

Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

**Does whole-body vibration training affect arterial stiffness,
cognitive ability, and quality of life in chronic stroke?**

A thesis presented in partial fulfilment of the requirements for the degree of

Master of Sport and Exercise
in
Exercise Prescription and Training

at Massey University, Manawatū, New Zealand.

Christie Emily Yule

2015

Acknowledgements

I would like to thank both my supervisors Doctor Darryl Cochrane and Doctor Lee Stoner. Both of you created a very supportive and positive environment for me to excel in. I am honoured to have worked with you on this thesis and have tremendous respect for you both. To Darryl, thank you for your continued patience, support, and countless hours reading over my thesis. From the very beginning when you told me this thesis was about what I wanted to study, I knew you would be a fantastic supervisor for me. Your undoubted and extensive knowledge in whole-body vibration, fantastic editing and endless positive attitude was invaluable. To Lee, thank you for your support, advice, and guidance throughout the course of my Masters. I knew you were the perfect man for the job and would be able to support me from a distance. Your superior knowledge, enthusiasm, and comments promoted me to think more broadly and therefore were invaluable.

A huge thank you to Amanda Harrison from the Stroke Foundation, your assistance in aiding me to recruit participants was simply amazing. To the Stewart Centre, and in particular Janet Webb and Terry Lloyd-West, I would like to express my sincere appreciation and gratitude for your support and patience throughout. Thank you for helping in my recruitment process and being so welcoming, without you my data collection would have been much more difficult. To all of my participants, thank you for your enthusiasm, humour, conversations, and patience, you are all fantastic characters whom made my study all worth it. I wish you all the very best in your future endeavours.

To my world-class parents, brother and twin sister, extended family, adopted family and Steph, thank you for your constant love, support and patience. I know at times it must have been challenging dealing with a stressed out, penniless, fulltime student but you humoured me on many occasions by laughing at my “dad” jokes when I was in desperate need. Also special appreciation to my closest friends and flatmates, all of whom, directly or indirectly, and probably unbeknownst to them, assisted me by keeping me “sane”.

Abstract

Background: Stroke is a type of cardiovascular disease, which has the third highest mortality rate in New Zealand. Risk factors of stroke have major consequences on the structure and function of blood vessels and their interaction with circulating blood; altering vascular structure through encouraging atherosclerosis and stiffening of arteries and by inducing thickening, narrowing, and tortuosity of capillaries and arterioles. Additionally, research has reported that the most significant effect of a stroke for a survivor is a decline in health-related quality of life (HRQOL). Studies state that stroke is associated with increased arterial stiffness, and even once established, arterial stiffness can be diminished by a programme of physical activity. Whole-body vibration (WBV) is a safe, easy to use, and time effective exercise intervention that has demonstrated significant improvements in arterial stiffness in healthy men and older sedentary adults. Therefore, it is worthwhile to explore the possibility of WBV as a valuable intervention in chronic stroke.

Purpose: To investigate whether 4 weeks of WBV would significantly reduce indices of arterial stiffness, and improve cognition and quality of life in chronic stroke.

Methods: Six participants with chronic stroke volunteered for this study. This was a cross-over design, where participants were exposed to WBV training for 4 weeks (3 times a week) on a commercialised Galileo vibration machine with an oscillating platform. WBV parameters were progressed throughout the 4 week intervention (5-7 sets of 60 sec bouts with 60 sec rest, 22-26 Hz, 2.1-6.5 mm, static squatting), and a 2 week washout period was prescribed between WBV and control (usual day-to-day living for four weeks) interventions. Arterial stiffness measurements (carotid arterial stiffness, PWV, PWA), cognition (ACE-III), and quality of life (SF-36), were conducted prior to each intervention and after the completion of each intervention. Additionally, rate of perceived exertion (Borg 15-point scale) was also recorded following every WBV session.

Results: No significant improvements were shown for central BPs, HR, or central $AIx@75$. Additionally, no significant improvements were seen in PWV between WBV and control. There was not significant interaction, or main effects for carotid arterial stiffness (β), DC or CC. However, carotid arterial stiffness did display a decrease over time for WBV, where arterial stiffness increased for control over time, but these measurements and their interaction effect were not found to be significant ($p=0.166$). No significant interaction or main effects were found for quality of life (SF-36) or cognitive ability (ACE-III). Finally, there was no significance of RPE over the 4 weeks.

Conclusions: Limited studies have investigated the effects of multiple sessions of WBV (short-term training) in stroke, with no study examining the effects of WBV on arterial stiffness, QOL or cognition. The present study found no significant improvements in indices of arterial stiffness, cognitive ability, or QOL. However, this was the first study to investigate the effects of WBV on these variables in chronic stroke; therefore further research with larger sample sizes are needed to investigate the aims of this study further.

Table of Contents

Acknowledgements	ii
Abstract	iii
Table of Contents	v
Abbreviations	vii
List of Figures	x
List of Tables	xi
Chapter 1 – Introduction	1
Chapter 2 – Literature Review	4
2.1 Stroke	4
2.1.1 Incidence and Prevalence in New Zealand.....	4
2.1.2 Types	6
2.1.3 Classification	9
2.1.4 Risk Factors	13
2.1.5 Aetiology	23
2.1.6 Acute vs. Chronic Stroke	26
2.1.7 Cognitive Ability	31
2.1.8 Quality of Life (QOL).....	34
2.1.9 Effects of Exercise	37
2.1.9.1 Benefits of Exercise.....	37
2.1.9.2 Exercise Prescription.....	41
2.2 Whole-body Vibration (WBV).....	45
2.2.1 Type.....	45
2.2.2 Parameters.....	48
2.2.3 Proposed Mechanisms	55
2.2.4 Effect on Short-term Training	58
2.2.4.1 Cognitive Ability and Quality of Life.....	58
2.2.4.2 Cardiovascular Indices	59
2.3 Cardiovascular Indices.....	64
2.3.1 Blood Pressure	64
2.3.2 Heart Rate	67
2.3.3 Arterial Stiffness.....	69
2.3.3.1 Principles of Arterial Stiffness.....	69
2.3.3.2 Mechanisms of Arterial Stiffness	71
2.3.3.3 Indices of Arterial Stiffness	75
2.3.3.4 Relationship with Age, Lifestyle, and Disease.....	89
Chapter 3 – Research Aim and Hypotheses	95

Chapter 4 – Methods	96
4.1 Study Design	96
4.2 Participants.....	98
4.3 WBV	100
4.4 WBV Training Protocol	102
4.5 SphygmoCor	104
4.5.1 Pulse Wave Analysis (PWA).....	105
4.5.2 Carotid-Radial Pulse Wave Velocity (PWV)	106
4.6 Ultrasound.....	107
4.7 Cognition and Quality of Life Measures	108
4.7.1 Addenbrooke’s Cognitive Examination (ACE-III)	108
4.7.2 Quality of Life (QOL).....	108
4.8 Statistical Analysis	109
Chapter 5 – Results	110
5.1 Participant Characteristics.....	110
5.2 SphygmoCor - PWA	110
5.3 SphygmoCor - PWV	111
5.4 Ultrasound.....	113
5.5 Quality of Life (SF-36)	115
5.6 Addenbrooke’s Cognitive Examination (ACE-III).....	115
5.7 Rate of Perceived Exertion (RPE).....	116
Chapter 6 – Discussion	118
6.1 Pulse Wave Analysis (PWA)	118
6.2 Pulse Wave Velocity (PWV)	119
6.3 Local Arterial Stiffness	122
6.4 Cognition and Quality of Life	124
6.5 Rating of Perceived Exertion	125
6.6 Limitations	126
6.7 Future Research.....	127
Chapter 7 – Conclusion	128
References	129
List of Appendices	167

Abbreviations

A

ACE-III	Addenbrooke's cognition examination
ACSM	American college of sports medicine
ADL	Activities of daily living
AIx	Augmentation index
AIx@75	Augmentation index at 75 beats per minute
AP	Augmentation pressure

B

β	Local arterial stiffness
BI	Barthel index
BP	Blood pressure
bpm	Beats per minute

C

$^{\circ}\text{C}$	Degrees celsius
CC	Compliance coefficient
cDBP	Central diastolic blood pressure
CI	Confidence interval
cm	Centimetres
cm s^{-1}	Centimetres per second
CNS	Central nervous system (check)
cPP	Central pulse pressure
CS	Canadian neurological scale
cSBP	Central systolic blood pressure

D

DBP	Diastolic blood pressure
DC	Distensibility coefficient
Ddia	Diastolic diameter
Dist	Distance between systolic diameter and diastolic diameter
Dsys	Systolic diameter

F

FP	Foot position
----	---------------

G

g	Gravitational acceleration
---	----------------------------

GOS Glasgow outcome scale

H

HR Heart rate

HRQOL Health-related quality of life

HRR Heart rate reserve

Hz Hertz

K

kg Kilograms

M

ms^{-2} Metres per second squared

MAP Mean arterial pressure

min Minutes

mm Millimetres

mmHg Millimetres of mercury

MRI Magnetic resonance imaging

mRS Modified rankin scale

ms^{-1} Metres per second

N

NIHSS National institutes of health stroke scale

NO Nitric oxide

P

PAR Population attributable risk

PARQ Physical activity readiness questionnaire

PP Pulse pressure

PWA Pulse wave analysis

PWV Pulse wave velocity

Q

QOL Quality of life

R

RM Repetition maximum

ROM Range of motion

RPE Rate of perceived exertion

RS Rankin scale

S

SAV	Side-alternating vertical sinusoidal vibration
SBP	Systolic blood pressure
SD	Standard deviation
sec	Seconds
SF-36	Short form-36
SSS	Scandinavian stroke scale
Sub	Subject
SV	Stroke volume
SV/PP	Stroke volume to pulse pressure ratio

T

TIA	Transient ischaemic attack
TUG	Timed up-and-go
TVR	Tonic vibration reflex

V

$\dot{V}O_2$	Volume of oxygen uptake
VV	Vertical synchronous vibration

W

WBV	Whole-body vibration
-----	----------------------

List of Figures

Figure 2.1. Stroke prevalence by age and gender (National Health Committee, 2013).....	5
Figure 2.2. Changes that occur in ischaemic stroke (NHLBI, 2014).	6
Figure 2.3. Changes that occur in haemorrhagic stroke (NHLBI, 2014).....	6
Figure 2.4. Structure of vessels (adapted from Cleaver and Melton (2003)).	23
Figure 2.5. Process of atherosclerosis (Maizels & Akademisk, 2011).....	24
Figure 2.6. The two commercial forms of vibration platforms: SAV and VV (Cochrane, 2010).	46
Figure 2.7. Parameters of sinusoidal oscillation (SAV) (adapted from Cochrane (2010) and Furness (2007)).....	48
Figure 2.8. Aortic pulse pressure waveform, adapted from Stoner et al. (2012).....	81
Figure 2.9. Radial applanation tonometry for aortic pulse pressure waveform (Fujime et al., 2012).	82
Figure 4.1. General overview of the study design	96
Figure 4.2. WBV Machine indicating foot positions and reflective tape markings.....	101
Figure 4.3. SphygmoCor	104
Figure 4.4. Electrode placements for PWV (AtCor Medical, 2008).....	106
Figure 5.1. Mean (\pm SD) for central augmentation index at 75 bpm	111
Figure 5.2. Mean (\pm SD) for pulse wave velocity.....	112
Figure 5.3. Mean (\pm SD) for carotid to radial pulse transit time standard deviation.....	112
Figure 5.4. Mean (\pm SD) for arterial stiffness	114
Figure 5.5. Mean (\pm SD) for distensibility coefficient.....	114
Figure 5.6. Mean (\pm SD) for compliance coefficient.....	114
Figure 5.7. Mean (\pm SD) of RPE for all participants across 12 WBV sessions.....	117

List of Tables

Table 2.1. Established risk factors for stroke	16
Table 2.2. Emerging risk factors for stroke	17
Table 2.3. Improvements due to exercise training in stroke survivors.....	39
Table 2.4. Exercise prescription for stroke survivors.....	42
Table 4.1. Participant characteristics.....	99
Table 4.2. WBV training protocol.....	103
Table 5.1. SphygmoCor values for pre and post WBV and control interventions (mean \pm SD)....	110
Table 5.2. Ultrasound values of pre and post WBV and control interventions (mean \pm SD)	113
Table 5.3. SF-36 scores for pre and post WBV and control interventions (mean \pm SD)	115
Table 5.4. ACE-III scores for pre and post WBV and control interventions (mean \pm SD).....	116

Chapter 1 – Introduction

Stroke is a type of cardiovascular disease, which has the third highest mortality rate in New Zealand. It occurs across all ethnicities and genders, and is a major cause of serious adult injury in New Zealand, of which many are disabled and need significant daily support. Therefore, it is not surprising that the most significant effect of a stroke for a survivor is a decline in health-related quality of life (HRQOL). Due to the great burden of stroke on mortality, morbidity, cognition, and quality of life (QOL), and its financial cost, there is a greater need to investigate interventions to reduce the severity of this disease. Consequently, these interventions need to be effective yet simple to administer, inexpensive, readily available, and elicit no adverse effects to participants.

Any intervention strategy should be underpinned by sound physiology. In terms of stroke, there are numerous non-modifiable and modifiable risk factors that have major consequences on the structure and function of blood vessels and their interaction with circulating blood; altering vascular structure through encouraging atherosclerosis and stiffening of arteries and by inducing thickening, narrowing, and tortuosity of capillaries and arterioles. As a result, one of the most common causes of stroke has been identified as atherosclerosis. These morphological changes are associated with arterial stiffness which is a sensitive marker of large artery health, and has been linked to future cardiovascular complications following stroke. Moreover, the carotid artery is the main artery to the brain and is a frequent site of atheroma formation. In relation to stroke, this artery is of particular importance as this formation can lead to thrombotic or embolic strokes. Therefore, measurement of carotid arterial stiffness may also provide important prognostic information. Research by Cameron and Dart (1994) has identified that once established, arterial stiffness can be diminished by a programme of physical activity. As a result, arterial stiffness may serve as an ideal target for exercise interventions designed to assist chronic stroke.

Various researchers have found exercise interventions can improve functional performance in stroke, and reduce stroke risk factors such as hypertension and lipid profiles, suggesting its potential as an exercise intervention for stroke survival. One exercise intervention that has received a lot of attention is WBV, with a growing interest in the use of WBV as an exercise intervention in compromised health. However, limited research has investigated the effects of WBV therapy in stroke, primarily research has focused on functional performance, with no studies examining indices of arterial stiffness, cognition, or QOL in chronic stroke. However, research has identified there are no adverse effects on stroke survivors after acute and short-term WBV interventions (Pang, Lau, & Yip, 2013a; van Nes, Geurts, Hendricks, & Duysens, 2004), and it is suggested that WBV may augment neurotransmission in the prefrontal cortex and in other surrounding regions by sensory stimulation (Regterschot et al., 2014). Therefore, the impact that multiple sessions of WBV have on arterial stiffness, cognition, and QOL in chronic stroke has not been examined. However, information regarding the interaction of these variables holds great potential in stroke populations due to the burden of the disease and WBV being a safe, easy to use, and time effective exercise intervention.

The aim of this thesis is to provide an extensive and current literature review that identifies reliable knowledge from which sensible hypotheses will be tested to investigate the impact of WBV on arterial stiffness, cognition, and QOL in chronic stroke. Chapter 2 will review the literature and explain the aetiology of stroke, its incidence and prevalence, the risk factors associated with it, and how it affects cognition and QOL. Following this, the effect of WBV and the possible benefits of this as an exercise regime for stroke shall be explored; along with the cardiovascular indices that are central to understanding stroke. From the knowledge identified in Chapter 2, the aim and hypotheses will be detailed in Chapter 3. The methodology, design, equipment, and procedures will be detailed in Chapter 4, whilst the results of the study will be

noted in Chapter 5. Chapter 6 will deliver a comprehensive discussion of the results found and comparison to previous research, and will culminate in a general conclusion with suggestions for possible directions for future research.

Chapter 2 – Literature Review

The literature will be examined in an attempt to bridge the gap of knowledge that currently exists between the effects of WBV on indices of arterial stiffness, cognition, and QOL in chronic stroke. In order to provide theoretical framework and background for later discussion on the effects of WBV on these variables in stroke, firstly an understanding of stroke and its risk factors, aetiology, and how it affects cognition and QOL and is affected by exercise is required. Secondly, understanding WBV and its proposed mechanisms, the effects on QOL, functional performance, and cardiovascular indices will allow insight into WBV as an exercise intervention. Finally, understanding the principles and mechanisms of arterial stiffness, and its relationship with age, lifestyle, and disease will highlight why this cardiovascular index is important to target and improve in chronic stroke.

2.1 Stroke

2.1.1 Incidence and Prevalence in New Zealand

Stroke has a significant effect on the mortality and morbidity of New Zealanders. Where stroke has the third highest mortality rate (about 2500 people every year), with approximately 24 New Zealanders suffering a stroke every day (The Stroke Foundation New Zealand, 2014). Furthermore, it is the major cause of serious adult injury in New Zealand with an estimated 60,000 stroke survivors, of which many are disabled and need significant daily support (The Stroke Foundation New Zealand, 2014). It has been stated that the most significant effect of a stroke for a survivor is a decline in health-related quality of life (HRQOL). It does not discriminate against gender or ethnicity affecting around 9000 New Zealanders every year; annually about 40 strokes are suffered by children and nearly 2000 strokes by people under retirement age (The Stroke Foundation New Zealand, 2014). In the years 2011 to 2012 the prevalence in New Zealand

was about 1.8% (62,000 people); with stroke risk increasing with age to 8% in those aged over 75 years (Figure 2.1) (National Health Committee, 2013). Additionally, Māori people were 1.3 times as likely to suffer a stroke as non-Māori when adjusted for sex and age (National Health Committee, 2013). These ethnic differences propose different risk factor profiles for diverse ethnic groups (Feigin et al., 2006). Financially, the National Health Committee (2013) estimates the total yearly cost of stroke is at \$378 million to \$432 million. Therefore, due to the great burden of stroke on mortality, morbidity, cognition, and quality of life (QOL), plus its financial cost, it is of high importance to investigate exercise interventions to reduce the severity of this disease.

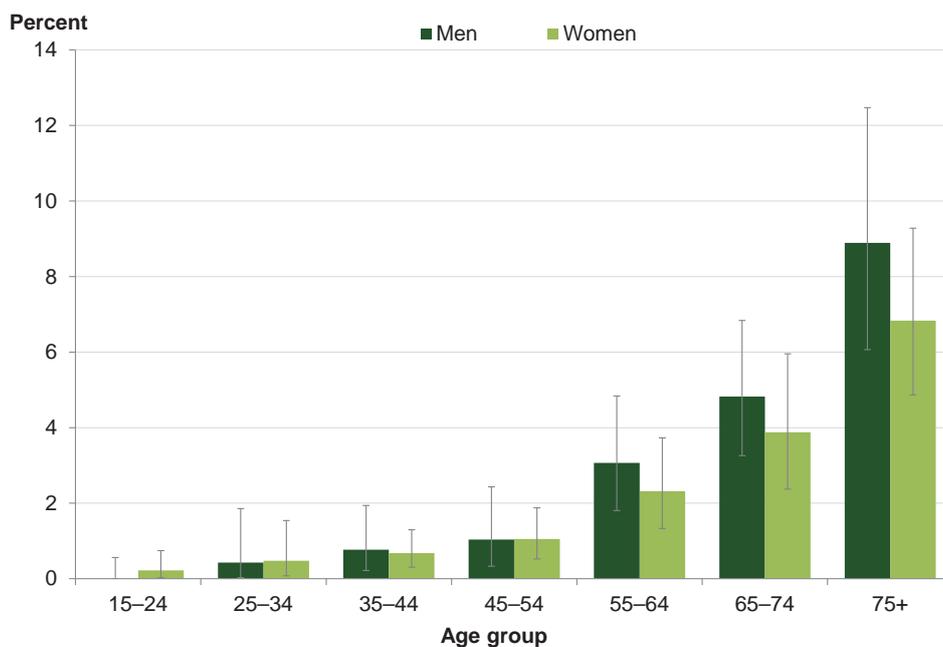


Figure 2.1. Stroke prevalence by age and gender (National Health Committee, 2013).

2.1.2 Types

There are two main types of stroke, ischaemic and haemorrhagic (Figures 2.2 and 2.3).

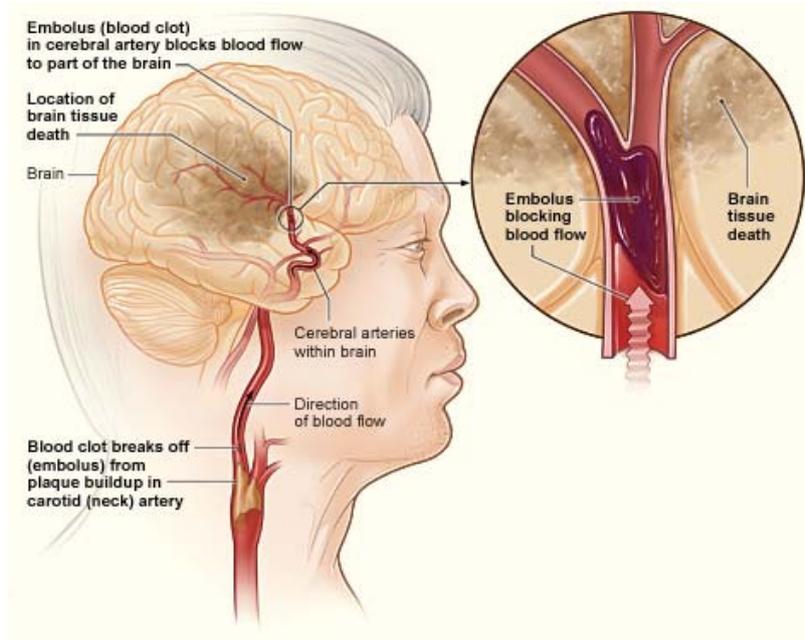


Figure 2.2. Changes that occur in ischaemic stroke (NHLBI, 2014).

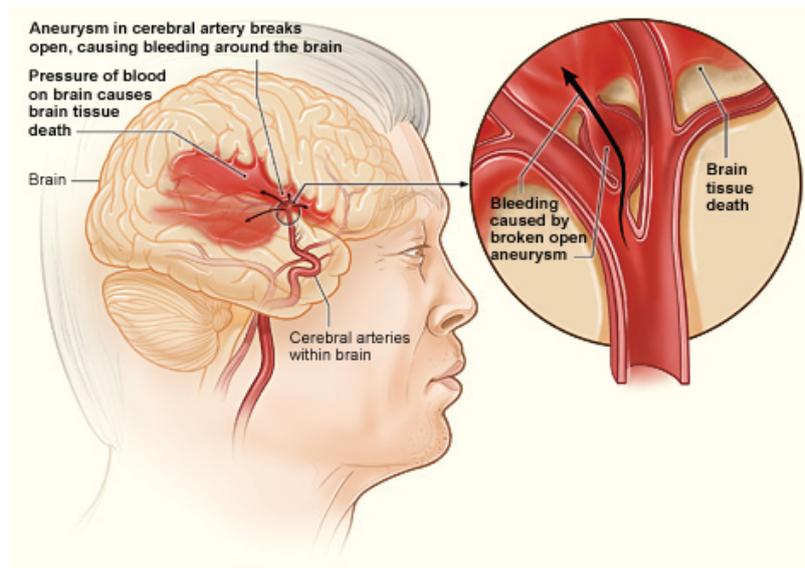


Figure 2.3. Changes that occur in haemorrhagic stroke (NHLBI, 2014).

Stroke is the sudden onset of symptoms of focal neurological dysfunction, which last more than 24 hours (or cause death) and results in acute vascular injury to part of the brain (Hankey & Blacker, 2015). This may be through inadequate blood supply via an obstruction (blood clot or fatty plaque) within a blood vessel supplying blood to part of the brain (ischaemic stroke), or a weakened vessel that ruptures and bleeds into (intracerebral haemorrhage) or over the surface (subarachnoid haemorrhage) of part of the brain (American Heart Association, 2012c; Hankey & Blacker, 2015). Ischaemic stroke is the most common type occurring 87% of the time compared to 13% in haemorrhagic strokes (10% intracerebral and 3% subarachnoid) (American Heart Association, 2013). However, there is another type referred to as a transient ischaemic attack (TIA), also known as a mini stroke. It shares the same pathophysiologic mechanisms as ischaemic stroke but the prognosis may vary depending on the cause and severity (Furie et al., 2011). As it displays focal neurological signs or symptoms lasting less than 24 hours and these stroke symptoms rectify before significant cell death (Furie et al., 2011; National Health Committee, 2013), it is often thought of as the mini stroke before the stroke (either ischaemic or haemorrhagic) and consequently not classed as one of the main types of stroke. Given that, all types of stroke will be considered in for the current study, it is important to understand how each can occur and consequently allow more comprehensive understanding when discussing future topics such as risk factors, aetiology, and research findings.

