E.M.; MOURA, J.B.; SOUZA, L.A.C.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Assessment of the strength of the lower limb muscles in subjects with stroke with portable dynamometry: a literature review. **Fisioterapia e Movimento,** v.29, n.1, p.193-208, 2016.

14. MARTINS, J.C.; AGUIAR, L.T.; LARA, E.M.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Assessment of grip strength with the modified sphygmomanometer test: association between upper limb global strength and motor function. **Brazilian Journal of Physical Therapy,** v.19, n.6, p.498-506, 2015.

15. MARTINS, J.C.; TEIXEIRA-SALMELA, L.F.; SOUZA, L.A.C.; AGUIAR, L.T.; LARA, E.M.; MOURA, J.B.; FARIA, C.D.C.M. Reliability and validity of the modified sphygmomanometer test for the assessment of strength of upper limb muscles after stroke. **Journal of Rehabilitation Medicine**, v.47, n.8, p.697-705, 2015.

16. MARTINS, J.C.; FARIA, C.D.C.M.; AGUIAR, L.T.; SOUZA, L.A.C.; LARA, E.M.; TEIXEIRA-SALMELA, L.F. Assessment of the strength of the trunk and upper limb muscles in stroke subjects with portable dynamometry: a literature review. **Fisioterapia e Movimento**, v.28, n.1, p.169-86, 2015.

PAPERS SUBMITTED IN PEER REVIEWED JOURNALS

1. MARTINS, J.C.; AGUIAR, L.T.; NADEAU, S.; SCIANNI, A.A.; TEIXEIRA-SALMELA, L.F.; FARIA, C.D.C.M. Measurement properties of self-report physical activity assessment tools in stroke: a systematic review. Submitted to **the Brazilian Journal of Physical Therapy.**

2. DUCLOS, N.C.; AGUIAR, L.T.; AISSAOUI, R.; FARIA, C.D.C.M.; NADEAU, S.; DUCLOS, C. Activity monitor placed at the non-paretic ankle is accurate in measuring step counts during community walking in post-stroke individuals: a validation study. Accepted for publication at **PM&R Journal**, 2019 (Appendix VI).

3. DUCLOS, N.C.; AGUIAR, L.T.; AISSAOUI, R.; NADEAU, S.; DUCLOS, C. *Collecter des informations sur l'activité des personnes à l'aide d'accéléromètres et les analyser: Pertinence et implication de l'actimétrie en réadaptation*. Accepted for publication at the journal **Encyclopédie Médico-Chirurgicale** (EMC), 2019.

4. FERREIRA, A.J.; AGUIAR, L.T.; MARTINS, J.C.; FARIA, C.D.C.M. Individuals with stroke have lower physical activity levels than healthy-control individuals matched by age, sex, and physical exercise levels. Submitted to the **Physiotherapy Theory and Practice Journal**.

JOURNAL REVIEWER

1. Annals of Physical and Rehabilitation Medicine
2. Brazilian Journal of Physical Therapy

3. International Journal of Sports and Exercise Medicine
4. Physiotherapy Theory and Practice
5. Topics in Stroke Rehabilitation
6. Trials

GRANTS AND AWARDS

1. Abstract selected as one of the best of the V Brazilian Congress of Neurofunctional Physiotherapy (COBRAFIN/ABRAFIN). 2018.
2. Grant for participation in scientific event. *Edital da Pró-reitoria de Pós-Graduação da UFMG* - PRPG Nº 02/2018.
3. Abstract selected as one of the best of the XXVII Scientific week of UFMG. 2018.
4. Abstract selected as one of the best of the XXII Brazilian Congress of Physiotherapy (COBRAF/ABF). 2018.
5. *Bourse de recrutement* 2016. École de réadaptation/Université de Montréal.
6. *Bourse d'exemption des droits de scolarité supplémentaires*. Université de Montréal. September 2016 – August 2018.
7. Graduate Scholarship of FAPEMIG. September/2016-August/2017.
8. Graduate Scholarship of FAPEMIG. March/2016-July/2016.
9. Graduate Scholarship of CAPES. March/2015-February/2016.