Ischaemic strokes result when there is an interruption to the blood supply to a certain area of the brain that can lead to lack of oxygen (ischaemia), infarction and eventual necrosis of tissue (American Heart Association, 2012c; Hankey & Blacker, 2015). This interruption may be an arterial occlusion or stenosis (Mohr et al., 1997). Haemorrhagic strokes are due to a rupture of a weakened blood vessel which causes compression of the brain tissue (American Heart Association, 2012c; Mohr et al., 1997). This pressure (due to an expanding hematoma) may result

in a loss of blood supply to the affected area, resulting in an infarction and ischaemia (Mohr et al., 1997).

Both ischaemic and haemorrhagic stroke can be divided into subtypes depending on the assumed mechanism of the focal brain injury, and the localisation and type of the vascular lesion (Furie et al., 2011). These subtypes have been identified as mechanisms that result in stroke (Adams et al., 1993; Furie et al., 2011; Zorowitz, Baerga, & Cuccurullo, 2004). Subtypes of ischaemic stroke are as follows: thrombotic (35% of all strokes), occurs when thrombus (blood clot) blocks blood flow to the brain either in the heart or the vessels; embolic (30% of all strokes) stroke occurs when an embolus (blood clot or fatty plaque) breaks away from the blood vessel wall, and flows to the brain blocking an artery; and lacunar infarction (20% of all strokes) is lacunes which are small infarcts seen in such places as the thalamus, pons, putamen, internal capsule, and caudate (Mohr et al., 1997; NHLBI, 2014; Zorowitz et al., 2004). Haemorrhagic stroke may be classified as either an intracerebral haemorrhage (10% of all strokes) or subarachnoid haemorrhage (3% of all strokes) (American Heart Association, 2013). Intracerebral haemorrhage commonly occurs in the thalamus, cerebellum, pons, and putamen, and will form a progressively enlarging haematoma. This haemorrhaging directly damages brain tissue and raises intracranial pressure producing vomiting, nausea, and headaches (Zorowitz et al., 2004). It is strongly linked to chronic hypertension and is preceded by formation of microaneurysms. It can also result from vascular malformations and ruptured aneurysms as well as systemic factors such as trauma, drugs and tumours (Zorowitz et al., 2004). Subarachnoid haemorrhage is the slow collection of blood in the subarachnoid space of the dura (Mohr et al., 1997). This type of haemorrhage can be spontaneous or traumatic. Spontaneous haemorrhages occur through extensions of intracranial haemorrhaging and the rupture of saccular aneurysms (Donnan, Fisher, Macleod, & Davis, 2008; Mohr et al., 1997). Aneurysms and arteriovenous malformations (AVM) typically result in haemorrhagic stroke. Aneurysms are a ballooning of a weakened portion of a blood vessel,

without treatment this ballooning proceeds to weaken the vessel and eventually ruptures and bleeds into the brain (American Heart Association, 2012c).

2.1.3 Classification

Classifying stroke can be challenging with numerous stroke scales available for clinical use, but currently there is no established clinical stroke scale. There are two main types, clinical (deficit) scales and outcome (handicap and disability) scales, of which many have been validated across numerous stroke studies (Barber, Fail, Shields, Stott, & Langhorne, 2003; Bonita & Beaglehole, 1988; Brott et al., 1989; Cavanagh & Gordon, 2002; D'Olhaberriague, Litvan, Mitsias, & Mansbach, 1996; Levine et al., 2006; Stavem, Lossius, & Ronning, 2002). Additionally, stroke scales have been found to be beneficial as they can be used in clinical research settings to summarise and categorise the deficits found in groups and individuals, and to communicate and document baseline deficits and changes over time whilst providing prognostic information (Levine et al., 2006). As a result, examining which stroke scales provide the most valid and reliable classifications of stroke type will allow for a more comprehensive understanding and comparison of participants' stroke severity and changes over time.

There are various clinical stroke scales such as; National Institutes of Health Stroke Scale (NIHSS), Canadian Neurological Scale (CS), Scandinavian Stroke Scale (SSS), and Oxfordshire Classification classify patients' baseline stroke severity (Bamford, Sandercock, Dennis, Warlow, & Burn, 1991; Brott et al., 1989; Cote et al., 1989; Cote, Hachinski, Shurvell, Norris, & Wolfson, 1986; Levine et al., 2006; Lyden et al., 2002; Rödén-Jüllig, Britton, Malmkvist, & Leijd, 2003). Outcome scales like the Rankin Scale (RS), modified Rankin Scale (mRS), Barthel Index (BI), and the Glasgow Outcome Scale (GOS) classify patients' level of disability and handicap after a stroke, quantifying their

prognosis and recovery (D'Olhaberriague et al., 1996; Jennett & Bond, 1975; Rankin, 1957; Sulter, Steen, & De Keyser, 1999; Van Swieten, Koudstaal, Visser, Schouten, & Van Gijn, 1988).

Whilst there is no ideal clinical stroke scale, the general consensus indicates that NIHSS is more applicable to rate clinical stroke severity (Levine et al., 2006). Research examining NIHSS found that intrarater agreement was good, particularly when the rater was a neurologist (mean $k = 0.77$), and the interrater agreement was excellent (mean $k = 0.69$) (Brott et al., 1989). Additionally, NIHSS correlated highly with infarction size on day 7 of a CT scan ($r = 0.78$) and 3 month outcome ($r = 0.71$) (Brott et al., 1989). More recent studies have stated that baseline severity as assessed by NIHSS is the most significant predictor of ultimate outcome (Derex et al., 2004; Schlegel et al., 2003; Schlegel, Tanne, Demchuk, Levine, & Kasner, 2004).

Unlike the NIHSS, the CS does not assess dysarthria, visual loss, sensory loss, or cognitive impairments affecting the right hemisphere such as neglect (D'Olhaberriague et al., 1996). The CS has been applied in clinical stroke trials, and has high validity and reliability (Brott et al., 1989; Cote et al., 1989; Stavem et al., 2002). Research states that a total score of <6.5 on the CS is a strong predictor of mortality at 1 month and 1 year (de Haan, Horn, Limburg, Van Der Meulen, & Bossuyt, 1993a; Muir, Weir, Murray, Povey, & Lees, 1996; Stavem et al., 2002). Furthermore, this scale correlates highly with the neurological examination ($r = 0.77$) (Cote et al., 1989), and with NIHSS (Muir et al., 1996). However, Muir et al. (1996) suggests that CS underestimates functional impairments.

The SSS has been applied in clinical stroke trials to either rate outcome severity or recruit patients (Lyden et al., 2002; Rödén-Jüllig et al., 2003). Research by Barber et al. (2003) investigated the reliability and validity of the SSS applied retrospectively to medical records. They found that the SSS score and the majority of its individual elements can be reliably estimated retrospectively from medical records. This scale has also been shown to have good construct validity when compared with the Barthel Index, Toronto Scale, Mathew Scale, and the Fugl-Mayer Scale (Rödén-Jüllig, Britton, Gustafsson, & Fugl-Meyer, 1994). However, a study by

Thommessen, Thoresen, Bautz-Holter, and Laake (2001) identified that the SSS aphasia score after stroke results in a higher rate of false positives and increases the prevalence for aphasia in epidemiological stroke studies.

Contrary, the Oxfordshire Classification has been noted as the simplest scale (Levine et al., 2006), dividing strokes into four categories: lacunar circulation syndrome (LACI), posterior circulation syndrome (POCI), total anterior circulation syndrome (TACI), and partial anterior circulation syndrome (PACI) (Bamford et al., 1991). The prognosis is strongly associated with the type of stroke classified of this scale, noting that those patients classified with TACI have the poorest prognosis (Dennis et al., 1993). Despite this scale not being comprehensively assessed for its reliability, validity, interrater, or intrarater reproducibility, a study by Mead, Lewis, Wardlaw, Dennis, and Warlow (2000) suggests that the scale would meet all these criteria because of the simplified nature. However, as research by D'Olhaberriague et al. (1996) identified the NIHSS and the CS as the most accurate scales, and suggests that these scales are likely to be superior than SSS.

As mentioned previously, outcome scales measure poststroke disability and handicap that have been defined by D'Olhaberriague et al. (1996). Disability denotes to the ability to execute activities of daily living (ADL) and involves performance and capacity, where handicap inhibits or restricts the completion of tasks that are normal for that individual. ADLs include self-care tasks necessary for personal independence: bathing, dressing, feeding, grooming, continence, toileting, mobility, and transfers (Bogouslavsky, 2002). Literature identifies commonly used and validated outcome scales to be the Rankin Scale (RS), modified Rankin Scale (mRS), Barthel Index (BI), and the Glasgow Outcome Scale (GOS) (D'Olhaberriague et al., 1996; Jennett & Bond, 1975; Rankin, 1957; Sulter et al., 1999; Van Swieten et al., 1988).

The Rankin Scale (RS) was constructed in 1957 to evaluate the amount of disability after a stroke (Rankin, 1957). This scale was later revised (mRS) by the Oxfordshire Community Stroke

Project to account for language and cognitive problems, and decrease the importance on walking (Burn, 1992). Research has stated that both the RS and mRS combine disabilities and impairments, but it does not measure handicap (Bloch, 1988; Bogousslavsky, 2002). Numerous studies have found the mRS to be substantially reliable (Bonita & Beaglehole, 1988; Broderick et al., 2000; Van Swieten et al., 1988; Wolfe, Taub, Woodrow, & Burney, 1991), and valid (Banks & Marotta, 2007). Numerous studies suggest that the mRS is more influential than the Barthel Index (BI) as a primary endpoint in clinical studies of stroke rehabilitation (Weir, Kaste, & Lees, 2004; Young, Lees, & Weir, 2003, 2005). However, a study by Uyttenboogaart, Luijckx, Vroomen, Stewart, and De Keyser (2007) suggests that when mRS is applied to multicentre stroke trials, it is a subjective global disability scale that considers changes in lifestyle and activity post-stroke that does not always cohere to ADLs measured by the BI. They continue to state that they are unsure whether presenting the mRS through a structured interview would improve the comparison to the ADLs measured by the BI, and additionally its validity in measuring functional outcome after stroke.

Thus, the Barthel Index (BI) assesses the amount of independence in performing ADLs, and is the most common applied measure of ADL competency in clinical stroke trials (Lyden, Broderick, Mascha, & Investigators, 1995). A study by Wilkinson et al. (1997b) reported that BI was an excellent scale for measuring stroke outcome over a long-term follow-up period (Levine et al., 2006). The major disadvantage of BI is that it does not assess social functioning, cognitive aspects, or household activities (Bogousslavsky, 2002). However, numerous studies have identified that the BI is valid (Granger, Albrecht, & Hamilton, 1979), it is highly correlated with poststroke status and has high internal consistency ($\alpha = 0.96$) (D'Olhaberriague et al., 1996), and has high interrater and test-retest reliability (Collin, Wade, Davies, & Horne, 1988; de Haan et al., 1993b).

The Glasgow Outcome Scale (GOS) was constructed to rate outcomes after head injury (Levine et al., 2006), but it has also been applied in stroke studies (Tirilazad International Steering

Committee, 2000; Yamaguchi et al., 1998). A study by Cavanagh and Gordon (2002) has shown an interrater reliability of 67% ($k = 0.52$), however, research has highlighted that it is challenging to differentiate between a score of 2 or 3 in this scale, and that the GOS significantly duplicates the information obtainable from the mRS (Broderick et al., 2000; Lyden & Lau, 1991). Nevertheless, Bogousslavsky (2002) has indicated that the scale is reliable and as sensitive as other stroke impairment scales at differentiating between treatment groups.

In summary, whilst numerous studies have validated the aforementioned scales for the use on stroke survivors, there is a general consensus to measure clinical severity using the NIHSS and the level of disability through the mRS after a stroke (Levine et al., 2006). Therefore, this establishes the use of the mRS as an appropriate classification scale in the present study.

2.1.4 Risk Factors

Stroke risk factors have major consequences on the structure and function of blood vessels and their interaction with circulating blood (Moskowitz, Lo, & Iadecola, 2010). Research by Van Dyke and Dave (2005) defines a risk factor as a characteristic or occurrence that has been connected with the amplified rate of a subsequently occurring disease. Furthermore, they state that risk factors may be modifiable, that is, usually behavioural or environmental in nature, or non-modifiable which are usually intrinsic to the person and so not easily changed (Van Dyke & Dave, 2005). Due to the consequences of stroke risk factors on the structure and function of blood vessels and their interaction with circulating blood, it is important to identify which risk factors contribute to stroke, and those that can be modified, that allows research to target the appropriate risk factors and aim to decrease their significance through interventions such as WBV.

Non-modifiable risk factors of stroke have been identified as: age, sex, race, ethnicity, and heredity or family history (American Heart Association, 2013; Hughes & Lip, 2008; Sacco et al., 1997). Whilst these factors cannot be modified, their presence aids in identifying those people at greatest risk, permitting aggressive treatment of those risk factors that can be modified (Sacco et al., 1997). A systematic review conducted by Hughes and Lip (2008), found that multiple studies indicated increasing age to have an independent effect on the risk of stroke, therefore making it one of the most important risk factors for stroke (Sacco et al., 1997). In 2002 the mean age at stroke death was 79.6 years (American Heart Association, 2013). Between the years of 1995 to 2002 there was a progressive incline in 30-day mortality rate as age increased; 9% in 65 to 74 years of age, 13.1% in 74 to 84 years of age, and 23% in those ≥ 85 years of age (American Heart Association, 2013). While age cannot be changed, an awareness of the accumulative effects of aging on the cardiovascular system and the progressive nature of stroke risk factors over a prolonged period, will allow for a greater understanding of non-modifiable risk factors contribution to stroke risk (Brown, Whisnant, Sicks, O'Fallon, & Wiebers, 1996; Goldstein et al., 2011; Wolf et al., 1992).

Research has identified that stroke is more prevalent in men (1.25 times higher) than in women (Sacco et al., 1997). However, each year approximately 55,000 more women than men have a stroke, this may be in part due to women tending to live longer than men (American Heart Association, 2013; Goldstein et al., 2011). Various studies support this finding, discovering that being female was a significant independent risk factor for stroke when assessed in general atrial fibrillation populations (Hart, Pearce, McBride, Rothbart, & Asinger, 1999; Hart et al., 2000; Van Latum et al., 1995; Wang et al., 2003). Furthermore, research has stated that women have a higher lifetime risk of stroke than men, with menopause and pregnancy being contributing factors (American Heart Association, 2013). Women who experienced a natural menopause before the age of 42 years had twice the ischaemic stroke risk of those women who experience natural menopause after the age of 42. Moreover, there is a 2.4 times greater risk of ischaemic

stroke or intracerebral haemorrhage during pregnancy and in the first 6 weeks post pregnancy (American Heart Association, 2013).

Stroke mortality and incidence rates vary greatly between racial and ethnic groups (Sacco et al., 1997). In terms of ethnicity, different studies highlight that Asians, particularly Japanese and Chinese, have high stroke incidence rates (He, Klag, Wu, & Whelton, 1995), and in the New Zealand population Māori people are 1.3 times more likely to suffer a stroke as non-Māori when adjusted for age and sex (National Health Committee, 2013). Racial groups such as African-Americans are more than twice as likely to die of stroke as whites (Howard et al., 1994a). However, a study by Otten, Teutsch, Williamson, and Marks (1990) suggests that some race-related risk of stroke may be associated to inherited risk factors or environmental factors other than race. In the National Health and Nutrition Examination Survey, mortality rate ratios were compared amongst black and white adults aged between 35 to 54 years old (Otten et al., 1990). This study found that when the mortality rate ratio was adjusted simultaneously for six well-established risk factors (systolic blood pressure, cholesterol level, smoking, diabetes, alcohol intake, and body-mass index) and family income, the mortality rate of blacks compared to whites decreased from 2.3 to 1.4. Therefore, this equated to approximately 31% of the surplus mortality being attributable to systolic blood pressure, cholesterol level, smoking, diabetes, alcohol intake, and body-mass index (Otten et al., 1990). In addition, a further 38% was attributable to family income, leaving 31% unexplained (Otten et al., 1990). In conclusion, they suggest that research should be targeted towards the causes of the mortality gap and increasing efforts aimed at modifiable risk factors. These findings are supported by Feigin et al. (2006), who states that similarly to race, ethnic differences propose dissimilar risk factor profiles for diverse ethnic groups.

Family history has long been noted as a risk factor for stroke incidence; with possible explanations being a common familial exposure to lifestyle or environmental risks, a genetic tendency for stroke, and a genetic determination of further stroke risk factors (Sacco et al.,

1997). The Framingham Study revealed that both parental and maternal histories were connected to an increased risk of stroke (Kiely, Wolf, Cupples, Beiser, & Myers, 1993). This is supported by later research by Liao et al (1997b), who examined whether familial history of stroke is linked with the prevalence of stroke in the Family Heart Study. After assessing personal and familial histories of stroke in over 3000 subjects and over 29,000 of their first-degree relatives, they found that a positive familial, paternal, and maternal history of stroke indicated an increased risk of stroke compared with those without a familial history of stroke. Furthermore, they concluded that this is consistent with the expression of a shared environment, genetic susceptibility, or both in the aetiology of stroke. This is supported by Hankey (2006), who states that the direct genetic influence of any single gene concerning ischaemic stroke is probably modest and only applied in selected patients, and in combination with environmental influences or through epistatic (gene-gene or environmental-gene) consequences.

Several studies have identified established (casual) modifiable risk factors for stroke (Table 2.1) (American Heart Association, 2013; Hankey, 2006; Moskowitz et al., 2010; Pearson et al., 2002; Sacco et al., 1997).

Table 2.1. Established risk factors for stroke

Classification	Risk Factor	References
Casual	Hypertension (>140/90 mmHg)	(American Heart Association, 2013; Hankey, 2006; Pearson et al., 2002; Sacco et al., 1997)
	Current cigarette smoking	(Goldstein et al., 2011; Hankey, 2006; Kissela et al., 2002; Longstreth, Nelson, Koepsell, & Van Belle, 1992; Pearson et al., 2002; Sacco et al., 1997; Shah & Cole, 2010)
	Blood lipid levels	
	Hypercholesterolaemia (total cholesterol \geq 240 mg/dL)	(American Heart Association, 2013; Hankey, 2006; Moskowitz et al., 2010; Sacco et al., 1997)
	Low HDL cholesterol (<40 mg/dL in adult males, <50 mg/dL in adult females)	(American Heart Association, 2013; Curb et al., 2004; Pearson et al., 2002)
	High fasting triglycerides (\geq 150 mg/dL in adults)	(American Heart Association, 2013; Pearson et al., 2002)

Diabetes mellitus	(Hankey, 2006; Kissela et al., 2005; Pearson et al., 2002; Sacco et al., 1997)
Atrial Fibrillation	(Hankey, 2006; Hughes & Lip, 2008; Pearson et al., 2002; Sacco et al., 1997; Wang et al., 2003; Wolf, Abbott, & Kannel, 1991)
Valvular heart disease	(Hankey, 2006; Kizer et al., 2005)
Ischaemic heart disease- Cardiomyopathy	(Hankey, 2006; Moskowitz et al., 2010)
Carotid stenosis	(Hankey, 2006; Rothwell et al., 2003)
History of stroke or TIA	(Howard et al., 1994b; Whisnant, 1997)

Table 2.2. Emerging risk factors for stroke

Classification	Risk Factor	References
Probable	Physical inactivity	(American Heart Association, 2013; Hankey, 2006; Hu et al., 2005; O'Donnell et al., 2010; Pearson et al., 2002)
	Obesity	(American Heart Association, 2013; Hankey, 2006; Hu et al., 2007; Pearson et al., 2002; Sacco et al., 1997)
	Low fruit and vegetable intake	(American Heart Association, 2013; Dauchet, Amouyel, Hercberg, & Dallongeville, 2006; Hankey, 2006; Pearson et al., 2002)
	Psychosocial stress	(Hankey, 2006; Simons, McCallum, Friedlander, & Simons, 1998)
	Excess alcohol	(O'Donnell et al., 2010; Sacco et al., 1997)
	Second-hand smoking	(Lee & Forey, 2006; Oono, Mackay, & Pell, 2011)
	Aspirin	(Pearson et al., 2002)
	Illicit drug use	(Sacco et al., 1997)
	Haemostatic and inflammatory factors	
	Elevated fibrinogen	(Kannel, Wolf, Castelli, & D'Agostino, 1987b; Rothwell et al., 2004; Sacco et al., 1997; Wilhelmsen et al., 1984)
	High concentrations of tissue plasminogen activator antigen	(Ridker, Hennekens, Manson, Vaughan, & Stampfer, 1994)
	Increased inflammatory markers (white blood cells, C-reactive protein, infection)	(Di Napoli et al., 2005)
	Hyperhomocysteinemia	(Sacco et al., 1997; Wald, Law, & Morris, 2002)
Dyslipidemia	(Holme, Aastveit, Hammar, Jungner, & Walldius, 2009)	

Raised Apo B-Apo A1 Ratio (represents the balance of antiatherogenic and proatherogenic lipoproteins)	(Hankey, 2006)
Patent foramen ovale	(Di Tullio, Sacco, Gopal, Mohr, & Homma, 1992; Hankey, 2006; Lechat et al., 1988; Nedeltchev et al., 2008; Ranoux et al., 1993)
Endothelial dysfunction	(Hankey, 2006)
Arterial compliance, elasticity, stiffness	(Hankey, 2006)
Structural heart disease	(Hughes & Lip, 2008; Sacco et al., 1997)
Peripheral arterial disease	(American Heart Association, 2013)
Chronic kidney disease	(Lee et al., 2010)
Sickle cell disease	(American Heart Association, 2013)
Multiple risk factors	(Sacco et al., 1997)
Pregnancy	(James, Bushnell, Jamison, & Myers, 2005; Kittner et al., 1996)
Early menopause (before 42 years)	(Lisabeth et al., 2009)
Obstructive sleep apnea	(Arzt, Young, Finn, Skatrud, & Bradley, 2005; Redline et al., 2010; Yaggi et al., 2005)

However, due to continual research into this area, new emerging (probable) risk factors have been identified but still require further study to be critically appraised (Table 2.2) (Hankey, 2006; Myers et al., 2009). Due to the pure number of both established and emerging risk factors for stroke, not all risk factors have been examined in detail. However, those that have been identified as major contributors to the overall risk of stroke have been examined in further detail below.

Casual risk factors are those that have demonstrated in randomised controlled trials to decrease stroke risk if improved, or for which a consistently strong and independent association with stroke has been recognised, whilst probable risk factors are less resolute and/or have not established a causative role (Hankey, 2006). Research has identified several modifiable risk factors that account for an estimated 60% to 80% of stroke risk in the general population (Donnan et al., 2008; Hankey, 2006; Moskowitz et al., 2010). Hankey (2006) stated increasing

blood pressure, cigarette smoking, blood cholesterol, diabetes mellitus, carotid stenosis, atrial fibrillation, and valvular heart disease to contribute to 60% to 80% of all ischaemic stroke. Several randomised controlled trials have demonstrated that treating increasing blood pressure, increasing blood cholesterol, atrial fibrillation, and carotid stenosis reduces the incidence of ischaemic stroke and as a result classifies these as certain casual risk factors for ischaemic stroke (Cholesterol Treatment Trialists, 2005; Hart, Benavente, McBride, & Pearce, 1999; Lawes, Bennett, Feigin, & Rodgers, 2004b; MRC Asymptomatic Carotid Surgery Trial Collaborative Group, 2004; Rothwell et al., 2003). Factors such as diabetes mellitus, cigarette smoking, valvular heart disease, and ischaemic heart disease are plausible casual risk factors for ischaemic stroke, as it is possible that associations found through epidemiological case-control and cohort studies may be confounded by other factors that have not been analysed or measured in epidemiological studies (Hankey, 2006). However, the aforementioned factors have shown a significant association with increased risk of stroke, specifically a strong association, biologically plausible, consistency among studies, and were independent of other factors that were examined (Bonita, Duncan, Truelsen, Jackson, & Beaglehole, 1999; Coulshed, Epstein, McKendrick, Galloway, & Walker, 1970; Kizer et al., 2005; Lawes et al., 2004a; Loh et al., 1997; Rodgers et al., 2004). Population-based studies in Rochester, Minn, supported these ischaemic stroke risk factors by means of multiple logistic-regression techniques. They found that the population-attributable risk (PAR) of ischaemic stroke due to 7 major risk factors was 57%; hypertension, cigarette smoking, diabetes mellitus, atrial fibrillation, mitral valve disease, ischaemic heart disease, and history of TIA (Whisnant, 1997). Additionally, if carotid stenosis and serum cholesterol had been included, it is probable that approximately 80% of all ischaemic strokes could be attributed to these risk factors (Cholesterol Treatment Trialists, 2005; Hankey, 2006; MRC Asymptomatic Carotid Surgery Trial Collaborative Group, 2004; Rothwell et al., 2003). Hankey (2006) also highlights that approximately 10% to 20% of atherosclerotic ischaemic strokes may be linked to newly established, casual risk factors for ischaemic heart disease: obesity, elevated apoB/apoA 1 ratio,

and physical inactivity, poor diet consisting of low fruit and vegetable intake, and psychosocial stress. However, it is debateable as to whether these risk factors are casual due to several studies indicating that stroke research has been limited to involving small sample sizes with differences in stroke subtype, lifestyle, and stroke severity, and also no randomised controlled trials have demonstrated that decreasing exposure to these risk factors lessens the risk of stroke (Ezzati, Lopez, Rodgers, Vander Hoorn, & Murray, 2002; Ezzati et al., 2003; Yusuf et al., 2004). As a result, research by Moskowitz et al. (2010) has classified these modifiable risk factors as probable (Table 2.2).