TEACHING EXPERIENCE

1. **2018 - Current** Professor at Universidade do Estado de Minas Gerais (UEMG). Courses: 1) Physiotherapy in children's health; 2) Supervised Internship III (Neurology and Geriatrics); 3) Interdisciplinary Studies.
2. **2018 - 2018** Invited Professor of the Specialization Course in Adult Neurofunctional Physiotherapy - UFMG. Courses: 1) Evidence Based Practice; 2) Instruments for Neurofunctional Assessment.
3. **2018 - 2018** Invited Professor of the Specialization Course in Adult and Child Neurological Physiotherapy of the Faculdade de Ciências Médicas de Minas Gerais (FCM-MG). Functional anatomy and Neuroanatomy applied to neurological physiotherapy.

4. **2018 - 2018** Invited Professor at the Stricto Sensu Postgraduate Program in Rehabilitation Sciences at UFMG. Measures and Instruments of Evaluation I.

5. **2018 - 2018** Invited Professor of the Specialization course in Orthopedic and Sports Physiotherapy of the Centro Universitário de Belo Horizonte, UniBH. Motor Control and Movement Disorders - Topic: International Classification of Functioning, Disability and Health (ICF).

6. **2017 - 2017** Invited Lecture: Constraint Induced Movement Therapy, Undergraduate course of Physiotherapy/Faculdade de Ciências Médicas de Minas Gerais (FCM-MG).

7. **2016 - 2016** Invited Lecture: Physiotherapist performance in adult neurologic area, Undergraduate course of Physiotherapy/UFMG.

8. **2016/1** Professor training: Kinesiotherapy, of the Undergraduate course of Physiotherapy/UFMG.

9. **2015/2** Professor training: Clinical Teaching I (Neurology) of the Undergraduate course of Physiotherapy/UFMG.

10. **2015/1** Professor training: Clinical Teaching I (Neurology) of the Undergraduate course of Physiotherapy/UFMG.

PARTICIPATION IN SHORT-TERM WORKSHOP

1. Practical methods of performing higher intensity exercises to improve lower limb function after stroke, 4h. ABRAFIN. 2018.

2. Reactivate, restore, preparing the nervous system to optimize function after spinal cord injury, 4h. ABRAFIN. 2018.

3. Application of the WHODAS 2.0 instrument, 40h. Universidade Federal do Ceará (UFC). 2018.

4. *eAEROBICS for Stroke Training Program*. Dalhousie University, D.U., Canada. 2018.

5. Emergency Cardiovascular Service, 4h. UFMG. 2017.

6. Formulating objectives in science: methodological and editorial dilemmas, 3h30. UFMG. 2017

7. Medline et Embase sur OvidSP. 1h15. Université de Montréal. 2016.

8. EndNote X7 sous Windows. 3h. Université de Montréal. 2016.

9. VII Journey of Formation of Higher Education Professors. 60h. Universidade Federal de Minas Gerais/Brazil. 2016

10. Rehabilitation in stroke. 4h. X Brazilian Congress of Cerebrovascular Diseases. Brazilian Society of Cerebrovascular Diseases and the Brazilian Academy of Neurology. 2015

11. Strategy and tips to write a high-quality article. 4h. Editage. 2015

SHORT-TERM WORKSHOP TAUGHT

1. **2018** - **Aguiar LT.** Mensuração de força muscular com o Teste do Esfigmomanômetro, Universidade do Estado de Minas Gerais (UEMG), 2h.

2. **2018** - **Aguiar LT**. Mensuração de força muscular com o Teste do Esfigmomanômetro, II Congresso de Ciências da Saúde, Faculdade de Sete Lagoas (FACSETE), 4h.

3. **2018** - Martins JC, **Aguiar LT**. Avaliação da força muscular com o Teste do Esfigmomanômetro. XXII Congresso Brasileiro de Fisioterapia (COBRAF), 8h.

PARTICIPATION IN SCIENTIFIC EVENTS

1. *Oficina - Projeto ADES-FIT - Aprimoramento Didático do Ensino Superior*, UFMG. 2018.

2. V Brazilian Congress of Neurofunctional Physiotherapy (COBRAFIN). 2018.

3. XXII Brazilian Congress of Physiotherapy (COBRAF). 2018.

4. I Home-Care Physiotherapy Symposium. 2018.

5. 9º Meeting between Science and Professional Practice. UFMG. 2017.