Feigin et al. (2005) conducted a systematic review of 37 longitudinal and case-control studies that investigated risk factors for subarachnoid haemorrhage published between 1966 to March 2005. They identified hypertension, smoking, and excessive alcohol as the most significant risk factors for subarachnoid haemorrhage. This is supported by Andersen, Olsen, Dehlendorff, and Kammergaard (2009); indicating that haemorrhagic stroke is strongly linked to high alcohol consumption and smoking. Furthermore, diabetes, atrial fibrillation, intermittent arterial claudication, and previous stroke or myocardial infarction all strongly favour ischaemic stroke, whilst hypertension favours neither but is a well-documented risk factor for both stroke types (Andersen et al., 2009).

Due to the emergence of new risk factors and the lack of research investigating risk factors of all types of stroke, a study by O'Donnell et al. (2010) investigated the association and contribution of casual and probable risk factors with all stroke. They performed a standardised case-control study in 22 countries across the world, which involved 3000 acute (within 5 days of symptoms onset) first stroke patients and 3000 age and sex matched controls with no history of stroke. They found that five significant risk factors attributed to more than 80% (PAR) of the worldwide risk of all stroke (ischaemic and intracerebral haemorrhagic): hypertension (34.6%), amount of regular physical activity (28.5%), abdominal obesity (26.5%), current smoking (18.9%), and diet

(18.8%). Furthermore, with the addition of five other significant risk factors, the PAR for all stroke increased to 90.3%: ratio of apolipoproteins B to A1 (24.9%), cardiac causes (6.7%), diabetes mellitus (5.0%), alcohol intake (3.8%), and psychosocial stress and depression (9.8%; 4.6% and 5.2%, respectively). All of the above stated risk factors were significant for ischaemic stroke, while smoking, hypertension, diet, alcohol intake, and abdominal obesity were the only significant risk factors for intracerebral haemorrhagic stroke. Interestingly for ischaemic stroke, O'Donnell et al. (2010) found a significant link with all nine risk factors acknowledged in the INTERHEART study, which stated nine modifiable risk factors that explained the majority of the risk of myocardial infarction globally (McQueen et al., 2008; Rosengren et al., 2004; Teo et al., 2006; Yusuf et al., 2005; Yusuf et al., 2004). These nine factors were hypertension, abdominal obesity, smoking, physical activity, diet, diabetes mellitus, alcohol intake, apolipoproteins, and psychosocial factors. However, the relative weight of hypertension, physical activity, apolipoproteins, and alcohol intake for stroke appear to be dissimilar compared with myocardial infarction. These recorded dissimilarities in risk factor profile may partially explain the worldwide differences in incidence of ischaemic stroke, intracerebral haemorrhagic stroke, and myocardial infarction (Johnston, Mendis, & Mathers, 2009; Truelsen et al., 2003). It is not surprising that the majority of stroke risk factor research has targeted ischaemic stroke, as approximately 87% of all strokes are ischaemic (American Heart Association, 2013). Pursuing ischaemic stroke risk factors would therefore target a large majority of the stroke population. However, previous research has identified different stroke types that are more favoured to certain risk factors, for example: diabetes and atrial fibrillation for ischaemic stroke compared to excess alcohol and smoking for haemorrhagic (Andersen et al., 2009). Therefore, a combination of these factors is required to target all stroke but more research is needed to identify these risk factors. Research has indicated that interventions that target reduction in blood pressure, ceasing smoking, drinking in moderation, regular physical activity, and encourage a well-balanced diet may substantially diminish the burden of stroke (Donnan et al., 1989; Donnan et al., 2008; He, Nowson, &

MacGregor, 2006; O'Donnell et al., 2010; Reynolds et al., 2003; Wendel-Vos et al., 2004). This is supported by Hankey (2006) who suggests research resources should target those risk factors that contribute up to 80% of all strokes, as opposed to the novel risk factors that only account for 20% of all strokes. Additionally, Hubner, Yagil, and Yagil (2006) recommends that future genetic research may be of more benefit from investigating the genetics of the established risk factors, such as; increased blood pressure, more than exploring new genes for stroke.

Research states that numerous established risk factors modify vascular structure through encouraging atherosclerosis, stiffening of the arteries, and stimulating thickening, narrowing, and tortuosity of arterioles capillaries (Allen & Bayraktutan, 2008; Iadecola & Davisson, 2008). In the brain, these morphological alterations are regularly linked to decreases in resting cerebral blood flow and marked changes in cerebral blood flow regulation (Moskowitz et al., 2010). Therefore, hypertension, aging, hypercholesterolaemia, and diabetes mellitus impair vital adaptive mechanisms that encourage the brain to be adequately perfused (Arrick, Sharpe, Sun, & Mayhan, 2007; Iadecola & Davisson, 2008; Iadecola, Park, & Capone, 2009; Kitayama, Faraci, Lentz, & Heistad, 2007). The endothelium's ability to regulate microvascular flow is compromised, whilst the rise in blood flow caused by neural activity is prevented, causing an inequality between the brain's energy supply and demand (Arrick et al., 2007; Iadecola & Davisson, 2008; Iadecola et al., 2009; Zou, Cohen, & Ullrich, 2004). Diabetes mellitus and hypertension weaken protective vascular mechanisms that keep cerebral blood flow stable during decreases in blood pressure, aiding the manifestation of ischaemia if intravascular pressure declines (Immink et al., 2004; Kim et al., 2008). As a result, these vascular changes escalate the brain's vulnerability to ischaemia following arterial occlusion (Moskowitz et al., 2010).

2.1.5 Aetiology

The aetiology of stroke involves: atherosclerosis; large-artery atherosclerotic infarction (thrombosis/embolus), and in turn perfusion failure distal to the site of severe occlusion or stenosis of major arteries; cardioembolism; small vessel disease (occlusion); lipohyalinosis; sickle cell disease; infarcts of undetermined cause; hypertension; ruptured aneurysms and vascular malformations (Adams et al., 1993; Furie et al., 2011; Mohr et al., 1997; Zorowitz et al., 2004). Atherosclerosis and lipohyalinosis (in the case of small vessel disease) have been linked to the formation of these causes; with atherosclerosis being one of the most common causes of stroke (Adams et al., 1993).

To better understand the process of atherosclerosis, an awareness of vessel structure is first required. All arteries have a three-layered structure (from outside to inside): the adventitia, media, and intima (Figure 2.4).

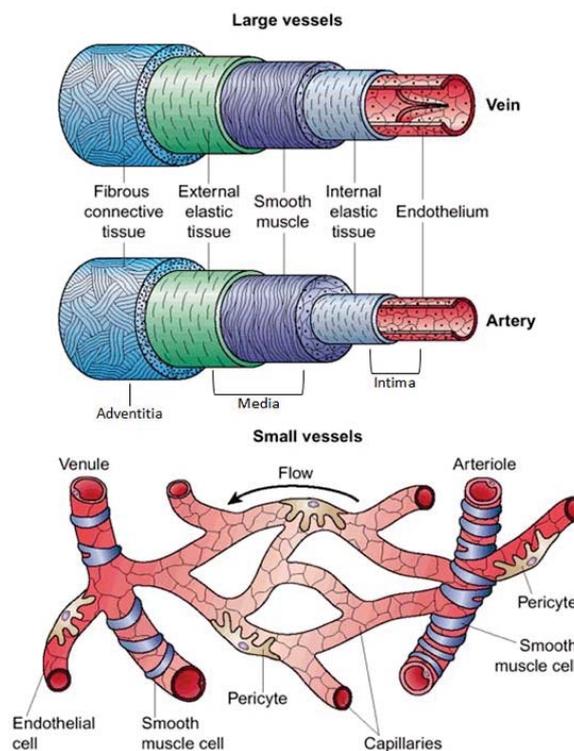


Figure 2.4. Structure of vessels (adapted from Cleaver and Melton (2003)).

The adventitia is a connective tissue sheath of the outermost layer; it maintains the vessel shape, provides nutrients to the media, and limits distension (Stoner & Sabatier, 2012; Young, 2011). The media is largely comprised of vascular smooth muscle cells that regulate blood flow via vasodilation and vasoconstriction (Stoner & Sabatier, 2012; Young, 2011). The intima is the innermost layer of the vessel, and contains a continuous monolayer of endothelial cells and thin layer of underlying connective tissue (Hurairah & Ferro, 2004; Stoner & Sabatier, 2012).

Atherosclerosis is the result of harmful agents associated with hypertension, hyperlipidemia, cigarette smoking, diabetes mellitus, and other agents that can change the condition of the artery wall, and consequently injure smooth muscle and the endothelium (Ross, 1995). A protective, inflammatory response occurs in excess to try and accommodate for these harmful agents; a process called atherosclerosis (Figure 2.5).

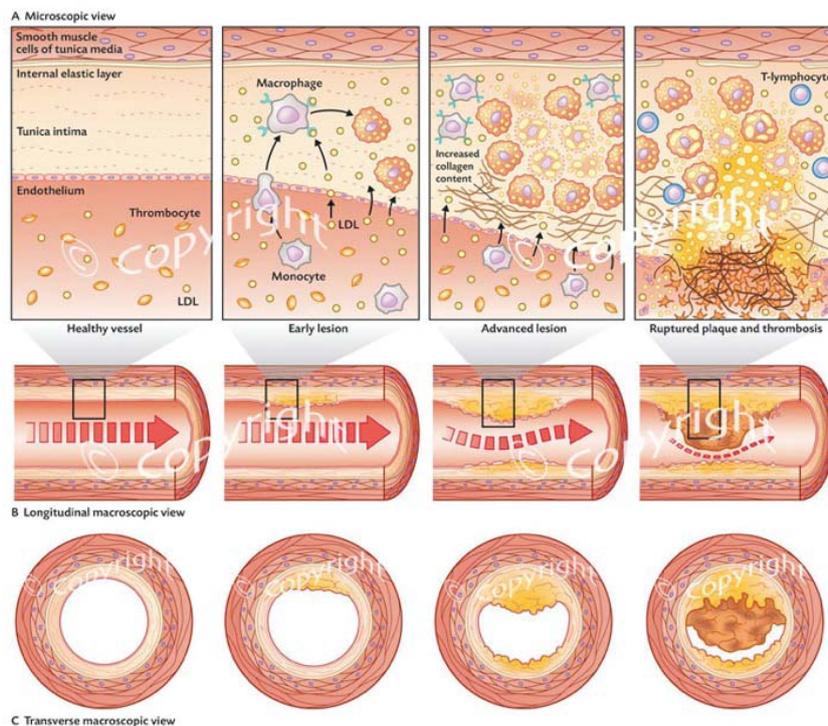


Figure 2.5. Process of atherosclerosis (Maizels & Akademisk, 2011)

The atherosclerotic process involves endothelial dysfunction that can result in alterations in adhesive characteristics, permeability, and growth-stimulatory characteristics (Davignon & Ganz, 2004). Initially, production of cytokines and perivascular microglia-macrophages upregulates adhesion molecule expression and encourages leukocytes to move and stick to the vessel surfaces (Zhang, Chopp, Zhang, Jiang, & Powers, 1998). These changes lead to neutrophils being recruited into the brain, followed by monocytes entering the subendothelium, becoming activated as macrophages and are joined by T lymphocytes (Moskowitz et al., 2010). These two cells in combination create the fatty streak. Activation of these cells can generate formation of molecules that can attract smooth muscle cells to migrate and replicate within the lesions (Paoletti, Gotto, & Hajjar, 2004). This in turn leads to the formation of fibrous plaques that have a fibrous cap that protects and covers a core of necrotic and lipid material (Munro & Cotran, 1988). This inflammatory response begins as a protective mechanism; however it can become excessive and destroy tissue, and ultimately cause a hyperplastic lesion. This lesion impacts on the lumen of the artery, reduces the blood flow through the artery, and consequently results in damage to the tissue (Ross, 1993; Ross, 1995). This build-up of plaque (the atherosclerotic process) is associated with ischaemic stroke and in particular thrombotic stroke as it blocks blood flow to the brain, but additionally it can be associated with embolic stroke if this plaque breaks free and floats to the brain.

Large-artery atherothrombosis or thromboembolism generally occurs during sleep and is associated with perfusion failure distal to the site of occlusion or stenosis (attributable to the process of atherosclerosis) of major vessels such as the carotid artery (Zorowitz et al., 2004). Cardioembolism or embolic stroke usually occurs during waking hours and is most often associated with an embolus blocking one of the branches of the middle cerebral artery (Zorowitz et al., 2004). This embolus can be attributed to the atherosclerotic process. The embolus may

cause significant neurologic deficits that are temporary, these symptoms rectify as the embolus fragments. This cause is most commonly due to a cardiac source such as chronic arterial fibrillation, valvular heart disease, myocardial infarction cardiomyopathy, or cardiac aneurysm (Zorowitz et al., 2004). Small vessel disease is the occlusion of deep penetrating branches of large vessels (50—200 μm in diameter) as a result of the process of atherosclerosis or lipohyalinosis (Lammie, 2000; Zorowitz et al., 2004). Lipohyalinosis is a destructive vessel lesion that is illustrated by a loss of normal arterial architecture (Lammie, 2000). As a result of this occlusion small lacunar infarcts occur (Mohr et al., 1997; Zorowitz et al., 2004). Finally, sickle cell disease can cause blood to cluster and block blood vessels (Furie et al., 2011; Zorowitz et al., 2004). Haemorrhagic strokes are strongly linked to chronic hypertension and are preceded by the formation of microaneurysms. Haemorrhagic strokes can also result from vascular malformations and ruptured aneurysms as well as systemic factors such as trauma, drugs and tumours (Zorowitz et al., 2004). Hypertension has been defined by the American Heart Association (2013), as a systolic blood pressure (SBP) of ≥ 140 mmHg or a diastolic blood pressure (DBP) of ≥ 90 mmHg. Chae, Lee, Rifai, and Ridker (2001) have identified some experimental evidence to suggest that hypertension may encourage endothelial expression of cytokines and stimulate inflammation. Their data suggests that high blood pressure may contribute to atherogenesis by encouraging inflammatory activation of the arterial wall, and consequently this may result in coronary artery disease or stroke.

2.1.6 Acute vs. Chronic Stroke

The focus of the present study is on chronic stroke, where acute stroke is <48 hours after stroke onset and chronic stroke is >6 months after stroke onset (Ochfeld et al., 2010). However, examining the process of how individuals are affected across time, that is acutely to chronically, will enable for further understanding of how patients are chronically affected but also whether

exercise interventions can have beneficial effects on stroke.

Research has described the process of stroke as having an acute onset, followed by an initial speedy recovery and improvement during the first six weeks, for a subsequent 6 months substantial improvement can occur, and thereafter this improvement gradually slows to a steady rate of recovery (Kirkevold, 2002). This suggests that many stroke survivors can and will adjust to the remaining effects of their stroke. This is supported by a New Zealand population based long-term follow-up study (Feigin et al., 2010), which investigated 418 stroke survivors up to five years post-stroke. They found that at 28 days post-stroke 26% of the survivors had significant activity restrictions (mRS= 3-5). Whereas, at five years post-stroke 68.6% of stroke survivors demonstrated good overall outcome (mRS= 3), with 70.6% displaying independence in activities of daily living (ADL), even though two-thirds self-reported incomplete recovery. Furthermore, they found no changes between 6-month and 5-year post-stroke on the SF-36 and activity restrictions. Additionally, their findings displayed that recurrent stroke significantly and independently increased the risk of moderate to severe neurologic impairment, dependency, participation limitations, and information processing speed limitations. Therefore the authors' findings are consistent with previous long-term (5 years) population-based stroke outcome research proposing a plateau (Toschke et al., 2010) or decline (Dhamoon et al., 2009) in recovery 6 months post-stroke (Feigin et al., 2010).

Research into stroke largely concentrates on short-term post-stroke outcomes and patients in hospital and rehabilitation settings (Feigin et al., 2010; Hackett, Duncan, Anderson, Broad, & Bonita, 2000), with minimal community-based stroke research into long-term outcomes for stroke survivors (Barker-Collo, Feigin, Parag, Lawes, & Senior, 2010). Long-term post-stroke research is vital in assisting the stroke community (survivors, families and healthcare providers) to effectively prepare and progress into the future, but also provide better outcomes for stroke

survivors through evidence-based long-term rehabilitation and education programs (Feigin et al., 2010; Gadidi, Katz-Leurer, Carmeli, & Bornstein, 2011).

Acute stroke symptoms and effects can vary depending on stroke severity, location of lesion, and stroke subtype (Sabaté & Wimalaratna, 2004), resulting in impairment in psychological, physical and social functioning (Kim, Warren, Madill, & Hadley, 1999). Symptoms of stroke include weakness of the face, arms or legs, loss of balance or coordination, trouble speaking or slurred speech, blurred vision, dizziness, and confusion (National Health Committee, 2013). Stroke has been associated with decreased motor functions, hemiparesis, paralysis, vision problems, memory loss, changes in behaviour, ataxia, and apraxia (American Heart Association, 2012a; Bohannon, 2007; Durstine, Moore, Painter, & Roberts, 2009; National Stroke Association, 2009). Moreover, as each of the brain's hemispheres control the opposite side of the body (American Heart Association, 2012b), depending on which side of the brain is effected by stroke this can result in different effects to the individual. For example, left hemisphere damage can cause impairments to the right side of the body such as: right side hemiparesis, paralysis, loss of visual awareness to the right, disconnected thoughts, an inability to read or write, difficulties speaking and understanding speech, slow and clumsy movement, and difficulty executing purposeful movements (The Stroke Foundation New Zealand, 1998). Right hemisphere damage can cause impairments to the left side of the body such as: left side hemiparesis, paralysis, loss of visual awareness to the left, difficulty recognising faces, eating or swallowing, spatial relationships and interpreting sound, difficulties with abstract sound, slurred speech, and memory problems (The Stroke Foundation New Zealand, 1998).

After enduring the acute effects of stroke, survivors are then confronted with the long-term outcomes and recovery of stroke (Hankey, Jamrozik, Broadhurst, Forbes, & Anderson, 2002). Research by Barker-Collo and Feigin (2006) state that short-term outcomes are considered to be the initial three months post-stroke, whilst long-term outcomes are considered to be one year

post-stroke onwards. Research suggests that at least 50% of stroke survivors have some form of long-term disability that can include cognitive, social, emotional, physical or vocational difficulties (O'Sullivan & Chard, 2010). As mentioned earlier, the outcome and amount of disability experienced as a result of a stroke is subject to factors linked with the brain lesion such as: the size, location, and type of lesion, premorbid functioning, and age (Barker-Collo & Feigin, 2006; Donnan et al., 2008; Hankey et al., 2002; Macciocchi, Diamond, Alves, & Mertz, 1998; Sabaté & Wimalaratna, 2004). Long-term outcome is predicted by elements of physical functioning, cognitive functioning, psychological functioning, and residual disability (Haacke et al., 2006; Hankey et al., 2002; Patel et al., 2006).

The ability to walk and function independently in everyday activities is compromised in stroke survivors (Almkvist Muren, Hütler, & Hooper, 2008). Consequently, insufficiencies in functioning and mobility in daily living is a sizeable concern as it has major effects on the wellbeing and psychological functioning of stroke survivors (White et al., 2007). Impairment in cognitive functioning is also common in stroke survivors, with deficits in functioning varying according to stroke severity, lesion site, ethnicity, and age (Feigin et al., 2010; Patel, Coshall, Rudd, & Wolfe, 2002; Viscogliosi et al., 2011). Research has found associations between cognitive dysfunction and the inability to participate in activities of daily living (ADL), depression, and poorer long-term outcomes (Feigin et al., 2010; Hackett & Anderson, 2005; Patel et al., 2002). Additionally, there is a lack of agreement on standardised cognitive assessments for stroke (Gottesman & Hillis, 2010), with the majority of studies usually focusing on short-term outcomes (Hochstenbach, den Otter, & Mulder, 2003). There is a high prevalence of psychological disorders in stroke survivors that can cause negative effects on their recovery process and lead to further physical impairment (Pohjasvaara, Vataja, Leppävuori, Kaste, & Erkinjuntti, 2001; Robinson & Spalletta, 2010; West, Hill, Hewison, Knapp, & House, 2010). Prominent psychological disorders in stroke survivors have been identified as depression and anxiety; with depression being reported as the most common, occurring in approximately 33% of stroke survivors most

frequently in the first 3 months post-stroke (Hackett, Yapa, Parag, & Anderson, 2005). Interestingly, whilst depression has been noted as the most common, a study by Morrison, Pollard, Johnston, and MacWalter (2005) found that in stroke survivors 3 years post-stroke, depression decreased overtime whereas anxiety remained stable 3 years after stroke. Impairment in physical functioning, cognitive functioning, and psychological distress post-stroke influences stroke survivors' quality of life (QOL) (Kim et al., 1999). A study by Aprile et al. (2006) identified the most significant effect of stroke as a decline in health related quality of life (HRQOL). Research by Hackett et al. (2000) highlighted the significant effect of stroke on HRQOL in stroke survivors six years post-stroke when compared to an age and sex-matched control group. They found that 77% of stroke survivors were living at home, and of this, 46% still needed support in at least one aspect of their daily living. Furthermore, whilst stroke survivors scored lower in areas of general health and physical functioning, no differences were noted in domains of bodily pain or mental health. They established that with significant continuing physical disabilities, stroke survivors had adjusted well psychologically to their disabilities. However, when a study by White et al. (2007) compared HRQOL and function in community-dwelling stroke survivors at one, three, and five-year gaps they discovered that whilst function did not change significantly over time, a large number of survivors still relied on community services. Additionally, they found that although high levels of perceived social supported was reported, emotional wellbeing was low overall. These findings are comparable to Patel et al. (2006) who discovered that at 3 years post-stroke, handicap and disability were still highly prevalent and patients' perception of health status was persistently low, however mental health perception was satisfactory. The residual effects of stroke restrict an individual's ability to participate in physical activities, leisure, hobbies, and social activities, with research stating that participation in these activities improves both mental and physical wellbeing (O'Sullivan & Chard, 2010). Consequently, it is important that stroke i target not only stroke survivors physical functioning, but also assist in the adjustment process so that survivors maintain a level of participation in

activities that promote both their health and wellbeing (Gadidi et al., 2011; Kirkevold, 2002; O'Sullivan & Chard, 2010; Robison et al., 2009).

2.1.7 Cognitive Ability

Cognitive impairment has a significant impact on activities of daily living and QOL by reducing the amount of independence of the individual, and is linked with long-term disability and morbidity (Douiri, Rudd, & Wolfe, 2013; Mellon et al., 2015). Where, stroke has been found to be the leading cause of acquired disability with around two-thirds having some form of neurological impairment at five years post-stroke (Feigin et al., 2010). Thus, it may be possible to prevent, postpone, or mitigate vascular cognitive impairment due to strokes significant association with vascular pathology (Mellon et al., 2015). Research has found that appropriate management of vascular risk factors post-stroke, such as adequate blood pressure (BP) control, lipid control, and anti-thrombotic therapy, is associated with longer term protective benefits and reduced risk of post-stroke cognitive impairment (Douiri, McKeivitt, Emmett, Rudd, & Wolfe, 2013). Therefore, it is important to investigate cognitive function and the effects of WBV therapy on this variable, as to attempt to reduce the burden of post-stroke cognitive impairment and consequently improve QOL.

As mentioned previously, the severity and type of cognitive impairment differs according to the location of stroke, and may involve problems with language, attention, perception, memory, or executive functioning (Nys et al., 2006; Nys et al., 2005a). Furthermore, cognitive difficulties affect an individual's ability to live independently, perform ADLs, and influence participation in activities (Claesson, Lindén, Skoog, & Blomstrand, 2004; Nys et al., 2005b; Viscogliosi et al., 2011). Viscogliosi et al. (2011) displayed deficits in language, visual perception, and memory three weeks after being discharged home after stroke. These deficits were associated with restriction in participation, and were most prominent in individuals aged 65 years and over.