6. XXVI Scientific week of UFMG. 2017.

7. AMAVC in combating stroke and in supporting people affected by stroke. UFMG. 2017.

8. 7º Meeting between Science and Professional Practice. UFMG. 2017.

9. 8th Annual Edith Strauss Interactive Day. 2017.

10. 11th Annual Canadian Neuroscience Meeting. 2017.

11. *Journée scientifique Andrée Forget et conférence Gustave Gingras*. 2017.

12. 2nd Quebec Congress in Adaptation-Rehabilitation Research. 2017.

13. *Journée Scientifique CRIUGM-CAREC*. 2017.

14. CRIR Student Colloquium. 2017.

15. The 3rd Annual PATH Symposium: Balance and mobility. 2016.

16. X Brazilian Congress of Cerebrovascular Diseases. 2015

PRESENTATIONS IN SCIENTIFIC EVENTS

1. **Aguiar LT**. [*Palestra: Treino aeróbio em indivíduos pós-acidente vascular encefálico*]. 2018.

2. **Aguiar LT**, Martins JC, Brito SAF, Mendes CLG, Teixeira-Salmela LF, Garcia LN, Souza DR, Faria CDCM. [*Força muscular de extensores de joelho indica força global do membro inferior pós-acidente vascular encefálico*]. 2018.

3. **Aguiar LT,** Nadeau S, Britto RR, Teixeira-Salmela LF, Martins JC, Quintino LF, Brito SAF, Faria CDCM. [*Eficácia do treino aeróbio no nível de atividade física de indivíduos pós-acidente vascular encefálico*]. 2018.

4. **Aguiar LT**. [*Palestra: Mensuração da força muscular pelo teste do esfigmomanômetro em indivíduos com disfunções neurológicas*]. 2018.

5. **Aguiar LT**. [*Palestra: Estimulação precoce em bebês pré-termos*]. 2018.

6. **Aguiar LT,** Nadeau S, Britto RR, Teixeira-Salmela LF, Martins JC, Faria CDCM. [*Eficácia do treino aeróbio em indivíduos pós-acidente vascular encefálico*]. 2018.

7. **Aguiar LT,** Martins JC, Brito SAF, Mendes CLG, Teixeira-Salmela LF, Faria CDCM. [*Força muscular de extensores de joelho indica força global do membro pós-AVE*]. 2018.

8. **Aguiar LT,** Martins JC, Nadeau S, Scianni AA, Teixeira-Salmela LF, Faria CDCM. [*Eficácia do treino específico da tarefa em indivíduos pós-acidente vascular encefálico*]. 2018.

9. **Aguiar LT,** Nadeau S, Martins JC, Teixeira-Salmela LF, Britto RR, Faria CDCM. Efficacy of interventions aimed to increase physical activity levels in individuals with stroke: A systematic review. 2017.

10. **Aguiar LT,** Nadeau S, Martins JC, Teixeira-Salmela LF, Britto RR, Faria CDCM. Efficacy of interventions aimed to increase physical activity levels in individuals with stroke: A systematic review. 2017.

11. **Aguiar LT,** Nadeau S, Caetano LCG, Basilio ML, Scianni AA, Teixeira-Salmela LF, Faria CDCM. Effects of Aerobic Exercise on Neuroplasticity in Subjects with Neurological Diseases: A Systematic Review. 2017.

12. **Aguiar LT,** Nadeau S, Martins JC, Teixeira-Salmela LF, Britto RR, Faria CDCM. Efficacy of interventions aimed to increase physical activity levels in individuals with stroke: A systematic review. 2016.

13. **Aguiar LT,** Lara EM, Martins JC, Teixeira-Salmela LF, Christo PP, Faria CDCM. Modified sphygmomanometer test for the assessment of trunk and lower limbs muscles strength in subjects with subacute stroke: Measurement properties. 2015.

14. **Aguiar LT,** Martins JC, Lara EM, Teixeira-Salmela LF, Faria CDCM. Modified sphygmomanometer test for the assessment of upper limbs muscles strength in subjects with subacute stroke: Measurement properties. 2015.