However, they found that cognitive impairment resulted in added restrictions in social roles than in ADL. Research by Rasquin et al. (2003) investigated the frequency of cognitive impairment in 198 stroke survivors up to one year post-stroke. They found that 65% of stroke survivors displayed mild cognitive impairment, and 10% presented with post-stroke dementia. Mental speed and calculation were most frequently affected, while memory displayed little deterioration. Performance on cognitive tests was improved for some at 6 and 12 months post-stroke, displaying that improvement of cognitive function is possible. However, to a lesser extent some participants displayed deterioration, but for most cognitive functioning remained stable. Previously, it has been reported that in 24% of first-ever cerebral stroke survivors at 6 months (Schmidt et al., 1993), 12.5% of stroke survivors at 12 months (Desmond, Moroney, Sano, & Stern, 1996), and 50% of stroke survivors at 15 months (Ballard, Rowan, Stephens, Kalaria, & Kenny, 2003), improvement in cognitive performance was noted. Hochstenbach et al. (2003) also displayed comparable rates of improvement at 2 years post-stroke, however this was mainly in language and attention, and only a low percentage of participants exhibited improvement in memory. A long-term observational study by Patel et al. (2002) identified that at 3 months post-stroke cognitive impairment was negatively associated with disability, long-term survival, and increased dependency up to 4 years post-stroke. This suggests that stroke survivors with cognitive impairment were more likely to be non-compliant with medication, experience more severe cerebrovascular disease, and experience more relationship difficulties with family and careers as a result of their reduced ability to manage their physical impairment. Furthermore, Barker-Collo et al. (2010) recognised that at 5 years post-stroke neuropsychological deficits were independently associated with HRQOL, handicap, and disability over and above age, stroke severity, and depression.

A study by Gottesman and Hills (2010) has identified there is a lack of agreement on standardised cognitive assessments for stroke. However, research has recognised published cognitive

screening tests such as; Mini Mental State Examination (MMSE), Cambridge Cognitive Assessment (CAMCOG), Middlesex Elderly Assessment of Mental State (MEAMS), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Montreal Cognitive Assessment (MoCA), and the Addenbrookes Cognitive Examination Revised (ACE-R). All of the above tests are designed to be suitable for bedside assessment, short to administer, and relatively easy to score and conduct (North Central London Cardiac and Stroke Network, 2012). Yet, none of these cognitive tests have proven to consistently identify cognitive impairments as no single test assesses the complete range of common cognitive difficulties post-stroke (North Central London Cardiac and Stroke Network, 2012). Therefore, research cannot recommend one test over another as no one measure can be applied universally. The MMSE is the most broadly applied cognitive measure, in stroke and other clinical settings (Shulman et al., 2006). But this measure has proven to have high levels of diagnostic validity for dementia (Tombaugh & McIntyre, 1992), where research has indicated that it has poor diagnostic validity in acute stroke populations and cannot accurately discriminate amongst people with and without cognitive impairment (Blake, McKinney, Treece, Lee, & Lincoln, 2002; Nys et al., 2005a). The MMSE does not adequately measure visuospatial abilities, executive functioning, or the ability to retain information over prolonged periods (Morris, Hacker, & Lincoln, 2012). On the other hand, the ACE-R covers a broader range of cognitive impairments than the MMSE, including normative data for five subscales and a measure of executive functioning (Morris et al., 2012). Studies have shown that when ACE-R is compared with the MMSE, higher specificity and sensitivity for the recognition of dementia has been displayed, although there is debate over the ideal cut-off score (Larner, 2007; Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000). Research by Gaber (2008) suggested that the ACE-R is a valid measure for detecting cognitive impairment after traumatic brain injury. Moreover, a study by Morris et al. (2012) investigated the validity of the ACE-R in detecting cognitive impairment post-stroke. They found that the ACE-R could not suitably measure the overall cognitive impairment in acute stroke survivors; however it could

identify impairment in visuospatial attention and executive domains. They also identified that ACE-R was more accurate than the MMSE for detecting cognitive impairment post-stroke, yet neither were a satisfactory measure. Due to the weaknesses in ACE-R domains, such as visuospatial, repetition, and comprehension, items on the ACE-R were substituted to form the ACE-III (Velayudhan et al., 2014). The ACE-III still contains five cognitive domains and has a maximum score of 100, but it can no longer derive an MMSE score. ACE-III cognitive domains were found to correlate significantly with standardised neuropsychological tests, its internal reliability was good ($\alpha = 0.88$), and had similar levels of specificity and sensitivity as the ACE-R (Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013).

2.1.8 Quality of Life (QOL)

QOL of stroke survivors is influenced by the amount of psychological distress, and impairment in cognitive and physical functioning post-stroke (Kim et al., 1999). Furthermore, a decline in HRQOL has been stated to be the most significant effect of a stroke for the survivor (Aprile et al., 2006). Commonly, QOL and HRQOL are used interchangeably in literature, but Doyle (2002) states that they are in fact two separate constructs. QOL is conceptualised as a broad construct that incorporates aspects of an individual's life that may affect or be related to their health state, such as spirituality, education opportunities, employment, housing, and standard of living (Campbell, Converse, & Rodgers, 1976; Doyle, 2002). Whereas, HRQOL denotes aspects of individual's lives that are linked to their health and health related outcomes (Salter, Moses, Foley, & Teasell, 2008). Outcome measures of HRQOL for stroke are most frequently investigated using measures of ADL, usually the mRS and the BI (Haacke et al., 2006; Kim et al., 1999). Because stroke affects more than just physical functioning, it is vital the potential multi-determinants that predict QOL and HRQOL post-stroke are considered (Haacke et al., 2006; Teoh, Sims, & Milgrom, 2009). To accomplish this QOL and HRQOL need to integrate a multidimensional framework, and

allow for global aspects of functioning in several areas (Salter et al., 2008). As a result, a study by Salter et al. (2008) investigated eight commonly used scales for assessment of HRQOL after stroke. Two-reviewers categorised scale items from three stroke-specific (30-item Stroke-Adapted Sickness Impacted Profile, Stroke Impact Scale, and the Stroke-Specific Quality of Life Scale) and five generic (Nottingham Health Profile, Medical Outcomes Study Short-Form 36, London Handicap Scale, EuroQol Quality of Life Scale, and the Sickness Impact Profile) scales within an established structure with nine dimensions; global judgements of health, symptoms, physical functioning, cognitive functioning, psychological wellbeing, social wellbeing, personal constructs, role activities, and satisfaction with care. These nine dimensions have been identified as important aspects of HRQOL (Fitzpatric, Davey, Buxton, & Jones, 1998). The aforementioned study found that whilst the majority of the scales included items to evaluate physical function, psychological wellbeing, social wellbeing, and role activities, there was a substantial variability between these scales with respect to the extensiveness of evaluation within each dimension and the combination of dimensions assessed. They concluded that no single scale contained items relating to all nine dimensions, and therefore no scale was a reasonable operationalization of HRQOL. Although, Anderson, Laubscher, and Burns (1996) found that the SF-36 avoids the 'ceiling effect' of most disability scales and had satisfactory internal consistency, whilst providing a valid measure of mental and physical health post-stroke. Furthermore, Ware (2004) identified that reliability statistics for the SF-36 have surpassed the minimum standard of 0.70 in over 25 studies and simulated over 24 patient groups.

According to a study by Aprile et al. (2006), post-acute and chronic stroke survivors (mean duration of disease 4 years) who exhibited high levels of disability as reported by their physician's perspective, described higher deterioration of physical performance and were restricted in some ADLs due to both physical and emotional problems. Additionally, in a multivariate analysis higher disability was associated with depression, higher age, and lower educational level. Those survivors with higher disability reported greater deterioration of mental

health; as a result this negatively predicted QOL for subsequent years post-stroke. Comparably, Choi-Kwon, Choi, Kwon, Kang and Kim (2006) recognised pain, dependency in ADL, and depression as predictors of QOL post-stroke. These domains continued to be associated with QOL 3 years post-stroke together with low socio-economic status. Gunaydin, Karatepe, Kaya, and Ulutas (2011) established at 3 months post-stroke depression negatively influenced QOL together with the ability to walk, functional status, and stroke severity. In terms of HRQOL, Patel et al. (2006) similarly found an association between disability and HRQOL to be apparent up to 3 years post-stroke, although mental health appeared to be satisfactory. Equally, mild residual disabilities have exhibited a reduced HRQOL in mild stroke survivors between 60-104 months post-stroke (Almkvist Muren et al., 2008). They found a decrease in functional capacity and HRQOL especially in areas associated to physical activity. Interestingly, a study by Darlington et al. (2007) identified that if stroke survivors were capable of persistent goal pursuit and could adjust their goals to allow for their disabilities they would state higher levels of QOL at one year post-stroke. Furthermore, they established that during the first 5 months post-stroke QOL was mostly determined by general functioning, however this became less associated with QOL after time (Darlington et al., 2007).

Whilst the physical effects of stroke are commonly considered a major determinant in both QOL and HRQOL, literature now highlights an improved awareness that psychosocial aspects additionally influence QOL (Gunaydin et al., 2011). Thus while dependency in self-care and mobility are the most acute issues, psychosocial and environmental factors have been proven to be more dominant in the stroke population (Gresham et al., 1979). Research has identified key predictors of QOL between 1 and 3 years post-stroke as depression and social support, and also improvement in functional status although this was not thought to be essential for effective rehabilitation (Kim et al., 1999). While key psychosocial predictors of HRQOL between 6 and 24 months post-stroke were self-esteem, depression, and perceived control, with higher levels of depression resulting in lower levels of HRQOL. Additionally, a population-based

10-year follow-up study by Wolfe et al. (2011) found rates of depression varied with a mean of 31% of stroke survivors suffering depression. However, depression has been shown to decrease over time (Hackett & Anderson, 2005; Morrison et al., 2005; Patel et al., 2006; Teoh et al., 2009).

2.1.9 Effects of Exercise

2.1.9.1 Benefits of Exercise

Research has found that exercise can reverse risk factors, improve cognitive function, and improve QOL (Bean, Vora, & Frontera, 2004; Goldstein et al., 2011; Gordon et al., 2004; Ivey, Ryan, Hafer-Macko, Goldberg, & Macko, 2007; Rimmer, Rauworth, Wang, Nicola, & Hill, 2009; Sherman, 2000; Wood et al., 1988). Therefore, exercise can be a valuable intervention for stroke.

Exercise capacity has been demonstrated to be substantially limited in stroke survivors between 1 and 6 months post-stroke, despite volume of oxygen uptake ($\dot{V}O_2$) peak and other indices of cardiovascular training improving during this time (MacKay-Lyons & Makrides, 2004). Furthermore, physical inactivity has been linked with several adverse health effects such as increased risk of cardiovascular morbidity, total mortality, cardiovascular mortality, and stroke (Goldstein et al., 2011). An observational 19-year follow up study conducted by Hu et al. (2005), who found that compared with sedentary physical activity (low leisure time), self-reported moderate physical activity (>4 hours per week of cycling, walking, or light gardening) was linked to an adjusted relative risk of ischaemic stroke of 0.87 (95% CI, 0.79-0.95). Furthermore, high physical activity (>3 hours per week of swimming, jogging, regular sports several times per week, or heavy gardening) was linked to an adjusted relative risk of ischaemic stroke of 0.80 (95% CI, 0.63-0.93), whilst active walking or cycling to work for 30 minutes or more daily, was linked with a significant decrease in relative risk of ischaemic stroke of 0.86 (95% CI, 0.76-0.96) (Hu et al., 2005). Do Lee, Folsom, and Blair (2003) found that the risk of stroke incidence or mortality in

highly active individuals is 27% lower than in low-active individuals (relative risk= 0.73; 95% CI, 0.67-0.79). Moderately active individuals had a 20% lower risk of stroke incidence or mortality than inactive individuals (relative risk= 0.80; 95% CI, 0.74-0.86). The authors concluded that moderate and high levels of physical activity are linked with a decreased risk of total, ischaemic, and haemorrhagic strokes.

Research suggests several possible mechanisms by which physical activity may cause a reduction in stroke risk. Hypertension and atherosclerosis of cerebral blood vessels are leading causes of stroke (Bronner, Kanter, & Manson, 1995; Gorelick et al., 1999). A direct dose-response relationship between stroke risk and blood pressure has been identified (Collins et al., 1990); with physical activity proving to lower blood pressure, improve lipid profiles, and enhance endothelial function which improves vasomotor function and vasodilation in vessels (Sherman, 2000; Wood et al., 1988). Additionally, research has identified that physical activity can play an antithrombotic role by decreasing blood viscosity, platelet aggregability, fibrinogen levels, and by improving fibrinolysis (Anderssen et al., 1995; Boman, Hellsten, Bruce, Hallmans, & Nilsson, 1994; Ernst, 1993; Gris et al., 1990; Koenig, Sund, Do, & Ernst, 1997; Rauramaa et al., 1986), which have all been associated with possible reductions in cardiac and cerebral events (Do Lee et al., 2003).

Physical inactivity has been stated to cause reductions in aerobic endurance, changes in body composition, skeletal muscle atrophy and bone loss, and weakness (Bean et al., 2004). However, regular physical activity has been associated with improved maximal cardiac output, reduction of resting blood pressure, improved lipid profiles, enhance endothelial function, improve arterial function, and enhance glucose regulation (Bean et al., 2004; Goldstein et al., 2011; Ivey et al., 2007; Rimmer et al., 2009; Sherman, 2000; Wood et al., 1988). Research has found numerous physiological changes as a result of exercise training in stroke survivors, such as improved: gait speed, timed up-and-go (TUG), walking distance, walking endurance, aerobic capacity, muscular

strength, muscular strength with little to no spasticity, muscular activity, functional activities and outcomes (especially when involving repeated step-ups or sit-to-stands), reduction in paretic knee spasticity, and favourable effects on ADL (Table 2.3). Additionally, these changes have been noted in different types of exercise training including: resistance training, aerobic exercise training, combined resistance and aerobic training, gait-oriented training, task-oriented circuit class, augmented exercise therapy (including physical and occupational therapy), home-based therapy (including aerobic training and normal therapy), and WBV training (Table 2.3), where paretic knee spasticity was seen to be reduced (Pang et al., 2013a). Moreover, studies have identified there were no adverse effects on stroke survivors after WBV interventions (Pang et al., 2013a; van Nes et al., 2004).

Table 2.3. Improvements due to exercise training in stroke survivors

Improvements	Type of Intervention	References
Gait speed	Resistance training	(Cramp, Greenwood, Gill, Rothwell, & Scott, 2006; Pak & Patten, 2008)
	Aerobic training	(Pang, Eng, Dawson, & Gylfadóttir, 2006; Saunders, Greig, Young, & Mead, 2004)
	Combined resistance and aerobic training	(Teixeira-Salmela, Olney, Nadeau, & Brouwer, 1999)
	Gait-oriented training	(Pappas & Salem, 2009; van de Port, Wood-Dauphinee, Lindeman, & Kwakkel, 2007)
	Task-oriented circuit class training	(Wevers, van de Port, Vermue, Mead, & Kwakkel, 2009)
	Home-based therapy (including aerobic training and normal therapy)	(Duncan et al., 2003)
Timed up-and-go	Gait-oriented training	(Pappas & Salem, 2009)
	Task-oriented circuit class training	(Wevers et al., 2009)
Walking endurance	Aerobic training	(Pang et al., 2006)
Walking distance	Gait-oriented training	(Pappas & Salem, 2009; van de Port et al., 2007)
	Task-oriented circuit class training	(Wevers et al., 2009)
Aerobic capacity	Aerobic training	(Chu et al., 2004; Pang et al., 2006; Potempa et al., 1995)
	Home-based therapy (including aerobic training and normal therapy)	(Duncan et al., 2003)
Muscular strength with little to no spasticity	Resistance training	(Bohannon, 2007; Cramp et al., 2006; Ouellette et al., 2004)
	Task-oriented circuit class training	(Yang, Wang, Lin, Chu, & Chan, 2006)
	Resistance training	(Ada, Dorsch, & Canning, 2006; Pak & Patten, 2008)
	Combined resistance and aerobic training	(Teixeira-Salmela et al., 1999)

Muscular activity	Resistance training	(Ada et al., 2006)
Reduction in paretic knee spasticity	WBV training	(Pang et al., 2013a)
Functional activities and outcomes (especially when involving repeated step-ups or sit-to-stands)	Resistance training	(Bohannon, 2007; Morris, Dodd, & Morris, 2004; Pak & Patten, 2008)
	Combined resistance and aerobic training	(Eng et al., 2003; Teixeira-Salmela et al., 1999)
	Gait-oriented training	(van de Port et al., 2007)
Favourable effects on ADL	Augmented exercise therapy (including physical and occupational therapy)	(Kwakkel et al., 2004)
HRQOL	Resistance training	(Flansbjer, Miller, Downham, & Lexell, 2008; Sims et al., 2009)
	Aerobic training	(Ada, Dean, Hall, Bampton, & Crompton, 2003)
	Combined resistance and aerobic training	(Duncan et al., 1998; Lai et al., 2006; Mead et al., 2007; Studenski et al., 2005; Teixeira-Salmela et al., 1999)

Additionally, research has stated QOL and HRQOL deteriorate following a stroke (Chen & Rimmer, 2011; Kim et al., 1999), but exercise may offset some of the deterioration in HRQOL by reducing secondary conditions such as pain and depression, and/or improving overall physical fitness which induces higher levels of physical functioning (for example better self-efficacy in executing ADLs) (Gordon et al., 2004). There have been a limited number of published systematic reviews on the effects of exercise on HRQOL in stroke survivors before 2007, but these three reviews indicate that exercise has limited (Saunders et al., 2004; van de Port et al., 2007), to no effect (Meek, Pollock, Potter, & Langhorne, 2003), in improving HRQOL in stroke survivors. However, a meta-analysis conducted by Chen and Rimmer (2011) investigated randomised controlled trials reporting the effects of exercise on stroke survivors' HRQOL between 1950 and March 2010. This study included additional new information on randomised controlled trials that were published after the three aforementioned systematic reviews (Meek et al., 2003; Saunders et al., 2004; van de Port et al., 2007). They found that exercise reported no adverse effects on stroke survivors, and exercise has a small to medium significant positive effect on HRQOL outcomes at post intervention, however not at follow-up 12 to 24 weeks after exercise intervention was ceased. Therefore, the results support the use of exercise to improve HRQOL in

stroke survivors, but more effective strategies are required to sustain these effects post intervention. This conclusion is supported by previous evidence suggesting there is an advantage of supervised exercise for quality of life and daily functioning post-stroke (Studenski et al., 2005). Stating that elimination of organised, supervised support may decrease motivation or access to continue to participate in exercise after supports have been removed (Chen & Rimmer, 2011). Research has identified social support or contacts in stroke survivors are positively and significantly associated to domain and global quality of life (King, 1996). Hence if social support and contacts is improved domain and global quality of life should also improve, this is especially important in stroke survivors, as numerous studies have found links between depression and stroke (Ahlsjö, Britton, Murray, & Theorell, 1984; Aström, Asplund, & Aström, 1992; Niemi, Laaksonen, Kotila, & Waltimo, 1988).

Literature has stated that interventions such as exercise are probably best tested in acute and subacute stroke and less in chronic stroke, as these populations are still in the recovery phase and would expect to see spontaneous improvements in controls (Studenski et al., 2005). However, research by Chen and Rimmer (2011) found no significant differences between subacute and chronic stroke survivors HRQOL after exercise interventions, but rather relatively greater benefits were seen in chronic stroke survivors. Moreover, they noted that exercise interventions applied in community-based settings found a significant positive effect size compared with non-significant effect size in clinical settings for HRQOL. But more research is required to conclude the effects of exercise on HRQOL by setting and time since stroke.

2.1.9.2 Exercise Prescription

It has been stated by Durstine et al. (2009) that exercise can aid in the improvement of affected bodily systems through implementation of appropriate exercise goals, such as: aerobic goals that increase independence of activities of daily living, walking speed, and decrease risk of cardiovascular disease; resistance goals that increase independence of activities of daily living;

flexibility goals that increase range of motion (ROM) of involved extremities and prevent contractures; and neuromuscular goals that improve levels of safety during activities of daily living. Therefore, targeting these goals through stroke exercise prescription will encourage improvement of bodily systems (Durstine et al., 2009). Due to the lack of literature stating appropriate and effective exercise prescription for stroke patients, research that identifies beneficial exercise modes through training studies and studies prescribing exercise prescription have been interpreted and combined (Table 2.4).

Table 2.4. Exercise prescription for stroke survivors

Type	Parameter	References
Aerobic	Mode	Cycle ergometry Arm ergometry Treadmill Seated stepper Water-based session Functional activities like sit-to-stand
	Frequency	3-5 days per week
	Intensity	40-70% $\dot{V}O_2$ max or 40-50% HRR (heart rate reserve), can progress to 60-80% HRR
	Duration	20-60 minutes per session (continuous training) or multiple 10 minute sessions (interval training)

Resistance	Mode	Isometric exercise Weight machine Free weights Body weight Elastic (resistance) bands Combination of functional and isolated exercises, with optional stability support	(Cramp et al., 2006; Durstine et al., 2009; Eng et al., 2003; Ouellette et al., 2004; Teixeira-Salmela et al., 1999; Yang et al., 2006)
	Frequency	2-3 days per week	(Cramp et al., 2006; Durstine et al., 2009; Ouellette et al., 2004; Yang et al., 2006)
	Intensity	20-50% 1RM or up to 70% 1RM if the subject is capable and in the chronic stage of stroke	(Cramp et al., 2006; Ouellette et al., 2004). (Teixeira-Salmela et al., 1999)
	Duration	1-3 sets of 8-10 repetitions	(Cramp et al., 2006; Durstine et al., 2009; Ouellette et al., 2004; Yang et al., 2006) (Teixeira-Salmela et al., 1999)
Combined	Mode	As stated in aerobic and resistance sections	(Duncan et al., 1998; Eng et al., 2003; Lai et al., 2006; Mead et al., 2007; Studenski et al., 2005; Teixeira-Salmela et al., 1999)
	Frequency	3 days per week	(Duncan et al., 1998; Eng et al., 2003; Teixeira-Salmela et al., 1999)
	Intensity	As stated in aerobic and resistance sections	(Duncan et al., 1998; Eng et al., 2003; Lai et al., 2006; Mead et al., 2007; Studenski et al., 2005; Teixeira-Salmela et al., 1999)
	Duration	Total:60-90 minutes per session Separately: As stated in aerobic and resistance sections	(Teixeira-Salmela et al., 1999)
Flexibility	Mode	Static Stretching	(Durstine et al., 2009)
	Frequency	2 days per week (before or after aerobic or resistance exercises)	(Durstine et al., 2009)
Neuromuscular	Mode	Coordination and balance activities	(Durstine et al., 2009)
	Frequency	2 days per week	(Durstine et al., 2009)

HRR, heart rate reserve; 1RM, 1-repetition maximum

The $\dot{V}O_2$ max and percentage heart rate reserve (HRR) prescribed can be decreased depending on the participants. Studies have shown that participants that were in the acute poststroke stage required slightly lower intensity compared to chronic participants. This was demonstrated in the Katz-Leurer et al. (2003a) and (2003b) studies, where acute patients were only prescribed up to 60% HRR but still produced beneficial results. Research by da Cunha Filho et al. (2001), da Cunha et al. (2002), Katz-Leurer et al. (2003a), and Katz-Leurer et al. (2003b) found that improvements

from aerobic training can still occur with a shorter duration but are more appropriate for acute stroke patients. Research by Cramp et al. (2006) stated that resistance trainings should incorporate some functional exercises as to optimise the chance of increasing functional ability, especially as this is compromised as a result of stroke. Additionally, they indicate that resistance training intensity can increase depending on the participant and what stage they are in (acute, subacute, chronic) (Cramp et al., 2006).

Therefore, after interpreting and combining various exercise studies in stroke, aerobic exercise prescription can involve cycle ergometry, arm ergometry, treadmill, and functional tasks like sit-to-stand. Aerobic exercise should be performed 3-5 days per week, at 40-70% $\dot{V}O_2$ max or 40-50% HRR, for 20-60 minutes or multiple 10 minute bursts. Resistance training can be isometric and involve both functional and isolated exercise, 2-3 days per week at 20-50% 1RM, for 1-3 sets of 8-10 repetitions. Stretching and neuromuscular exercises can also be included 2 days a week. Additionally, combined exercise (aerobic and resistance training combined) prescription is the same as aerobic and resistance exercise prescriptions, except the two types are combined together in one session that is approximately 60-90 minutes in duration, 3 days a week.

In summary, numerous types of interventions have been applied to stroke populations, finding physiological improvements such as walking speed and duration, improved cardiorespiratory fitness, muscular strength, functional activities, and HRQOL. However, little research has investigated the effects of alternate exercise modalities such as WBV on stroke populations. The limited evidence to date, suggests that this form of exercise produces no adverse effects to stroke and can produce positive improvements in paretic knee spasticity (Pang et al., 2013a; van Nes et al., 2004). Therefore, it is possible that WBV may be a beneficial therapy to apply to stroke survivors without the risk of any adverse effects.

2.2 Whole-body Vibration (WBV)

WBV has shown to improve functional performance such as muscle strength, functional mobility, balance control and postural control in compromised health populations, and affect cardiovascular indices such as blood flow, heart rate (HR), BP, and arterial stiffness. However, it is unknown if WBV has any effect on cognitive ability and QOL as no research to date has investigated these variables. Therefore, in an attempt to understand how and why WBV may improve different variables, this section will discuss the types, parameters, proposed mechanisms, and effects of short-term WBV training on cognitive ability and QOL, functional performance, and cardiovascular indices.

2.2.1 Type

Vibration exercise may also be called vibration training, vibration therapy, whole-body vibration (WBV), biomechanical stimulation, or biomechanical oscillation (Cochrane, 2010). WBV can be experienced in a range of environments (occupationally, recreationally, and in laboratory and field settings) (Furness, 2007), and examined after a single (acute) or multiple bouts (chronic) of vibration; where chronic bouts of WBV can be prescribed to training studies or programmes over a number of sessions, over a number of weeks. Over the years different vibrating units have been developed. In 1895, John Harvey Kellogg developed a vibrating chair, oscillating platform, and vibrating bar for health benefits (Calvert, 2002). Additionally vibrating units have been placed under cycle ergometers (Samuelson, Jorfeldt, & Ahlborg, 1989), attached to resistance training equipment (Issurin & Tenenbaum, 1999), placed directly on muscles or tendons (Jackson & Turner, 2003; Warman, Humphries, & Purton, 2002), or custom built for flexibility training (Kinser et al., 2008; Sands, McNeal, Stone, Haff, & Kinser, 2008; Sands, McNeal, Stone, Russell, & Jemni, 2006). In more recent years, vibrating dumbbells have also been developed (Cochrane & Hawke, 2007). At this point in time two commercial forms of vibration platforms have been commercially

manufactured for the health and fitness industry; those that produce vertical synchronous vibration (VV), or those that produce side-alternating vertical sinusoidal vibration (SAV) (Figure 2.6) (Cochrane, 2010; Crewther, Cronin, & Keogh, 2004; Rubin et al., 2003; Torvinen et al., 2002c). Commercial machines such as Power Plate®, Vibra Pro®, Nemes®, and Soloflex®, produce VV where the plate moves in the vertical direction vibrating both legs simultaneously (Cochrane, 2010). This causes symmetrical and synchronised movement of both sides of the body throughout the exposure (Cochrane, 2010). Side-alternating vertical sinusoidal vibration is produced from teeterboard platforms such as the Galileo® which rotate about an anteroposterior horizontal axis (Cochrane, 2010). Consequently, the further the feet are away from the axis the larger the vibration amplitude (Furness, 2007). Moreover, the side-alternating movement of these platforms are asynchronous, resulting in unilateral vibration being applied alternately to the left and right foot (Cochrane, 2010).

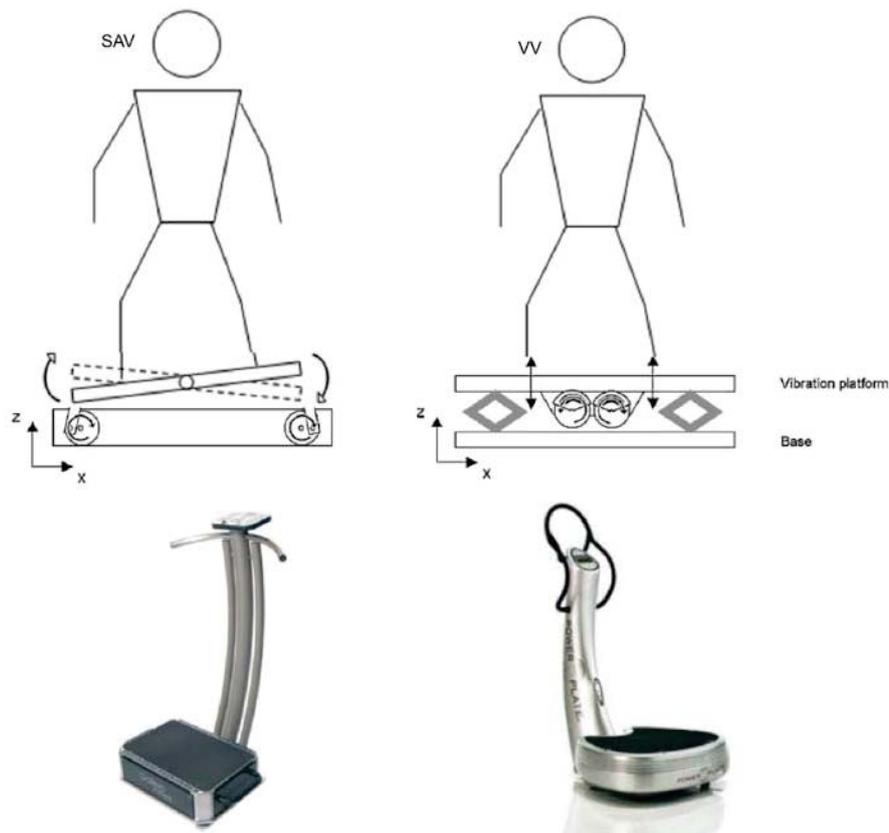


Figure 2.6. The two commercial forms of vibration platforms: SAV and VV (Cochrane, 2010).

Research has debated which type of vibration platform is more superior to the other. A study by Abercromby et al. (2007a) identified that lower limb extensors were activated significantly more during SAV, but the tibialis anterior was activated significantly more during VV. Additionally, they found during both static (18.5° knee flexion) and dynamic squatting (from 10° to 35° of knee flexion, with a tempo of 4 sec up 4 sec down), that SAV produced better activation of the lower limb muscles than VV. However, Rittweger, Schiessl and Felsenberg (2001) identified that during SAV, vibration transmission to the head is decreased due to the feet being alternated up and down causing a rotation of the pelvis and flexion of the spinal column. Another study by Abercromby et al. (2007b) supported this hypothesis stating that as a result of the pelvis damped the vibration energy during SAV more than during VV, VV was found to be superior to SAV across a range of different knee angles (5° to 35° knee flexion), and the vibration was transmitted to the head and upper body 71% to 189% more during VV than SAV. However, no kinematic analyses have been conducted on VV and SAV to validate this hypothesis. Moreover, a study by Ritzmann, Gollhofer, and Kramer (2013) aimed to clarify the debate by assessing SAV and VV machines to determine the effect of various WBV determinants on electromyographic (EMG) activity during vibration, and therefore present optimal training conditions. This randomised cross-over study analysed EMG activity of six leg muscles in 18 individuals with respect to: (1) vibration type (SAV versus VV), (2) stance (normal versus forefoot), (3) knee flexion angle (10° to 60°), (4) load (no extra load versus extra one-third of body-weight), and (5) frequency (5 Hz to 30 Hz). Their results showed: EMG activity was greatest during SAV compared to VV; forefoot stance was more beneficial; EMG was superior for knee extensors when the knee was flexed at 60°; additional load resulted in increased EMG activity; and a progressive increase in frequency caused a progressive rise in EMG activity. They concluded that high vibration frequencies with, an additional load, a knee flexion of 60°, in a forefoot stance on a SAV platform, produces the greatest amount of EMG activity. Therefore, this suggests that SAV platforms produce higher EMG activity, and

consequently may be more beneficial than VV platforms. However, from a practical perspective far more conditioning exercises can be performed on the VV compared to the SAV platform; as the side-alternating of the SAV platform purposes difficulty in performing exercises such as prone and lateral bridge holds, abdominal crunches, and tricep dips (Cochrane, 2010).

2.2.2 Parameters

The load of vibration is dependent on numerous parameters such as; frequency (Hz), amplitude (mm), duration (sec or min), acceleration (ms^{-2}), posture and exercises (Cochrane, 2010). Frequency is determined by the repetition rate of the oscillations (Hz); amplitude is the maximum displacement of vibration from the equilibrium position (mm); duration is the exposure time (sec or min); and acceleration (g or ms^{-2}) determines the magnitude (Figure 2.7) (Cochrane, 2010; Jordan, Norris, Smith, & Herzog, 2005).

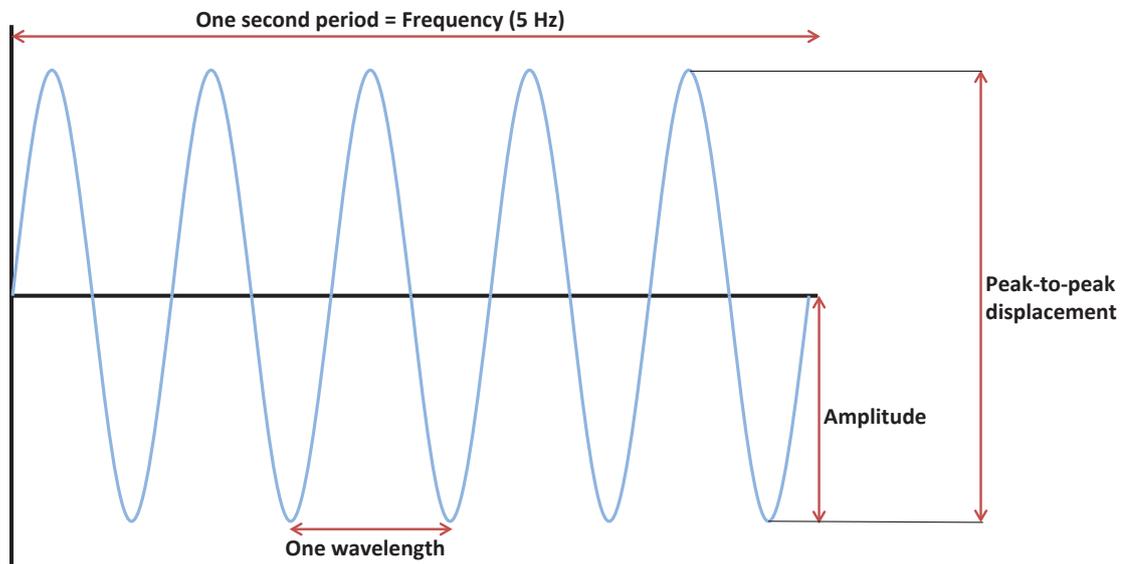


Figure 2.7. Parameters of sinusoidal oscillation (SAV) (adapted from Cochrane (2010) and Furness (2007)).

Furthermore, research has also identified magnitude as the displacement multiplied by acceleration (Cardinale & Lim, 2003). With amplitude/peak-to-peak displacement defined as the height from the highest to lowest vibration wave (Cochrane, 2010). Normal prescribed ranges of WBV are 25 Hz to 45 Hz and amplitude of 2 mm to 6 mm (peak-to-peak displacement) for strength and power increases (Cochrane, 2010).

The optimal vibration dosage (frequency, amplitude, and duration) is unestablished. Literature suggests this is due to differences in protocol designs, participants and outcome measures, such as; participant characteristics (age, gender, body/muscle mass, training status, health status), types of vibration (SAV or VV), vibration parameters (frequency, amplitude, duration, rest interval), and prescribed dosage (number of repetitions, sets, exercises) (Cochrane, 2010). Nevertheless, a study conducted by Cardinale and Lim (2003) analysed EMG activity of the vastus lateralis across varying vibration frequencies (30 Hz, 40 Hz, and 50 Hz). They found that when performing a static squat (knee angle of 100°) on a VV (Nemes®) platform for 60 seconds that the root mean square was significantly higher during 30 Hz compared to 40 Hz and 50 Hz. However, this frequency was prescribed on a VV platform. A study by Lythgo, Eser, de Groot, and Galea (2009) conducted their study on a SAV (Galileo®) platform, analysing a range of vibration frequencies to determine leg blood flow of individuals from 60 second WBV bouts. Interestingly, these authors also established that 30 Hz displayed the greatest increase, with an approximate 50% increase in mean blood cell velocity in the femoral artery compared to resting values. Furthermore, they found that increasing the frequency (10 Hz to 30 Hz) significantly raises mean blood cell velocity in the femoral artery. This is supported by a study mentioned earlier, finding that a progressive rise in frequency caused a gradual increase in EMG activity (Ritzmann et al., 2013). In terms of neuromuscular performance, Da Silva et al. (2006) investigated the effects of different frequencies (20 Hz, 30 Hz, and 40 Hz) of 60 second WBV (SAV) bouts on 31 physically active individuals. They found that whilst both 20 Hz and 30 Hz frequencies elicited

neuromuscular improvements, the greatest increases in squat jump, counter movement jump, and power were seen at 30 Hz. In contrast, at 40 Hz all analysed parameters were decreased. Whilst many studies prescribe either fixed vibration frequency or increase vibration frequency during or after finishing a session(s), a study by Di Giminiani, Tihanyi, Safar, and Scrimaglio (2009) showed individualised vibration frequencies elicit more beneficial effects than fixed (30 Hz) or no vibration. The authors displayed that after eight weeks of three sessions per week performing a half squat, mean power of jump height and squat jump increased 11% and 18% respectively compared to fixed (30 Hz), and no vibration. Therefore, this suggests that vibration frequency should be individualised to produce maximal benefits from WBV training. However, it should be noted that the aforementioned study determined this 'optimal' vibration frequency through analysing the EMG of only one muscle (vastus lateralis). Therefore, more research into EMG activity with other muscle groups would be more beneficial in determining whether this is an optimal frequency, or if it is just applicable to the vastus lateralis. In summary, studies have prescribed a fixed frequency, such as 18 Hz (Rittweger, Just, Kautzsch, Reeg, & Felsenberg, 2002b), 26 Hz (Bosco et al., 1999b; Bosco et al., 2000; Kerschman-Schindl et al., 2001; Rittweger, Beller, & Felsenberg, 2000; Rittweger et al., 2001), and 30 Hz (Abercromby et al., 2007a; de Ruiter, Van Der Linden, Van der Zijden, Hollander, & De Haan, 2003), for acute and long-term bouts of vibration exposure. Other studies have increased vibration frequency throughout or post the cessation of a session(s) (Delecluse, Roelants, & Verschueren, 2003; Torvinen et al., 2002a; Torvinen et al., 2002c).

Amplitude differs according to the vibration platform the exercise is performed on. On a VV platform, the machine has a pre-setting function (0 mm to 2 mm or 2 mm to 4 mm) and foot placement is independent of amplitude. Whereas, the amplitude on an SAV platform depends on the individual's foot placement. For example, when the foot placement is close to the middle of the plate it results in small peak amplitude (≈ 3 mm), however, a wide foot placement results in larger amplitude (≈ 12 mm). As foot placement determines amplitude on an SAV platform, this

may affect vibration transmission to numerous areas of the body (Cochrane, 2010); however this theory is yet to be proven. Limited studies have investigated the optimal amplitude of vibration, and of those that have, they have lacked the necessary scientific accuracy and consistency to allow comparisons amongst studies (Cochrane, 2010). One study by Cardinale, Leiper, Erskine, Milroy, and Bell (2006) investigated the differences of high (3 mm), low (1.5 mm), and no (0 mm) amplitudes of vibration at a fixed frequency (30 Hz) on testosterone and insulin growth factor 1. They found no differences in testosterone and insulin growth factor 1 levels across the amplitude range. However, the authors did not state which vibration platform was used, and thus if a VV platform with a low amplitude was used this could account for the lack of difference across amplitudes. Rittweger et al. (2002a) also analysed various vibration amplitudes (2.5 mm, 5 mm, 7.5 mm) with a fixed frequency (26 Hz); but they stated the use of a SAV platform where individuals stood in an upright stance with a 10° knee flexion, and investigated oxygen cost of vibration. They found that oxygen cost rose across all three amplitudes compared to baseline levels, with amplitude of 7.5 mm producing the highest oxygen cost (7.3 ml/kg/min compared to baseline of 3.6 ml/kg/min). Research by Pollock, Woledge, Mills, Martin, and Newham (2010) analysed the effects of high (5.5 mm) and low (2.5 mm) amplitude WBV (SAV) at several frequencies (5 Hz to 30 Hz) on acceleration and EMG activity throughout the body. They found that EMG activity was greater during high amplitudes at all frequencies; however, this was not always significant. Adams et al. (2009) utilised a VV platform (Power Plate®) and reported that high vibration frequency (50 Hz) with high amplitude (4 mm to 6 mm), and low frequency (30 Hz) with low amplitude (2 mm to 4 mm) effectively increased vertical jump power in 11 untrained healthy men.

In the literature, the majority of WBV exercise duration has consisted of intermittent 20 to 60 second exposures and continuous exposures from 3 minutes to 6 minutes (Adams et al., 2009; Bosco, Cardinale, & Tsarpela, 1999a; Bosco et al., 1998; Bosco et al., 2000; Cardinale et al., 2006; Cardinale & Lim, 2003; Cochrane & Stannard, 2005; Cormie, Deane, Triplett, & McBride,

2006; de Ruyter et al., 2003; Rittweger et al., 2002a; Rittweger et al., 2001; Torvinen et al., 2002c). However, like frequency and amplitude, there is little scientific evidence stating the optimal duration for either intermittent or continuous WBV sessions (Cochrane, 2010). Moreover, Adams et al. (2009) found no significant difference in vertical jump peak power in 11 untrained healthy men across 30 second, 45 second, and 60 second WBV durations; with frequencies ranging from 30 Hz to 50 Hz and amplitudes of 2 mm to 4 mm and 4 mm to 6 mm. Intermittent protocol commonly used by studies is one developed by Bosco et al. (1998; 1999b), but there is little justification for its use. It comprises of 10 repeated 60 second exposures with 60 seconds rest and has shown improvements in muscular power (Bosco et al., 1998; Bosco et al., 1999b). Nevertheless, Stewart, Cochrane, and Morton (2009) identified that standing with a 5° knee flexion on a SAV platform (with a fixed frequency of 26 Hz and amplitude of 4 mm), produced a 3.8% increase in isometric peak torque after 2 minutes of continuous WBV, compared to decreases in isometric peak torque at 4 and 6 minutes. Long-term WBV studies have adopted various exposure durations for studies run over 6 to 12 weeks and 3 to 8 months; these ranged from 2 to 20 minute total duration or WBV exposure in one session (Delecluse et al., 2003; Roelants, Delecluse, Goris, & Verschueren, 2004; Torvinen et al., 2002b; Torvinen et al., 2003). Cochrane (2010) states that there appears to be a lack of knowledge concerning the effectiveness of continuous WBV exercise in enhancing performance measures, with more research required to determine the optimal duration of WBV exposure for both acute and long-term studies. Additionally, he states acute vibration causes temporary increases from 1 to 10 minutes post vibration exposure, but further research should target the dosage (duration, frequency, and amplitude) and the potential after vibration (Cochrane, 2010).

Research has identified that WBV exercise generates mechanical vibration causing acceleration, which is the product of amplitude and angular velocity, where acceleration has also been labelled magnitude and expressed as g (gravity, $1g = 9.81 \text{ ms}^{-2}$) or ms^{-2} (Cochrane, 2010). Cardinale and Wakeling (2005) state that acceleration is proportional to the force being applied;

therefore, acceleration is dependent on changes in frequency and amplitude to cause a rise in acceleration of vibration being transmitted to the body. As force appears to be the main variable to elicit alterations within the body, WBV exercise is dependent on increasing acceleration to increase force (Cochrane, 2010). However, Wakeling, Nigg, and Rozitis (2002) identified there is reduced transmission of vibrational force through the body due to damping by the passive action of soft and hard tissues, muscle contractions, and joint kinematics. As stated by Lorenzen, Maschette, Koh, and Wilson (2009), all studies should report peak acceleration (g or ms^{-2}) and describe how this was determined. However, numerous studies report acceleration but have not described how they measured or calculated it (Bosco et al., 1999b; Bosco et al., 2000; Cardinale et al., 2006; Kerschman-Schindl et al., 2001; Rittweger et al., 2000; Torvinen et al., 2002a; Torvinen et al., 2002b). Some studies have stated they measure peak acceleration by fixing accelerometers to vibration plates (Delecluse et al., 2003; Di Giminiani et al., 2009; Lythgo et al., 2009; Roelants et al., 2004), while others attached accelerometers on body landmarks to calculate acceleration transmission through various joints (Abercromby et al., 2007b; Crewther et al., 2004).

The posture (or stance) and type exercises performed on vibration platforms also contribute to the load of vibration (Cochrane, 2010). With research by Harazin and Grzesik (1998) stating that the position of the spine and degree of muscular tension in the lower extremities and trunk alters the damping and elastic properties of the body. The most common exercises performed on vibrating platforms are static and dynamic squats (Abercromby et al., 2007a; Abercromby et al., 2007b; Bosco et al., 1999b; Bosco et al., 2000; Cardinale et al., 2006; Cardinale & Lim, 2003; de Ruitter et al., 2003); although, a combination of upper- and lower-body exercises have similarly been executed on numerous vibrating plates (Bosco et al., 1998; Cochrane & Stannard, 2005; Torvinen et al., 2002a). It is still unclear if a greater knee angle causes a decrement in EMG activity for static and dynamic squatting (Cochrane, 2010). As mentioned previously, a study by Ritzmann et al. (2013) investigated the influence of different vibration determinants on EMG activity during WBV as to identify optimal training conditions. Amongst

those determinants was knee flexion angle (10°, 30°, 60°) and stance condition (normal versus forefoot stance). Their results displayed that EMG activity was greatest for the knee extensors when knee flexion was 60°, and plantar flexors when adopting the forefoot stance. They concluded that 60° knee flexion and forefoot stance may be an optimal body position to elicit positive effects on knee extensors and plantar flexors (Ritzmann et al., 2013). Research by Abercromby et al. (2007a) found that acceleration of the head reduced as knee angle enlarged from 10° to 30°, with the VV platform producing higher accelerations than SAV platform. Furthermore, they found the greatest mechanical impedance transpired at a knee angle of 10° to 15° (fixed frequency was 30 Hz and amplitude was 4 mm). They concluded that performing a squat at knee angles of 26° to 30° dissipates head vibration, whereas, small knee angles increased the chances of negative side effects to WBV exercise as the highest mechanical energy is most probably transmitted to the head and upper-body, and consequently should to be avoided (Abercromby et al., 2007a). Meanwhile, Harazin and Grzesik (1998) investigated WBV transmission through an electromagnetic vibrator (constructed by I.O.M, Sosnowiec) at the metatarsus, ankle, knee, hip, shoulder, and head joints during 10 different postures. They found that transmission was similar through all body landmarks when standing feet apart with a 110° knee flexion. This suggests that having a knee angle of 110° during WBV creates a more even transmission of vibration. Other studies state that, to avoid injury but to still produce beneficial results, frequency and amplitude should be between 26 Hz to 44 Hz and 1 mm to 10 mm (Crewther et al., 2004; Cronin, Oliver, & McNair, 2004). Where vibration frequencies below 12 Hz and amplitude as high as 3 mm have resulted in muscle soreness and chronic tendonitis of the lower limbs in healthy individuals (Cronin et al., 2004; Mester, Spitzenfeil, Schwarzer, & Seifriz, 1999).

2.2.3 Proposed Mechanisms

The exact mechanism(s) of WBV presently remain unclear due to early theories being based on findings from direct vibration to the muscle or tendon (Adams et al., 2009; Cochrane, 2010; Furness, 2007). Unlike WBV, the whole-body or areas of the body are vibrated stimulating numerous muscles, tendons, organs and bones. Therefore, Cochrane (2010) suggests that caution should be taken when evaluating findings from direct vibration studies in an attempt to explain the possible mechanism(s) of WBV exercise. However, several proposed mechanisms have been identified in the literature and are based on neurogenic potentiation (Adams et al., 2009; Cochrane, 2010). The first mechanism has concentrated on spinal reflex, also known as tonic vibration reflex (TVR), which causes excitatory responses of the muscle spindle and consequently increases muscle activity (Rittweger, Mutschelknauss, & Felsenberg, 2003). The second proposed mechanism is focused on a muscle tuning response, where the muscular system damps the vibration stimulus to encourage muscle activity (Cochrane, 2010). The last mechanism is based on neural adaptations identical to power and resistance training, such as motor unit recruitment, synchronisation, and co-contraction (Cochrane, 2010); where WBV may elicit neural changes (Bosco et al., 1999a).