15. **Aguiar LT**. [*Palestra: Uso do teste do esfigmomanômetro modificado*]. 2015.

16. **Aguiar LT**. [*Palestra: Teste do esfigmomanômetro modificado*]. 2015.

PARTICIPATION IN THE JURY OF FINAL CONCLUSION WORK (UNDERGRADUATE STUDENTS)

1. **Aguiar LT.** Functional and independence assessment of activities of daily living in injured athletes and non-athletes: a cross-sectional study. Students: Karine Braga e Kamilla Batista. Faculdade Ciências Médicas de Minas Gerais. 2018.

PARTICIPATION IN THE JURY OF FINAL CONCLUSION WORK (GRADUATE STUDENTS)

1. **Aguiar LT**. Effects of physical therapy treatment in patients with diabetic neuropathy: literature review. Student: Flávia Cristina de Melo Carneiro. Universidade Federal de Minas Gerais. 2018.

2. **Aguiar LT**. Efficacy of mobilization in reducing pain and improving function in individuals with ankle dysfunction: literature review. Student: Bruna Daniele Gonçalves Santos. Universidade Federal de Minas Gerais. 2018.

3. **Aguiar LT**. Humanized community elderly care through the Rehabilitation Problems Assessment Protocol: experience report for a comprehensive action strategy in primary care in Ribeirão das Neves, Minas Gerais. Student: Natália de Pádua Ferreira Barbosa. Universidade Federal de Minas Gerais. 2018.

4. **Aguiar LT**. Use of intratissicular percutaneous electrolysis in patellar tendinopathy in volleyball athletes: a narrative review. Student: Gustavo Oliveira e Silva. Universidade Federal de Minas Gerais. 2018.

5. **Aguiar LT**. Risk factors leading to the development of canelitis (medial tibial stress syndrome or medial tibial periostitis) in runners: a review of the literature. Student: Marcus Vinicius Ribeiro de Almeida. Universidade Federal de Minas Gerais. 2018.

6. **Aguiar LT**. High-intensity exercise improves balance and gait in Parkinson's disease: a systematic review. Student: Laira Rodrigues Módulo. Universidade Federal de Minas Gerais. 2017.

7. **Aguiar LT**. Efficacy of aquatic physiotherapy in the functionality of adult and elderly individuals with neurological disease: a systematic review of the literature. Student: Lilian Bicalho Mendes Von Randow. Universidade Federal de Minas Gerais. 2017.

8. **Aguiar LT**. Use of the pilates method in adult neurofunctional rehabilitation: literature review. Student: Thiago Leonardo Simão. Universidade Federal de Minas Gerais. 2017.

9. **Aguiar LT**. Characterization of the injuries of the athletes attended by the physiotherapy sector CTE/UFMG. Student: Jéssica dos Santos Bueno. Universidade Federal de Minas Gerais. 2017.

SUPERVISION OF UNDERGRADUATE STUDENT

1. Student: Ludimylla Brennar. Relationship between muscle strength and gait speed in individuals in the sub-acute and chronic phase after stroke. 2015. Universidade Federal de Minas Gerais.

2. Student: Lorena Dadores Estarlino. Relationship between muscle strength and gait speed in individuals in the sub-acute and chronic phase after stroke. 2015. Universidade Federal de Minas Gerais.

SUPERVISION OF GRADUATE STUDENT

1. Post-graduate student (*latu sensu*): Ordália Evangelista Gomes. Efficacy of aerobic training in subjects with Parkinson's disease: a systematic review. 2018 – In progress. Universidade Federal de Minas Gerais.

2. Post-graduate student (*latu sensu*): Lílian Lazzeri. Evaluation of the muscular strength of individuals after stroke. 2018 – In progress. Universidade Federal de Minas Gerais.

3. Post-graduate student (*latu sensu*): Carla Meliane Barbosa de Souza. Measurement properties of exercise capacity tests in post-stroke patients: a systematic review. 2015. Universidade Federal de Minas Gerais.

DEVELOPMENT OF EDUCATIONAL MATERIAL

1. **2018 -** Practical Guide for Measuring Muscular Strength with the Modified Sphygmomanometer Test.
2. **2015 -** Video (Pitch) Modified Sphygmomanometer Test.