Mechanical stimuli transmitted via the vibration unit through the body causes short and fast changes in the length of the muscle-tendon complex (Cardinale & Bosco, 2003). These alterations in length are identified by sensory receptors that control muscle contraction through reflex muscular activity by activating muscle spindles and the stretch-reflex loop (Adams et al., 2009; Cardinale & Bosco, 2003). Leading to the activation of alpha motoneurons and causing reflexive muscle contractions, this is referred to as the TVR (Delecluse et al., 2003; Roelants et al., 2004). Research by Roelants, Verschueren, Delecluse, Levin, and Stijnen (2006) state that polysynaptic and monosynaptic pathways facilitate this response, subsequently causing an increase in activation of motor units and therefore muscle activation. Additionally, Jordan et al. (2005) states that TVR is most likely dependent on muscle length, body position, and the

frequency of vibration. Moreover, they suggest that voluntary muscle contractions may be improved by the TVR when applied in combination with strength training protocols (Jordan et al., 2005). This mechanism and its consequences are supported by research indicating increases in EMG activity (Bosco et al., 1999a; Cardinale & Lim, 2003). However, Cochrane (2010) states that TVR requires high vibration frequencies (>100 Hz) and directly applied vibration to the muscle or tendon, whilst, WBV is not typically applied to the body and frequencies are lower (20 Hz to 45 Hz) with longer exposure time (>30 sec). Consequently, the author suggests that it is unlikely that WBV acts through a spinal mechanism, such as TVR (Cochrane, 2010). However, vibration may well cause an indirect participation of muscles spindles, with other sensory inputs influencing gamma motoneurons activity, resulting in changes to the spindle input (Gandevia, 2001).

Nigg (1997) suggests that the body is capable of tuning its muscle activity as to decrease the vibrations that are transmitted through the soft tissue and may well bring about a detrimental effect. The extent of muscle activity necessary to allow this is dependent on the intensity of vibration, where maximal muscle activation can decrease or eradicate oscillations within the tissues (Cochrane, 2010). Impact forces from the collision of the heel with the ground during everyday activities have been shown to produce 10 Hz to 20 Hz of vibrations to the lower limbs (Wakeling & Nigg, 2001). As a result of the impact force, shortly before the heel hits the ground, an input signal produces a muscle tuning (activity) response to decrease soft tissue vibrations and prevent resonance (Cochrane, 2010; Nigg, 1997; Wakeling et al., 2002). This results in sensory organs sending impulses to the central nervous system and, in turn, the central nervous system responds by adjusting joint stiffness and increasing muscle activity (Cochrane, 2010). Therefore, muscle tuning relies on three components: the level of muscle activity, the vibration resonance of the soft tissue, and the frequency and amplitude of the input force (Cochrane, 2010). Additionally, the damping of vibration depends on the individual's neuromuscular response of the proportion of muscle fibre types and viscoelastic (stiffness) elements, the sensitivity of joint and skin receptors, and the muscle spindle (Bazett-Jones, Finch,

& Dugan, 2008). The viscoelastic elements of the muscles are important as the mechanical energy produced from the vibration is capable of being stored and returned from elastic elements of the muscle-tendon complex, where damping of vibrations causes a net dissipation of mechanical energy which may be absorbed by activated muscle (Albansini, Krause, & Rembitzki, 2010).

WBV has shown to increase muscle power and force similarly to that of resistance training (Bosco et al., 1999a; Bosco et al., 1998; Bosco et al., 1999b; Cardinale & Bosco, 2003; Delecluse et al., 2003). Moreover, Cardinale and Bosco (2003) notes that improvements in strength and power are attributed to neuromuscular facilitation for both resistance training and WBV, as both training types place load on the neuromuscular system. Unlike resistance training which adds extra load via dumbbells, barbells, manual or elastic resistance, WBV adds load by adjusting vibration frequency and/or amplitude and therefore increasing acceleration. Increasing the load can alter neuromuscular facets through neurogenic and myogenic factors (Cochrane, 2010). Possible factors have been identified such as; motor unit firing, motor unit synchronisation, central motor command, and inter-muscular coordination (Cardinale & Bosco, 2003; Cochrane, 2010). However, further research is required to validate these factors.

Additionally, other less prominent mechanisms have been identified as probable causes, such as: muscle hypertrophy, due to the small load placed on the muscle tendon unit during an acute bout of vibration (Issurin, 2005); warm-up effect, where friction created between the vibrating tissues increases muscle temperature (Issurin & Tenenbaum, 1999), in combination with increased blood flow due to vibration (Kerschan-Schindl et al., 2001); and tensegrity (tensional integrity), where WBV has the potential to prompt mechanochemical conversion in which cytoskeletal filaments and heat stress proteins explain the beneficial effects WBV has on blood vessel and tissues (Albansini et al., 2010).

In summary, it is probable that spinal reflexes, muscle tuning and neural mechanisms improve muscular performance, however research by Cochrane (2010) makes it apparent that

this will not be working in isolation. Rather, other body systems similarly contribute, such as; muscle temperature, blood flow, hormone secretion, skin, and joint receptors (Cochrane, 2010).

2.2.4 Effect on Short-term Training

2.2.4.1 Cognitive Ability and Quality of Life

Research assessing WBVs effect on quality of life (QOL) and cognition is limited, both in healthy populations and compromised health. A study conducted by Bruyere et al. (2005) investigated the effects of 6 weeks of WBV in elderly individuals. Forty-two elderly individuals were randomly allocated to either a WBV (SAV) or physical therapy group (WBV= 4 repetitions of 60 second bouts, 3 times per week, frequency 10 Hz to 26 Hz, amplitude 3 mm to 7 mm; physical therapy= 10 minutes, 3 times per week) or a physical therapy alone group (10 minutes, 3 times per week). Where, physical therapy consisted of strengthening exercises with resistive mobilisation of the lower limbs, transfer skill training, gait and balance exercises. They found that after 6 weeks of WBV, elderly individuals significantly improved their HRQOL compared to the physical therapy alone group (Bruyere et al., 2005). Furthermore, noting that 8 of the 9 items assessed in the SF-36 significantly improved from baseline (physical function, social function, role-physical, role-emotional, mental health, vitality, pain, general health; where health change did not significantly improve) (Bruyere et al., 2005). Therefore, concluding that WBV can improve HRQOL in elderly individuals (Bruyere et al., 2005). Contrary, a study by Arias, Chouza, Vivas, and Cudeiro (2009) found that after 5 weeks of WBV (12 sessions, 5 repetitions of 60 second bouts, frequency 6 Hz, amplitude not stated, platform not stated) in Parkinson disease patients, no difference in QOL was reported when compared to the placebo group. However, this study used a Parkinsonian specific QOL assessment that involves 39 items rated 0 to 4, with a higher score indicating poorer QOL. Thus this makes comparisons between these two studies challenging. Research suggests that as WBV stimulates vibration-sensitive mechanoreceptors in the skin (Dykes, 1983; Johansson

& Vallbo, 1983), and afferent signals of cutaneous mechanoreceptors are transmitted to sensory brain areas that are connected to prefrontal brain regions (Braak, Braak, Yilmazer, & Bohl, 1996; Martin, 2003), WBV may augment neurotransmission in the prefrontal cortex and in other surrounding regions by sensory stimulation (Regterschot et al., 2014). However, no study to date has investigated the effects of WBV on cognitive ability and/or on QOL in stroke. But, research has identified that the most significant effect of stroke is a decline in HRQOL (Aprile et al., 2006), whilst stating that WBV has no adverse effects on stroke survivors (Pang et al., 2013a; van Nes et al., 2004). Therefore, these areas would benefit from future investigative research work.

2.2.4.2 Cardiovascular Indices

WBV training may improve vascular health indirectly through improvement in vascular risk factors (such as cholesterol and blood sugar), or directly through rises in blood flow and increased shear stress, which as long as it is antegrade (forward travelling), will improve endothelial function. However, research on the effect of WBV on the cardiovascular system is limited. But favourable effects in blood flow, BP, HR, and arterial stiffness have been reported as a result of WBV, nonetheless further examination is required.

Blood flow has been found to create shearing stress on the endothelial cells (Frangos, Eskin, McIntire, & Ives, 1985; Rubanyi, Romero, & Vanhoutte, 1986). As blood flows through a vessel, it applies a physical force on the vessel wall. This force generates stress that can be parallel or perpendicular to the vessel wall. Shear stress parallel to the vessel wall is characterised by the frictional force that blood flow applies on the endothelial surface of the vessel wall (White & Frangos, 2007). Stress perpendicular to the vessel wall is tensile stress, and characterises the dilating force of BP on the vessel wall (White & Frangos, 2007). Shearing stress stimulates endothelial-derived vasodilators, most notably nitric oxide (NO), which promotes smooth muscle

relaxation and increased blood flow to the exercising region (Green, O'Driscoll, Blanksby, & Taylor, 1996; Laughlin, Oltman, & Bowles, 1998). However, the blood flow has to be antegrade (forward travelling) or positive, as retrograde (backward) or negative (turbulent) flow promotes atherosclerosis (White & Frangos, 2007). Thus, a strong correlation has been found between endothelial cell dysfunction and regions of low mean shear stress and oscillatory flow with flow recirculation (White & Frangos, 2007). Conversely, steady shear stress stimulates cellular responses that are essential for endothelial cell function and are atheroprotective (White & Frangos, 2007). NO has been found to perform a myriad of anti-atherogenic functions and is considered the most important molecule governing endothelial health (Gao, 2010; Michel & Vanhoutte, 2010; Moncada & Higgs, 2006; Napoli et al., 2006). Moreover, where flow patterns continue to be relatively positive and undisturbed mean wall shear stress is high and as a result the occurrence of plaque formation (associated with the process of atherosclerosis) is correspondingly low (Svindland, 1983). Conversely, in regions of recirculating flow (negative or turbulent flow) mean wall shear stress is relatively low and therefore the occurrence of plaque formation is correspondingly high (Svindland, 1983). Thus, the key to improving vascular function is to regularly increase blood flow, which induces a positive shear stress on the endothelium.

A study conducted by Kerschman-Schindl et al. (2001) were the first to report an increase in arterial blood flow of the popliteal artery (100% with mean blood flow velocity increasing from 6.5 cm s^{-1} to 13.0 cm s^{-1}) as a result of WBV (3 repetitions of 3 minute bouts, 26 Hz, 3 mm [amplitude], SAV) of standing and static squatting in 20 healthy participants. Moreover, Lythgo et al. (2009) reported an increase in mean blood cell velocity of the femoral artery after intermittent WBV (12 repetitions of 60 second bouts, 5 Hz to 30 Hz, 2.5 mm to 2.5 mm, SAV) of static squatting in 9 healthy males where 30 Hz produced the greatest rise in mean blood flow compared to baseline levels. Conversely, Hazell, Thomas, DeGuire, and Lemon (2008) found that intermittent WBV (15 repetitions of 60 second bouts, 45 Hz, 2 mm, VV) of seated passive vibration and static squatting in 8 healthy men produced no increases in femoral artery blood

flow after 3 minutes of WBV. However, it should be noted that differences between these protocols (Hazell et al., 2008; Lythgo et al., 2009), specifically the vibration platforms used and frequencies prescribed, may contribute to the differences in the findings. In terms of skin blood flow, research by Lohman, Petrofsky, Maloney-Hinds, Betts-Schwab, and Thorpe (2007) found that when both calf muscles were rested on a VV platform (3 minutes, 30 Hz, 5 mm to 6 mm, 45 healthy participants) the gastrocnemius skin blood flow was raised by 250% compared to baseline levels and remained elevated (200%) 10 minutes after intervention. However, performing an isometric squat and calf raises with and without vibration using the same parameters, displayed little increase in gastrocnemius skin blood flow. Previously WBV has been shown to increase blood flow (Kersch-Schindl et al., 2001), and the mechanisms associated to arterial stiffening are related to atherosclerosis, it is possible that WBV may elicit improvements in arterial stiffness, and therefore be of benefit as an exercise intervention in chronic stroke.

Heightened BP may play an important role in vascular alterations over time (Daniels, 2012), and is of particular importance in stroke populations as hypertension has been identified as a major risk factor for stroke (Kannel, 2009). Research has found that chronic hypertension augments atherosclerosis and encourages complex pathological alterations in the medias of arteries and arterioles (Baumbach & Heistad, 1989; Chobanian, 1983). Moreover, this may be seen as fracturing and disarray of elastin as a result of elevated arterial pressure and may cause greater deposition of calcium and collagen, and a stiffer arterial system (Daniels, 2012). These structural alterations increase vascular resistance and protect the cerebral microcirculation from the adverse effects of systemic hypertension (Baumbach & Heistad, 1988). Remarkably, however, the structural alterations may predispose to cerebral ischaemia by impairing vasodilator responsiveness (Baumbach & Heistad, 1991). Moreover, these changes result in a cruel cycle of events in which heightened BP, in addition with other factors, results in alterations in the vascular system that consequently encourages arterial stiffening and further elevation of BP

(Daniels, 2012). In terms of HR, evidence shows that resting HR is linked to cardiovascular morbidity and mortality in patients with cardiovascular disease and general population (Benetos, Rudnichi, Thomas, Safar, & Guize, 1999; Diaz, Bourassa, Guertin, & Tardif, 2005; Heidland & Strauer, 2001; Jouven et al., 2005; Kannel, Kannel, Paffenbarger, & Cupples, 1987a). Where clinical and experimental data suggests that continued elevation of HR contributes to the pathogenesis of vascular disease (Custodis et al., 2010). Research has stated a positive correlation between increased resting HR and circulating markers of inflammation, such as high-sensitivity C-reactive protein (Rogowski et al., 2007; Sajadieh et al., 2004). Therefore, elevated HR may add to endothelial dysfunction by up-regulation of inflammatory cytokines (Custodis et al., 2010). Furthermore, in coronary heart disease patients, increased resting HR may encourage atherosclerotic disease via facilitation of plaque disruption and progression of coronary atherosclerosis (Zhu & Friedman, 2003). Additionally, aerobic cycle ergometry training (3 sessions per week for 10 weeks, 30 minutes, 30% maximal effort) in 42 stroke patients has shown to significantly lower SBP at submaximal workloads (Potempa et al., 1995). Also WBV training (3 sessions per week for 12 weeks, VV) in 25 postmenopausal women with prehypertension and hypertension has shown to significantly improve BP (SBP, DBP, MAP) whilst HR significantly decreased after WBV exercise training (Figuroa, Kalfon, Madzima, & Wong, 2014). This may suggest that WBV intervention may elicit improvements in BP, HR and in turn arterial stiffness in chronic stroke. However, minimal research has examined the effect of WBV on BP and HR.

A single WBV session (10 repetitions of 60 second bouts, 26 Hz, 2 mm to 4 mm, VV) in 10 healthy men has shown no significant effects on BPs (SBP, DBP, PP) post 60 minutes of WBV (Otsuki et al., 2008). This is supported by Kerschman-Schindl et al. (2001) who found no change in HR, systolic and DBP values post WBV. However, studies by Figuroa et al. (2011) and Rittweger et al. (2000) illustrated significant changes in BP; with acute intermittent WBV, and values returned to baseline 15 minutes post WBV intervention (Figuroa et al., 2011). Additionally, Rittweger et al. (2000) demonstrated a significant decrease in DBP after exhaustive WBV but also

an increase in HR (30%) and SBP (15%) compared to control (bicycle ergometry). Contrary, multiple sessions of WBV over 3 months (5 minutes, 3 times per week) in middle-aged and older adults displayed no significant improvements in SBP and DBP (Lai et al., 2014). However, Figueroa et al. (2011) and Rittweger et al. (2000) noted that changes in BP dissipate to baseline by 15 minutes post WBV. This may suggest that the possible additive effect of multiple sessions of WBV may have no continued effect on BP.

To date, there are only three studies that have investigated the effects of WBV on arterial stiffness (Figueroa et al., 2011; Lai et al., 2014; Otsuki et al., 2008). Of these three, all studies found that acute WBV (one session) significantly decrease arterial stiffness in healthy men (Figueroa et al., 2011; Otsuki et al., 2008), and following 3 months of WBV in middle-aged and older sedentary adults (Lai et al., 2014). Otsuki et al. (2008) demonstrated significant reductions in arterial stiffness, through brachial-ankle pulse wave velocity, at 20 and 40 minutes post intermittent WBV exercise (10 repetitions of 60 second bouts, 26 Hz, 2 mm to 4 mm, static squatting, VV, 10 healthy men) compared to control (static squatting without vibration). In a similar study, the WBV protocol was modified slightly in 15 healthy men to include a higher frequency (40 Hz) that acquired pulse wave velocity (PWV) from carotid-femoral, brachial-ankle, and femoral-ankle sites (Figueroa et al., 2011). Femoral-ankle PWV was significantly reduced at 5 minutes in both WBV and without WBV (control), where it continued to remain low during the 30 minute recovery post-WBV but the control returned to baseline. However, there were no significant changes in carotid-femoral PWV or brachial-ankle PWV after either trial. The study also states that prolonged reduction in leg PWV after WBV exercise could be linked to a local effect of vibration on the leg arteries (Figueroa et al., 2011). Finally, Lai et al. (2014) displayed significant reductions in bilateral brachial-ankle PWV following multiple continuous WBV sessions in 38 middle-aged and elderly participants (5 minutes, 3 times per week, 30 Hz, 3.2 g, full standing position, VV). While all three studies produced significant reductions in arterial stiffness,

these were across different measurement techniques (brachial-ankle PWV compared to femoral-ankle PWV), WBV protocols, and subject characteristics. Therefore, there is a lack of evidence to conclude WBV effect on arterial stiffness and requires further investigation.

2.3 Cardiovascular Indices

2.3.1 Blood Pressure

As mentioned previously, heightened BP may play an important role in vascular alterations over time (Daniels, 2012), and is of particular importance in stroke populations as hypertension has been identified as a major risk factor for stroke (Kannel, 2009). Research has found that chronic hypertension augments atherosclerosis and encourages complex pathological alterations in the medias of arteries and arterioles (Baumbach & Heistad, 1989; Chobanian, 1983). Moreover, it is suggested that elevated BP may promote atherogenesis by modulation of the biomechanical stimuli from pulsatile blood flow, such as increased cyclic strain or hydrostatic pressure, and in turn this effects endothelial cell gene expression and function (Chae et al., 2001). These changes result in a vicious cycle of events in which heightened BP, in addition with other factors, results in alterations in the vascular system that consequently encourages arterial stiffening and further elevation of BP (Daniels, 2012). Therefore, it is important to investigate and understand if and how BP is affected as a result of WBV therapy in chronic stroke, as improvement in BP may consequently benefit arterial stiffness and reduce the risk of future stroke.

The influence of mechanisms on BP response to exercise depends on variables including muscle fiber type, recruited muscle mass, exercise intensity, and the mode of exercise (Leicht, Sinclair, & Spinks, 2008; Lewis et al., 1985; Mitchell, Payne, Saltin, & Schibye, 1980). Where BP response to exercise is important as it has been found to be an independent predictor of cardiovascular morbidity and mortality (Dlin, Hanne, Silverberg, & Bar-Or, 1983; Mundal et al., 1994), it is also

important as abnormal SBP response to exercise can accurately predict endothelial dysfunction in hypertensive patients (Tzemos, Lim, Farquharson, Srtuthers, & MacDonald, 2000), and exercise BP reflects the exercise-induced peripheral vasodilatory capacity. Consequently, as this is at least in part due to NO release as a result of increased vascular wall stress, failure of NO release during exercise would dull the normal fall in peripheral vascular resistance, causing an abnormal increase in exercise BP, resulting in a heightened risk of future cardiovascular events (Tzemos, Lim, & MacDonald, 2002).

Research by Lind and McNicol (1967) identified two main types of muscular contraction: static or isometric exercise where muscular tension is exerted continuously, and dynamic or rhythmic exercise which consists of short periods of contraction alternating with periods of relaxation. The authors conclude that cardiovascular responses are different depending on the type of exercise.

It has been stated that dynamic activities such as walking, running, swimming, and cycling have modest effects on arterial BPs (Laughlin, 2000). Early research that investigated the cardiovascular response to dynamic and static muscular actions showed a strong increase in SBP and minimal changes in DBP during dynamic exercise, whilst isometric exercise induces marked rises in SBP and in particular DBP (Chapman & Elliott, 1988; Laird, Fixler, & Huffines, 1979; Lindquist, Spangler, & Blount, 1973; Tuttle & Horvath, 1957). Initially there is a rapid increase in MAP and SBP from the resting level, with SBP increasing linearly with exercise intensity, and DBP remains constant or decreases marginally with higher exercise levels (Katch, McArdle, & Katch, 2011; Laughlin, 2000). When healthy fit individuals perform maximal dynamic exercise, SBP may increase to 200 mmHg or more despite decreased peripheral resistance (Katch et al., 2011). It is suggested that this is a result of the heart's sizable cardiac output during maximal exercise in individuals with high aerobic capacity (Katch et al., 2011). Research by Fagard (2006) suggests that aerobic endurance training decreases BP through a reduction of systemic vascular resistance and positively affects associated cardiovascular risk factors. Dynamic resistance exercise, such as

heavy resistance, increases BP severely due to strained muscular force compressing peripheral arterioles which augments the resistance to blood flow (Katch et al., 2011). MacDougall, Tuxen, Sale, Moroz, and Sutton (1985) supports this, demonstrating that when performing weightlifting exercises in healthy young individuals, the mechanical compression of blood vessels combines with a Valsalva response to create severe elevations in BP. As a result, the additional workload placed on the heart due to acute elevations in BP increases the risk for individuals suffering from coronary heart disease or hypertension (Katch et al., 2011). However, a study by Gordon et al. (1995) found no significant cardiovascular events were suffered after determining 1RM strength testing in over 6600 healthy individuals aged 20 to 69 years, who all had resting BPs over or equal to 160/90 mmHg. Haslam, McCartney, McKelvie, and MacDougall (1988) supports this finding that in 8 coronary artery disease patients, intra-arterial BPs during weightlifting were within clinically acceptable ranges at 40% and 60% of 1 RM. Furthermore, when comparing dynamic leg exercise with dynamic arm exercise, it has been stated that the extent of increase in arterial pressure is approximately 10% higher in arm exercise than in leg dynamic exercise (Laughlin, 2000). It is suggested that this is due to the smaller arm muscle mass and vasculature, which proposes higher resistance to blood flow compared to the larger and more vascularised lower-body areas; signifying that arm exercise requires much larger SBP, myocardial workload, and vascular strain (Katch et al., 2011).

Isometric exercise has been found to produce increased mean arterial pressure with increases in isometric contractile force; this rise in BP is far superior to the metabolic cost of the exercise (Laughlin, 2000). Furthermore, the magnitude of increase in arterial BPs is proportional to the duration of constant contraction and the size of muscle mass stimulated (Laughlin, 2000). When compared to dynamic exercise, research suggests that isometric exercise may produce a stronger chemoreflex response due to limited release of metabolites and blood flow within the muscle (Weippert, Behrens, Rieger, Stoll, & Kreuzfeld, 2013). This chemoreflex causes BP to rise via sympathetic vasoconstriction, but additionally it appears to affect sympathetic HR modulation

(Iellamo et al., 1999; Rowell & O'Leary, 1990). Moreover, when comparing isometric exercise to dynamic exercise when active muscle mass, intensity, and duration are similar, research has shown BP increases produced by isometric exercise are higher than that of dynamic exercise (Laughlin, 2000). This is supported by numerous studies that report higher BP response for isometric exercise compared to dynamic (González-Camarena et al., 2000; Lindquist et al., 1973; Weippert et al., 2013). However, a study by Chapman and Elliot (1988) disagrees with this concluding that when the same muscle groups are used for both moderate isometric and dynamic exercise, the effect of the exercise types on cardiovascular response is more comparable than often identified. Interestingly, whilst cardiovascular adjustments to dynamic exercise reach a steady state, after several minutes of isometric exercise, HRs and BPs continue to rise (Laughlin, 2000).

2.3.2 Heart Rate

Evidence shows that resting HR is linked to cardiovascular morbidity and mortality in patients with cardiovascular disease and general population (Benetos et al., 1999; Diaz et al., 2005; Heidland & Strauer, 2001; Jouven et al., 2005; Kannel et al., 1987a). Where clinical and experimental data suggests that continued elevation of HR contributes to the pathogenesis of vascular disease (Custodis et al., 2010). Furthermore, increased resting HR may encourage atherosclerotic disease via facilitation of plaque disruption and progression of coronary atherosclerosis (Zhu & Friedman, 2003). Therefore, due to the effects of HR on the vascular system, it is important to investigate how this parameter is affected by exercise interventions, as a reduction in resting HR through WBV therapy may consequently reduce the risk of future cardiac event in these already high risk stroke patients.

Literature by Katch et al. (2011) states that the heart is 'turned on' for exercise due to four causes: (1) increased sympathetic activity, (2) reduced parasympathetic activity, combined with

(3) feedback information from activation of receptors in muscles and joints as exercise commences, and (4) input from the brain's central command. Additionally, the HR response to exercise is associated to a multifaceted interaction between factors such as age, gender, sympathetic drive, physical conditioning, venous return, and baroreceptor reflexes (Lauer, Okin, Larson, Evans, & Levy, 1996). Research has shown that the initial rise in HR during exercise, up to about 100 bpm, is a result of the withdrawal of parasympathetic tone (Rowell, 1986). But when exercise intensity or work rates are increased, stimulation of the SA and AV nodes via the sympathetic nervous system is accountable for rises in HR (Rowell, 1986). Therefore, the parasympathetic nervous system reduces and stimulation of the sympathetic nervous system increases (Jagoda, Myers, Kaminsky, & Whaley, 2014).

Submaximal steady-rate exercise results in the HR increasing rapidly but levelling off within several minutes (Vokac, Bell, Bautz-Holter, & Rodahl, 1975). With each subsequent increase in exercise intensity, HR will increase to a new plateau as the body endeavours to meet the cardiovascular response to the metabolic demands (Katch et al., 2011). Furthermore, Vokac et al. (1975) found that when comparing submaximal arm exercise to that of leg exercise, HR was significantly higher in arm cranking than in cycling at workloads above 300 kpm/min. Whilst HR rapidly levelled off in cycling, during arm cranking HR increased steadily throughout the initial 6 minutes of work, levelling off around 8 minutes. The reduction in HR regularly observed among highly conditioned endurance individuals is a result of adaptations of increased parasympathetic activity, with some reduction in sympathetic discharge (Katch et al., 2011). Highlighting that endurance training produces an imbalance between parasympathetic depressor and sympathetic accelerator activity to support increased vagal parasympathetic dominance (Katch et al., 2011). Early research that investigated the cardiovascular response to dynamic and static muscular activities showed a large increase in HR during dynamic exercise, whilst only a moderate increase in HR through isometric exercise (Laird et al., 1979; Lindquist et al., 1973). This was supported by Chapman and Elliott (1988), who found a significant increase in HR during moderate intensity

dynamic exercise. While González-Camarena et al. (2000), found a lower HR was associated with isometric exercise when compared to dynamic exercise. Research by Rowell (1986) also identifies that a rise in body temperature above normal causes an increase in HR, however reductions in body temperature below normal results in a lower HR.

2.3.3 Arterial Stiffness

2.3.3.1 Principles of Arterial Stiffness

Arterial stiffness is a broad term that jointly describes compliance, distensibility, and elastic modulus of the arterial vascular system; therefore arterial stiffness is the pressure necessary to achieve a given dilation in an arterial segment or in the whole arterial tree (Schillaci & Parati, 2008). These properties are not identical along the arterial tree, and elastic and muscular vessels differ (Stoner, Young, & Fryer, 2012).

The competence of the buffering function is reliant on viscoelastic properties of arterial walls and the geometric characteristics of the arteries, comprising of their diameter, length, and cross-section. Thus, stiffening of the vasculature develops from a complex interaction between stable and dynamic alterations including cellular and structural elements of the vessel wall (Zieman, Melenovsky, & Kass, 2005). These vascular changes are influenced by: hemodynamic forces (shear stress and/or cyclic tensile stress) (London, Marchais, Guerin, & Pannier, 2003; Wolinsky & Glagov, 1964, 1969); direct injury; atherogenic factors (such as atherosclerosis); and extrinsic factors such as salt, glucose regulation, and hormone regulation (Gibbons & Dzau, 1994; Zarins, Zatina, Giddens, Ku, & Glagov, 1987; Zieman et al., 2005). The characteristics of arterial remodelling are largely dependent on the existence of an intact endothelium and the type of hemodynamic stimuli being applied to the vessel (Gibbons & Dzau, 1994; Tozzi, Poiani, Harangozo, Boyd, & Riley, 1989; Tronc et al., 1996). Research has stated the principal determinant of tensile stress and arterial wall stretch is BP (London et al., 2003). A rise in BP or

arterial radius results in the thickening of the vessel wall with normal internal diameter as to maintain tensile stress within the physiological range (London et al., 2003). However, shear stress is altered by changes in blood flow, where acute and chronic rises in arterial blood flow cause a proportional increase in vessel lumen and decreases in blood flow reduce arterial inner diameter (Kamiya & Togawa, 1980; Langille & O'Donnell, 1986; London et al., 2003). Increased arterial stiffness requires a greater amount of force to dilate and take up the blood ejected from the heart. The heart provides this increased force, which results in the heart producing more forceful contractions to accommodate for the arteries (Acampa et al., 2014). Transforming mechanical forces into remodelling of the vascular system implies there are “sensors” within the vasculature (London et al., 2003), introducing endothelial cells.

Endothelial cells are cleverly located at the blood-vessel wall interface allowing them to detect and transmit physical forces to effector cells, and thus contribute to the process of arterial remodelling (Traub & Berk, 1998). Moreover, these cells make up the endothelium layer of vessels, where an important role is played by the vascular endothelium in the maintenance of vascular homeostasis, not just by serving as a barrier, but additionally by making use of autocrine, paracrine, and classical endocrine signalling, causing the stimulation and release of circulating agents that alter vessel wall phenotype (Luescher & Barton, 1997; O'Rourke & Kelly, 1993; Vita & Keane, 2002). In turn, the endothelium releases a variety of agonistic and antagonistic molecules, comprising of vasodilators and vasoconstrictors, inflammatory and anti-inflammatory, pro-coagulants and anti-coagulants, oxidising and anti-oxidising, fibrinolytics and anti-fibrinolytics, and several others (Luescher & Barton, 1997). Additionally, the effects of the endothelium include maintenance of vascular tone, smooth muscle cell proliferation, platelet aggregation and adhesion, and leukocyte adhesion (Moncada & Higgs, 1993). Furthermore, the endothelium's ability to regulate vascular tone can be used to establish the health of the endothelium (Stoner et al., 2012). When in a state of homeostasis the endothelium maintains its function, preserving blood fluidity and vascular tone, as well as little to no expression of pro-

inflammatory mediators (Moncada & Higgs, 1993). Research has stated the most significant molecule derived from the endothelium as nitric oxide (NO), where great amounts of evidence support its numerous anti-atherogenic properties (Vallance & Chan, 2001). As well as its vasodilatory effects, NO prevents crucial events in the development of atherosclerosis, namely: smooth muscle cell proliferation, adhesion and migration into the arterial wall, and platelet adhesion and aggregation (Vallance & Chan, 2001).

Arterial stiffness can be measured by two indices; local arterial stiffness of the carotid artery via ultrasound producing a measurement known as β -index and regional arterial stiffness via SphygmoCor producing a measurement of pulse wave velocity (PWV). Additionally, pulse wave analysis (PWA) can be performed as a composite measure of aortic wave reflection and systemic arterial stiffness (O'Rourke, Pauca, & Jiang, 2001; Oliver & Webb, 2003). Carotid arterial stiffness and PWV are important to stroke because of their direct association with vascular health; where research has shown arterial stiffness, as measured by carotid-femoral PWV and local arterial stiffness of the carotid artery, is strongly associated with atherosclerosis at numerous sites in the vascular tree (van Popele et al., 2001). A major contributing cause of stroke is atherosclerosis (Adams et al., 1993), and as PWV reflects the presence and severity of underlying cerebral or systemic atherosclerosis (Kim et al., 2014), this measurement becomes important in the assessment of arterial stiffness in stroke. Additionally, as the carotid artery is a frequent site of atheroma formation (Laurent et al., 2006a), and as carotid arterial stiffness has been associated cross-sectionally with atherosclerosis at different sites in the vascular tree (van Popele et al., 2001), measurement of carotid arterial stiffness becomes important in stroke populations also.

2.3.3.2 Mechanisms of Arterial Stiffness

It is suggested that arterial stiffness develops from a multifaceted interaction between both dynamic and stable alterations in structural and cellular features of the vessel wall (Zieman et al.,

2005). Changes in the vascular wall are influenced by structural, cellular and genetic implications, where arterial stiffness has been associated with endothelial dysfunction, altered vascular smooth muscle cell number, expression of modified vascular wall matrix proteins, inflammation, structure and function, and potential genetic determinants (Wang, Keith Jr, Struthers, & Feuerstein, 2008). Additionally, stiffness is not homogenous throughout the vascular tree, rather it is often patchy and arising in central and conduit vessels, and less so in peripheral arteries (Bassiouny, Zarins, Kadowaki, & Glagov, 1994; Beattie, Xu, Vito, Glagov, & Whang, 1998; Benetos, Laurent, Hoeks, Boutouyrie, & Safar, 1993). Aging, hypertension, diabetes mellitus and other common diseases augment the vascular alterations that cause arterial stiffening and can do so in diverse, yet synergistic, ways (Benetos et al., 1993; Ziemann et al., 2005).

The compliance, resilience, and stability of the vascular wall are dependent on the contribution of two scaffolding proteins: collagen and elastin (Ziemann et al., 2005). Usually these two proteins are held in balance due to a slow, but yet dynamic, process of production and degradation (Ziemann et al., 2005). However, dysregulation of this balance causes a reduction in normal elastin and an overproduction of abnormal collagen, which in turn contribute to arterial stiffness (Johnson, Baugh, Wilson, & Burns, 2001). Examination of the intima of stiffened vessels shows disarrayed and abnormal endothelial cells, raised collagen, broken and frayed elastin molecules, increased matrix metalloproteinases, intercellular cell adhesion molecules, cytokines, infiltration of vascular smooth muscle cells, and mononuclear and macrophage cells (Lakatta, 2003). Moreover, arterial stiffness is strongly affected by vascular smooth muscle cell tone and endothelial cell signalling (Ziemann et al., 2005). Vascular smooth muscle cells are vital for compliance and function of the vasculature. By contraction and relaxation, vascular smooth muscle cells control the lumen diameter and support blood vessels to sustain a suitable BP. Additionally, these cells synthesise extracellular matrix components and increase migration and proliferation (Wang et al., 2008). As a result of these properties, smooth muscle cells contribute to short-term regulation of the vessel diameter and also long-term adaptation through structural

remodelling by altering connective tissue composition and cells numbers (Wang et al., 2008). Smooth muscle cells release numerous matrix metalloproteinases which in turn can degrade elastin through creating uncoiled, less affective collagen and frayed and broken elastin molecules (Zieman et al., 2005). This loss of elastin from the vascular media adds to arterial stiffness (Wang et al., 2008).

Endothelial dysfunction is a prominent process that contributes to atherosclerosis and is seen in many pathophysiological conditions such as obesity, hypertension, type 2 diabetes mellitus, dyslipidemia, hypercholesterolaemia, heart failure, and metabolic syndrome (Anderson, 2006; Charakida et al., 2009; Elkayam, Khan, Mehboob, & Ahsan, 2002; Ghiadoni, Taddei, & Viridis, 2012; Hadi & Al Suwaidi, 2007; Kullo & Malik, 2007; Lupattelli et al., 2000; Meyers & Gokce, 2007; Tziomalos, Athyros, Karagiannis, & Mikhailidis, 2010). Furthermore, research has found that endothelial dysfunction is linked to vasoconstriction, inflammation, increased leukocyte adhesion and infiltration, platelet aggregation and thrombosis, and vascular smooth muscle cell proliferation (Young, 2011). Not only does endothelial dysfunction contribute to arterial stiffness but it also precedes plaque formation and in turn atherosclerosis (Gibbons & Dzau, 1994; Ross, 1999); where endothelial responses are seen to be reduced early in the process of atherogenesis, preceding evidence of the atherosclerotic plaque (Luscher & Barton, 1997). Furthermore, endothelial dysfunction is the imbalance between the release of agonistic and antagonistic endothelium-derived factors, where the main mechanism has been noted as the reduction of NO bioactivity causing an increase in production of endothelial reactive oxygen species (Russo, Leopold, & Loscalzo, 2002; Young, 2011). NO is a crucial endothelium-derived relaxing factor that has a pivotal role in the maintenance of vascular tone and reactivity (Kinlay et al., 2001). Disruption of the functional integrity of the endothelium plays a significant role in all stages of atherogenesis, extending from the initiation of lesions to plaque rupture (Stoner & Sabatier, 2012; Young, 2011). Endothelial dysfunction causes increased permeability to lipoproteins, foam cell formation, T-cell activation, plus smooth muscle migration into the arterial

wall (Ross, 1999). The initial step in formation of the plaque arises upon activation of an inflammatory response and fatty streaks emerge (Stoner & Sabatier, 2012). If these conditions continue, these fatty streaks progress and the plaques become susceptible to rupture (Ross, 1999).

Studies have suggested that arterial stiffness is in part influenced by genetic predisposition, which is independent of the influence of cardiovascular risk factors and BP (Cecelja & Chowienczyk, 2012; Mahmud & Feely, 2005). Research by Riley et al. (1986) showed that arterial stiffness was greater in adolescents with parental history of diabetes mellitus or myocardial infarction than those without parental history. Twin and family studies support the idea of genetic factors contributing to arterial stiffness, with the heritability of arterial stiffness reported amongst 38% to 54% (Cecelja et al., 2011; Ge et al., 2007). In terms of hypertension, offspring of families with hypertension were found to have a higher arterial stiffness than control subjects (Falzone & Brown, 2004). Whereas, research suggests that hypertension-induced vascular wall thickening is not connected to an increase in arterial stiffness in subjects with essential hypertension (Laurent, Boutouyrie, & Lacolley, 2005). A genome-wide scan of the population from the Framingham Heart Study reports that having chronically raised arterial PP has moderate inheritability (0.51 to 0.52) (Levy et al., 2000). Furthermore, studies that have implemented a candidate gene approach, found the renin-angiotensin-aldosterone system, which is involved in hypertension and BP control, plays a key role in arterial stiffness (Benetos et al., 1995; Lajemi et al., 2001). Studies examining the heritability of atherosclerotic lesions as measured by ultrasound, report low to non-significant heritability scores (Hunt et al., 2002; Moskau et al., 2005; Sayed-Tabatabaei et al., 2005). In contrast, O'Donnell et al. (2002) found that the contribution of genetic factors to vascular calcification was 49% in Framingham Heart Study participants. Therefore, arterial stiffness is in part influenced by genetic factors (Cecelja & Chowienczyk, 2012).

2.3.3.3 Indices of Arterial Stiffness

Non-invasive measurement of arterial stiffness involves assessing surrogate indices that are intrinsically connected with arterial stiffness, these indices include: elastic modulus, arterial distensibility, arterial compliance, PWV, augmentation index (Aix), brachial PP, and PWA (Pannier, Avolio, Hoeks, Mancia, & Takazawa, 2002; Schillaci & Parati, 2008). Numerous methodologies have been used in the in vivo assessment of arterial stiffness (Stoner et al., 2012), where they can be classed into three main methods: (1) direct stiffness estimation using measurements of distending pressure and diameter, measured by ultrasound or magnetic resonance imaging (MRI) (local determination of stiffness), (2) analysis of the arterial pressure pulse and its wave contour, that is, pulse wave analysis (systemic/central determination of stiffness), and (3) pulse transit time, that is, pulse wave velocity (regional determination of stiffness) (Pannier et al., 2002; Stoner et al., 2012; Van Bortel et al., 2002). Therefore local stiffness is the stiffness in a small section of a blood vessel under study, systemic stiffness is the stiffness of the entire circulation, and regional stiffness is the stiffness of a segment of the arterial tree (Parati & Bernardi, 2006). Numerous computerised devices exist to quantify local, systemic, and regional measurements of arterial stiffness. For example, the SphygmoCor device (AtCor Medical, Sydney, Australia) and a commercial B-mode device (Sonoite Micromaxx equipped with a 6-13 MHz linear array transducer) are often used to quantify local, systemic, and regional arterial stiffness (Stoner et al., 2012).

2.3.3.2.1 Pulse Pressure (PP)

Pulse pressure (PP) is the simplest surrogate index of arterial stiffness, where it expresses the degree of impairment of the buffering function of large arteries (Hamilton, Lockhart, Quinn, & Mcveigh, 2007). It is the resultant of subtracting DBP from SBP (Katch et al., 2011; Powers &

Howley, 2015), and is determined by stroke volume (SV) and arterial stiffness (Dart & Kingwell, 2001). As total arterial compliance is a measure of arterial stiffness, this means that PP is the result of SV divided by total arterial compliance (Nakayama & Azuma, 1977). However, this calculation is incomplete as more than just SV and the compliance of large vessels influences PP, research states that early reflected pulse waves also influence PP (O'Rourke, 1990; Safar, 1989; Van Bortel, Hoeks, Kool, & Struijker-Boudier, 1992). Stiffening of the arterial tree causes a simultaneous increase in SBP and a decrease in DBP, subsequently resulting in a wide PP (Tsvigoulis et al., 2006). Several studies illustrate that increased PP values may influence arterial remodelling at the sites of both the intracranial and extracranial arteries, increase the possibility of plaque ulceration and rupture (Lovett, Howard, & Rothwell, 2003), the development of carotid artery stenosis (Franklin, Sutton-Tyrrell, Belle, Weber, & Kuller, 1997), the incidence and severity of cerebral white matter lesions (Liao et al., 1997a) as well as the prevalence of cerebrovascular disease (Domanski, Davis, Pfeffer, Kastantin, & Mitchell, 1999). Moreover, numerous studies have shown the predicative value of PP leading to cardiovascular disease in various populations, such as: healthy populations, general populations, hypertensive patients, and in patients with Type 2 diabetes mellitus (Assmann, Cullen, Evers, Petzinna, & Schulte, 2005; Cockcroft et al., 2005; Fang, Madhavan, Cohen, & Alderman, 1995; Franklin, Khan, Wong, Larson, & Levy, 1999; García-Palmieri et al., 2005; Mannucci et al., 2006; Millar, Lever, & Burke, 1999; Panagiotakos et al., 2005). Research has reported measuring PP centrally is more beneficial and depicts endothelial function more strongly than PP measured at the brachial artery (Laurent, Tropeano, & Boutouyrie, 2006b; McEniery et al., 2006). Furthermore, research by Mannucci et al. (2006) suggests that PP measured over a 24 hour period is a stronger predictor of mortality than a single measurement. PP is influenced by numerous physiological factors and is consequently difficult to interpret in the presence of arteriovenous fistulae or aortic valve insufficiency (Cohn, Quyyumi, Hollenberg, & Jamerson, 2004). As activation of β -Adrenergic has displayed an increase PP without altering aortic PWV (Lemogoum et al., 2004), this indicates that an alteration in PP does

not always suggest an alteration in aortic stiffness. Due to conduit arteries (elastic arteries) exhibiting a non-linear pressure-volume relationship, PP is therefore directly associated to mean arterial pressure (MAP) (Hamilton et al., 2007). Therefore, if BP is reduced this will in turn decrease PP but without necessarily causing a direct effect on the arterial wall (Cohn et al., 2004). Due to this a more sophisticated index which includes PP is the SV/PP ratio (Hamilton et al., 2007). However, whilst SV/PP ratio has been applied as a measure of systemic arterial stiffness in past research, it is considered as a very crude approximation, and it is suggested that this method be avoided (de Simone et al., 1999; Lind, Andrén, & Sundström, 2004; Van Bortel et al., 2002).

While PP has been associated with stroke in longitudinal studies and its predicative value remains controversial (Laurent et al., 2003), it has been found to be a strong predictor of heart disease (Blacher et al., 2000; Franklin et al., 1999), associated with adverse effects following stroke (Faulkner et al., 2013), and display a relationship with atherosclerosis and arterial stiffness, as a rise in PP at rest may reflect an increase in large artery stiffness and increased peripheral vascular resistance (Blacher et al., 2000; Franklin et al., 1999). Moreover, research has shown that increased PP values may influence arterial remodelling at sites of both intracranial and extracranial arteries, increase the development of carotid artery stenosis (Franklin et al., 1997), heighten the probability of plaque ulceration and rupture (Lovett et al., 2003), increase the severity and prevalence of cerebral white matter lesions (Liao et al., 1997a), and also heighten the incidence of cerebrovascular disease (Domanski et al., 1999). Thus, measuring PP has its merits to analysing chronic stroke.

2.3.3.2.2 Local (Ultrasound of Carotid)

Distensibility coefficient (DC) is the relative rise of arterial cross-sectional area for a given increase in pressure (Hamilton et al., 2007; van der Heijden-Spek et al., 2000). Whilst compliance coefficient (CC) is the absolute rise in cross-sectional area for a given increase in arterial pressure,

this assumes that the length of the vessel is unaltered by the pulse wave (Hamilton et al., 2007; van der Heijden-Spek et al., 2000). Subsequently the measured change in cross-sectional area is meant to correspond to the volume change per unit of length. Therefore, distensibility is associated to the elastic properties of the arterial wall and is considered a determining factor of strain on the vessel wall, and compliance demonstrates the buffering capacity of an artery (Van Bortel, Kool, & Boudier, 1995; van der Heijden-Spek et al., 2000). It is stated that a reduced distensibility may increase the risk of arterial wall damage, a central feature of atherosclerotic disease, and hence a preserved local distensibility may be essential in protecting the arterial wall of each particular artery, especially those arteries that are at a higher risk of vascular disease (Van Bortel et al., 1995; van der Heijden-Spek et al., 2000). Additionally, a decrease in total arterial compliance contributes to an increased cardiac afterload and the risk of cardiac hypertrophy, therefore it is also important to preserve or increase compliance of arteries (Van Bortel et al., 1995; van der Heijden-Spek et al., 2000). As arterial compliance is related to arterial distensibility and arterial volume it may imply that an increase in arterial compliance consequently means an increase in distensibility, yet a study by Van Bortel et al. (1995) states otherwise. Research by Stork et al. (2004) states that compliance coefficient and distensibility coefficient are inversely related to stiffness, therefore if arterial stiffness decreases then a reduction in compliance and/or distensibility may be seen.

Determination of local arterial stiffness encompasses the assessment of cross-sectional arterial distensibility (Pannier et al., 2002). Where it has been identified that changes in diameter of numerous arteries, such as the aorta, carotid, brachial, and radial, can be associated to the distending pressure, and therefore provide several direct measurement sites of arterial stiffness (Wang et al., 2008). For the arterial segment being assessed, it is assumed that the segment is a cylindrical tube (Pannier et al., 2002). However, it should be noted that arteries are not homogenous tubes, and therefore compliance can differ at various parts of the same vessel (Hamilton et al., 2007). Moreover, due to the relationship between compliance and distensibility,

a combination of diameter measurement along with simultaneous, or within a few minutes, local BP measurement (commonly at the brachial artery) is required to assess local arterial stiffness (Hamilton et al., 2007; Pannier et al., 2002; Wang et al., 2008). Thus, devices such as ultrasound and magnetic resonance imaging (MRI) have been identified as capable devices for noninvasively assessing local arterial stiffness (known as β -index) due to their vascular echo tracking abilities involving echo imaging or the Doppler shift principle (Kullo & Malik, 2007; Nelson et al., 2009; Ohayon et al., 2011; Pannier et al., 2002; Wang et al., 2008). Although MRI is capable of higher resolution, it was found to be far more costly when compared to ultrasound (Nesbitt et al., 2000). The resultant β -index is obtained from a logarithmic alteration of the curvilinear relationship between diameter and pressure, as measured using an ultrasound probe and an oscillometric arm cuff (Kawasaki, Sasayama, Yagi, Asakawa, & Hirai, 1987). Furthermore, research has identified that β index is considered to be independent of changes in blood pressure through normalizing dimension change to the diastolic mean diameter according to its formula: β -index = $\ln(\text{SBP}/\text{DBP}) / (\Delta D/D_d)$ (Nakatani et al., 1995; Störk et al., 2004). An even more accurate measurement of the diameter-pressure relationship can be determined invasively using an intravascular ultrasound device with luminal pressure transducer (Bank & Kaiser, 1998; Oliver & Webb, 2003).

Carotid arterial stiffness has been linked with atherosclerosis at different sites along the vascular tree, spontaneous cervical artery dissection and generalised narrowing of the retinal arterioles (Tsvigoulis et al., 2006). Therefore, measurement of local carotid stiffness may offer vital prognostic information (Laurent et al., 2006a). However, research has expressed that although there is a good relationship between brachial and carotid artery pulse pressures (Reneman, van Merode, Brands, & Hoeks, 1992), the application of brachial pulse pressure as a surrogate for carotid artery pressure could also cause incorrect conclusions, principally in the presence of early reflected pulse waves (Van Bortel et al., 1995). It has been stated that early reflected pulse waves may increase pulse pressure in the carotid artery and ascending aorta but

not in the brachial artery (O'Rourke, 1990), and consequently may disrupt the relationship between carotid and brachial artery pulse pressure (Van Bortel et al., 1995). Moreover research by Mattace-Raso et al. (2006) and Oliver et al. (2003) concurs that using brachial pulse pressure instead of carotid pulse pressure may lead to an underestimation of distensibility, which is different in individuals with and without cardiovascular disease. Thus, research suggests to derive carotid pulse pressure through the direct measurement of brachial pulse pressure (Mattace-Raso et al., 2006).

There are many common causes of stroke but one of the most common causes is atherosclerosis (Adams et al., 1993; Furie et al., 2011; Mohr et al., 1997; Zorowitz et al., 2004), where this process can be added to by various stroke risk factors such as hypertension, hypercholesterolemia, diabetes mellitus, cigarette smoking, and coronary heart disease (Ross, 1995; Sugioka et al., 2002). Furthermore, research has found that arterial stiffness is a risk factor for atherosclerosis and cardiovascular events (Laurent et al., 2006a; Wada et al., 1994). As the carotid artery is a frequent site of atheroma formation (Laurent et al., 2006a), the carotid artery has been examined to investigate the effects of atherosclerosis and in turn arterial stiffness, as carotid arterial stiffness has been associated cross-sectionally with atherosclerosis at different sites in the vascular tree (van Popele et al., 2001). Therefore, the measurement of carotid arterial stiffness becomes important in stroke populations.

2.3.3.2.3 Systemic/Central (PWA)

Systemic arterial stiffness affects the global buffering properties of the arterial system by displaying the overall opposition of large arteries to the pulsatile effects of ventricular ejection (Stoner et al., 2012). PWA can be used to estimate systemic arterial stiffness, with applanation tonometry being considered the “gold standard” and the most widely used technique (Compton et al., 2008; Stoner et al., 2012). Performing radial artery tonometry and then applying a transfer

function to calculate the aortic pressure waveform will provide these central estimations of SBP, PP, and augmentation index at 75 beats per minute (AIx@75) (Figures 2.8 and 2.9). Research identifies that central blood pressures are more strongly linked to vascular disease than brachial pressures (De Silva et al., 2008). Where an increase in central PP (SBP-DBP) is linked to arterial stiffness and can possibly favour the occurrence of cerebrovascular disease (Tsvigoulis et al., 2006).

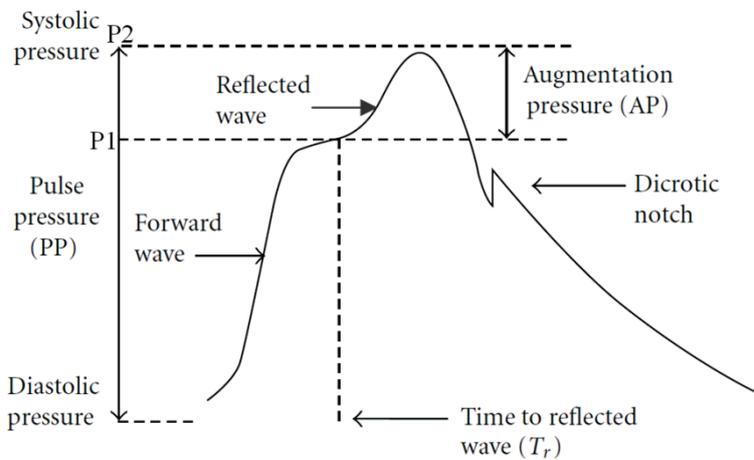


Figure 2.8. Aortic pulse pressure waveform, adapted from Stoner et al. (2012).

Systolic and diastolic pressures are the peak and trough of the waveform. Augmentation pressure is the additional aortic systolic pressure caused by the return of the reflected waves at the central aorta. Augmentation index (AIx) is the AP as a percentage of central PP and is a combined measure of aortic wave reflection and systemic arterial stiffness. The dicrotic notch denotes closure of the aortic valve and is a calculation of ejection duration. Time to reflection is calculated as the time at the onset of the incident wave to the onset of the reflected wave (Stoner et al., 2012).

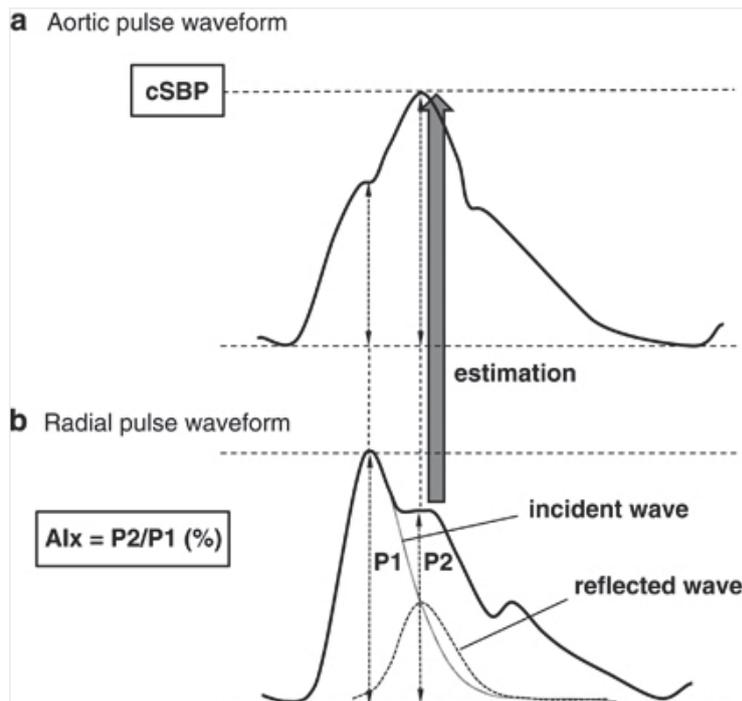


Figure 2.9. Radial applanation tonometry for aortic pulse pressure waveform (Fujime et al., 2012).

P1 indicates the systolic peak of the aortic pressure wave as a result of a forward traveling wave created by stroke volume, P2 is the systolic peak of a reflected wave returning to the ascending aorta from the peripheral arteries. Alx was standardised to a HR of 75 beats/min (Alx@75); due to the linear relationship between HR and Alx (Figuroa et al., 2001).

Arterial pulse waveform encompasses a summation of a forward pressure wave and a reflection pressure wave from peripheral sites of impedance (Stoner, Lambrick, Westrupp, Young, & Faulkner, 2014). Alx is the difference between the second and first systolic peaks (P2-P1) conveyed as a percentage of the pulse pressure (Figure 2.9) (Laurent et al., 2006a). In arteries with greater stiffness, PWV increases and the reflected wave arrives back at the central arteries earlier, consequently this adds to the forward wave and augments the systolic pressure (Laurent et al., 2006a). There are a number of variables known to influence Alx such as HR, DBP, height, age, vasomotor tone of the arterial system, and aortic PWV (Figuroa et al., 2011; Laurent et al., 2006a; Wang et al., 2008). Prominent tapering of the aorta has also been positively correlated with the Alx, proposing a significant influence of the arterial diameter along with arterial length (Stoner et al., 2014). Furthermore, Alx has been found to be influenced by vasoactive drugs independently of aortic pulse wave velocity (Stoner et al., 2014). This suggests that Alx is to some

extent determined by the intensity of wave reflection, and this in turn, is expressed by the diameter and elasticity of small arteries and arterioles (Stoner et al., 2014). HR has been shown to have a major influence on Alx, stating that an increase of just 10 bpm can result in a 4% reduction in Alx (Wilkinson et al., 2000). This increase in heart rate, and consequently decrease in Alx, displays an inverse relationship between the two variables and hence Alx should be normalised for a HR of 75 beats per minute (Alx@75) ((Figuroa et al., 2011; Wilkinson et al., 2000). Furthermore, research by Figuroa et al. (2011) suggests that HR does not influence the reduction in wave reflection post WBV, rather the reduction is due to vasodilation of peripheral arteries. Thus, stating that WBV counteracts the increase in Alx caused by static squat and decreases wave reflection magnitude through a local effect on arterial stiffness. Additionally, as mentioned earlier, Wilkinson et al. (2000) found a significant, inverse, relationship between HR and Alx with every 10 bpm increment, Alx decreased by around 4%. The study notes that it is unlikely that changes in aortic stiffness account for the inverse relationship between Alx and HR. Rather there is a higher chance that this relationship is due to the reduction in ejection duration, linked with increasing heart rate, producing a shift of the reflected wave into diastole (Wilkinson et al., 2000).

Unlike the PWV, which is a direct measure of arterial stiffness, the Alx, which is derived from PWA, is actually an indicator of arterial wave reflection (Stoner et al., 2012). Additionally, PWA has emerged as a non-invasive, reliable, valid, and widely implemented technique to examine central BPs and systemic arterial wave reflection (Alx) (Stoner et al., 2014). More specifically, the Alx is thought to reflect the merging of forward and backward (reflected) pressure waves (Laurent et al., 2006a). The forward travelling wave is determined by cardiac function, including heart rate and stroke volume (Figuroa et al., 2001)(Kelly, Millasseau, Ritter, & Chowienczyk, 2001). The reflected wave is dependent on large artery stiffness, particular that of the aorta (Kelly et al., 2001); however, additional sources of wave reflection also include large artery

geometry, including tapering of the aorta and bifurcations throughout the vascular tree, as well as the tone of the small vessel beds (Kelly et al., 2001; London, Guerin, Pannier, Marchais, & Stimpel, 1995; Soga et al., 2008; Voges et al., 2012). Research suggests that Alx depends, at least partially, on large artery and aortic PWV (Kelly et al., 2001). Where increased PWV causes an earlier arrival of reflected waves and, as a result, increased augmentation during early systole (Merillon et al., 1983). Additionally, evidence suggests that PWV is inversely related to arterial distensibility (Kelly et al., 2001). Thus, it is proposed that Alx is an index of arterial stiffness (Wilkinson, Cockcroft, & Webb, 1997a), and consequently has been used as a measure of this (Westerbacka et al., 1999). Moreover, Alx has been shown to be a significant predictor of major adverse cardiovascular events and all-cause mortality in patients with angiographic coronary artery disease (Chirinos et al., 2005). A major cause of stroke is atherosclerosis, which has been correlated with arterial stiffness (Laurent et al., 2001), and as Alx is a measure of wave reflection and a proposed index of arterial stiffness (Wilkinson et al., 1997a), this measure becomes important in stroke populations.

2.3.3.2.4 Regional (PWV)

Arterial stiffening causes a rise in PWV and influences the transit time of pressure waves (London et al., 2001). As a result of an increase in PWV, arterial stiffness decreases the transit time from the peripheral reflection sites toward central arteries, thus changing the timing of incident and reflected waves (London et al., 2001). Whilst arterial stiffening is accountable for the acceleration of the pressure wave transmission, the intensity of wave reflection is reliant on the reflective properties of the vascular tree that can be changed independently of arterial stiffness (Glasser et al., 1997). Arterial stiffening, in addition to contributing to cardiovascular alterations, heightens the appearance of abnormal reflective properties of the vasculature in the central arteries and aorta by accommodating an early return of reflected waves (London et al., 2001). The increase of wave reflections on the central arteries and aorta causes greater pressure during systole and

reduced DBP and/or diastolic tension-time index (O'Rourke & Kelly, 1993). It is known that the elastic properties of conduit arteries differ along the arterial tree; with more elastic proximal arteries (i.e. central arteries) and stiffer distal arteries (i.e. peripheral arteries) (Laurent et al., 2006a). As a result of numerous branches along a viscoelastic tube, a pressure wave progressively amplifies from central to distal conduit arteries due to wave reflections (Laurent et al., 2006a). In peripheral arteries wave reflections can augment the pressure wave as reflection sites are nearer to the peripheral sites than to central arteries, and PWV is increased in a peripheral stiffer artery. As a consequence, the amplitude of the pressure wave is higher in peripheral arteries than in central arteries (Laurent et al., 2006a). Thus in stiff arteries, PWV increases and the reflected wave arrives back at the central arteries earlier which adds to the forward wave and augments SBP (Laurent et al., 2006a).

Several devices can be used to measure PWV, such as tonometric, oscillometric, photo plethysmographic, and volume plethysmographic devices (Liu, Hsu, Chen, & Wu, 2011; Naidu, Reddy, Yashmaina, Patnaik, & Rani, 2005; Salvi et al., 2004; van Leeuwen-Segarceanu et al., 2010). Research states that methods using mechanotransducers or high-fidelity applanation tonometers are well accepted for carotid-femoral PWV measurement (Laurent et al., 2006a). For example, the SphygmoCor system (AtCor Medical, Sydney, Australia) involves using a single high-fidelity applanation tonometer to find a proximal (carotid artery) and distal (radial artery) pulse. As stated above high-fidelity applanation tonometers are well accepted, with numerous studies having used this device for the measurement of aortic PWV (Laurent et al., 2006a). Additionally, research has found that the non-invasive measurement of carotid pulse wave compared to the invasive measurement of ascending aortic pulses has been shown to produce close similarities in both the frequency and time domains (Kelly, Daley, Avolio, & O'Rourke, 1989; Kelly, Hayward, Avolio, & O'rourke, 1989). Furthermore, after directly measuring carotid pulse pressure via applanation tonometry it was found that the pulsatile component of BP is underestimated by the measurement of brachial artery sphygmomanometric BP (Benetos et al., 1993).

A study by Ueda et al. (2008) evaluated the reproducibility and comparability of carotid-femoral PWV measured by an automatic waveform analyser known as Form (AT-Form PWV/ABI) compared to a mechanotransducer (Complior, Complior II; Colson, Paris, France). They measured carotid-femoral PWV twice in 21 normotensive males using both the Form and Complior devices. Their results showed that carotid-femoral PWV measured by Form was similar to, and indeed may be more reproducible than, that measured by Complior that has been implemented in numerous studies as a predictable marker for cardiovascular events (Ueda et al., 2008).

Research has shown differences in PWV dependent on the sites used (Ueda et al., 2008). Carotid-femoral sites are central measurements as they are measured along the aortic and aortoiliac pathway (Laurent et al., 2003), brachial-ankle sites are peripheral measurements and as such represents systemic arterial stiffness as it mainly encompasses aortic PWV and leg PWV (Sugawara et al., 2005). Due to the reasons stated previously, PWV obtained from peripheral sites will be higher compared to that of central sites like carotid-femoral (Laurent et al., 2006a; London et al., 2001).

Carotid-femoral PWV is a direct measurement and is considered the most clinically relevant, as the aorta and its principal branches are responsible for the majority of the pathophysiological effects of arterial stiffness (Laurent et al., 2003). Carotid-femoral PWV has been proven as a valid index of arterial stiffness to predict cardiovascular risk and events (Laurent et al., 2006a; Zhang et al., 2011). Notably Tillin et al. (2007) have stated that carotid-femoral PWV, measured using an ultrasound technique, is a more superior indicator of atherosclerosis than either carotid-radial or femoral-posterior tibial PWV. Additionally, carotid-femoral PWV should be used preferentially in studies of atherosclerosis and in determining risk in clinical settings (Tillin et al., 2007). However, some studies have identified that carotid-femoral PWV has limitations such as the femoral waveform may be challenging to record accurately in patients with obesity, diabetes, peripheral artery disease, and metabolic syndrome (Van Bortel et al., 2002). Furthermore, abdominal obesity and large bust size can result in inaccurate distance

measurements (Van Bortel et al., 2002). Whilst this is a limitation for carotid-femoral PWV, differences in any PWV may be attributable to inaccuracies in distances measured at any of the recording sites. Distances need to be measured precisely as small inaccuracies can influence the absolute value of PWV (Chiu, Arand, Shroff, Feldman, & Carroll, 1991). The shorter the distance between the two recording sites, the larger the absolute error in defining the transit time (Laurent et al., 2006a).

A study by Ueda et al. (2008) evaluated the validity of brachial-ankle PWV as a substitute of carotid-femoral PWV across two different PWV devices, the Complior (Complior, Complior II; Colson, Paris, France) and the automatic waveform analyser known as Form (AT-form PWV/ABI; Omron-Colin, Komaki, Japan) devices. They found that there was no correlation between carotid-femoral PWV, measured by either the Complior or Form devices, and brachial-ankle PWV. They suggest that brachial-ankle PWV may not be a valid substitute for carotid-femoral PWV. However, it has been expressed that Japanese researchers advocate the use of brachial-ankle PWV due to its simplicity compared to other measurement sites, disclosing that the aortic PWV was the primary independent link of brachial-ankle PWV, followed by leg PWV (Sugawara et al., 2005). Thus brachial-ankle PWV is an index of systemic arterial stiffness, which largely encompasses leg PWV and aortic PWV (Figuroa et al., 2011). Therefore, it should be noted that brachial-ankle PWV involves both central and peripheral arterial stiffness, where aortic and leg PWV are the main independent correlates explaining 58% and 23% of the total variance in brachial-ankle PWV respectively (Sugawara et al., 2005), and as a result any changes in this measure of arterial stiffness should be interpreted carefully (Otsuki et al., 2008). Research has identified that in small groups of either coronary heart disease patients or elderly community-dwelling people (Matsuoka et al., 2005; Tomiyama et al., 2005), that brachial-ankle PWV was an independent predictor of cardiovascular events or deaths. Whilst Urbina et al. (2010) declares that brachial-ankle PWV is an index of arterial stiffness displaying comparable characteristics to those of aortic PWV. A study by Tanaka et al. (2009) supports these findings asserting that there

is a significant positive relation between brachial-ankle PWV and carotid-femoral PWV, and that they are both indices of arterial stiffness that display a comparable degree of links with cardiovascular disease risk factors and clinical events. Moreover other studies agree that PWV as an index of aortic stiffness, is an independent predictor of fatal stroke in patients with uncomplicated essential hypertension (Boutouyrie et al., 1999; Laurent et al., 2003), and an independent predictor of stroke and coronary heart disease in apparently healthy subjects (Mattace-Raso et al., 2006). In particular the study by Laurent et al. (2003) found that PWV was significantly linked with a 72% increase in stroke risk for each 4 ms^{-1} increase in PWV, this 4 ms^{-1} increase in PWV is equivalent to that of 7 years of aging.

Whilst carotid-femoral PWV is considered the most clinically relevant, a study by Di Iorio, Cucciniello, Alinei, and Torraca (2010) identify that carotid-radial measurement delivers an accurate analysis with a high reproducibility in relation to carotid-femoral PWV measurement. Additionally, Schillaci et al. (2006) validates that carotid-femoral and carotid-radial PWV do correlate weakly with each other. Carotid-radial PWV mostly reflects peripheral muscular arterial stiffness of the upper limb (Zhang et al., 2011), and studies express that carotid-radial PWV is not affected by age significantly whereas carotid-femoral PWV is (Schillaci et al., 2006; van der Heijden-Spek et al., 2000). Research has shown that carotid-femoral PWV measurement is less tolerable for patients and less simple for the investigator, whilst carotid-radial PWV measurement is convenient for both patients and the investigator (Di Iorio et al., 2010; McCall et al., 2010). Additionally, this measurement also incorporates the carotid artery, a known major site of occlusion or stenosis in stroke (Zorowitz et al., 2004), and therefore suggests its relevancy to arterial stiffness measurement in stroke.

As mentioned earlier, there are many common causes of stroke but one of the most common causes is atherosclerosis (Adams et al., 1993; Furie et al., 2011; Mohr et al., 1997; Zorowitz et al., 2004), where this process can be added to by various stroke risk factors such as hypertension,

hypercholesterolemia, diabetes mellitus, cigarette smoking, and coronary heart disease (Ross, 1995; Sugioka et al., 2002). Furthermore, research has found that arterial stiffness is not only a marker of atherosclerosis but also a modulator of its progression (Kaess et al., 2012; Oberoi et al., 2013). Therefore, arterial stiffness has shown to be correlated with atherosclerosis (Laurent et al., 2001), most likely through the effects of cyclic stress on arterial wall thickening (Boutouyrie et al., 1999; Lyon, Runyon-Hass, Davis, Glagov, & Zarins, 1987). Due to PWV being measured at arterial sites of major physiologic importance it is generally accepted as the simplest, most robust, non-invasive, and reproducible method to establish regional arterial stiffness (Laurent et al., 2006a; Laurent et al., 2003; Stoner et al., 2012). Additionally, PWV has been shown to be an independent predictor of stroke (Laurent et al., 2003; Mattace-Raso et al., 2006), and therefore PWV becomes an important measurement in stroke populations.

2.3.3.4 Relationship with Age, Lifestyle, and Disease

Arterial stiffness is the hallmark of the aging process and the result of numerous disease states such as atherosclerosis, hypertension, diabetes mellitus, chronic renal failure, and hypercholesterolaemia (Acampa et al., 2014). Some authors have reported a linear relationship between arterial stiffness and age (Avolio et al., 1983), whilst others have identified accelerated arterial stiffening between the age of 50 and 60 years (McEniery, Hall, Qasem, Wilkinson, & Cockcroft, 2005). Changes in the vascular wall attributed to aging are through structural modifications, such as an increase in calcification of the media and collagen content, accumulation and migration of vascular smooth muscle cells in the arterial walls, and elastic lamellae creasing and breakage (Paini et al., 2006). Research by Van Bortel et al. (1995) identifies that large conduit arteries do not react similarly to changes in physiological conditions or disease states. Advancing age decreases elasticity of the common carotid artery (Benetos et al., 1993; Reneman, Van Merode, Hick, & Hoeks, 1985), and aortic artery through decreased distensibility and compliance (van der Heijden-Spek et al., 2000), increased diameter (Samijo et al., 1998), and

can be seen to have increased wall thickness (Benetos et al., 1993; Boutouyrie et al., 1992; Reneman, Van Merode, Hick, Muytjens, & Hoeks, 1986). However, no significant correlation with age was seen in the femoral artery (Benetos et al., 1993) or with the distensibility of the brachial artery (van der Heijden-Spek et al., 2000). This is supported by Laurent et al. (1994) who found that femoral, brachial, and radial arteries, which all have a muscular structure, are resistant to age-induced stiffening compared with the carotid artery. Yet, research by Van der Heijden-Spek et al. (2000) found that brachial artery diameter increased with age and its compliance was not reduced but even augmented in women. Additionally, they found that the effect of age on large artery wall properties is asymmetrical and depends on vascular territory and gender (van der Heijden-Spek et al., 2000). Moreover, in patients with hypertension, compliance and distensibility of elastic arteries decrease (Safar, Simon, & Levenson, 1984), but compliance of the radial artery does not (Laurent et al., 1993). This may indicate a compensation for the loss in compliance in elastic arteries (Laurent et al., 1993). Research has also found that aging of the arterial media is connected with increased expression of matrix metalloproteinases, which are involved in the degradation of vascular elastin and collagen fibres, and therefore contribute to arterial stiffness (Cecelja & Chowienczyk, 2012).

Cardiovascular risk factors, such as lifestyle, disrupt endothelial dysfunction and contribute to the development and progression of atherosclerosis (Young, 2011). Lifestyle factors that have been identified as important in this process are; obesity, physical inactivity, alcohol consumption, salt intake, and cigarette smoking (Ambrose & Barua, 2004; Tanaka & Safar, 2005; Zieman et al., 2005). The pathophysiology that connects stiffening of the arteries to abdominal adiposity is largely unknown (Safar, Czernichow, & Blacher, 2006). However, visceral adipocytes have a heightened lipolytic activity that causes an increase in fatty free acids released in the portal vein with an accumulation (pancreas, liver, and muscles) that adds to insulin resistance (Safar et al., 2006). Moreover, other suggested mechanisms are increases in circulating leptin or proinflammatory cytokines (Singhal et al., 2002; Visser, Bouter, McQuillan, Wener, & Harris,

1999). It is suggested that adipose tissue releases a large number of bioactive mediators that influence insulin resistance and body weight homeostasis, and additionally alter BP, lipids, fibrinolysis, coagulation, and inflammation, leading to endothelial dysfunction and atherosclerosis (Van Gaal, Mertens, & De Block, 2006). Studies have suggested that arterial stiffness is less pronounced in those who participate in regular endurance exercise (Tanaka et al., 2000; Vaitkevicius et al., 1993). Moreover, aerobic exercise at medium intensity (cycling at 65% maximal oxygen uptake for 30 minutes) has displayed an acute decrease in systemic arterial stiffness (Kingwell, Berry, Cameron, Jennings, & Dart, 1997). A meta-analysis conducted by Miyachi (2013) found that in young individuals with low baseline levels of arterial stiffness, that high-intensity resistance exercise is linked with increased arterial stiffness. Furthermore, acute resistance exercise (85% 1RM) to volitional fatigue found that arterial stiffness of the exercised leg decreased; however, there was no effect on the non-exercised leg or central arterial stiffness. Furthermore, previous research has indicated that the reduction in leg PWV after acute resistance (Heffernan et al., 2006), endurance (Kingwell et al., 1997; Sugawara et al., 2004; Sugawara et al., 2003), and static exercise (Davies, Frenneaux, Campbell, & White, 2007) has been linked to contraction-related vasodilatory factors (Figuroa et al., 2011). Furthermore, even once arterial stiffness is established, large artery stiffening can be decreased through participation in physical exercise (Cameron & Dart, 1994). Low physical activity and poor cardiovascular fitness are determinants of greater arterial stiffness (Boreham et al., 2004). However, the nature of the associations is not clear due to physical activity and cardiorespiratory fitness both mediating and confounding the associations with each other with arterial stiffness (Boreham et al., 2004), and as a result it is unclear how physical inactivity directly contributes to arterial stiffness. However, what has been identified is how physical activity improves bodily functions that may consequently contribute to arterial stiffness. Research has stated physical activity improves glucose tolerance and sensitivity, decreases triacylglycerols decreases platelet aggregation, increases fibrinolysis, lowers resting HR by increasing vagal tone, improves oxygen

uptake in the heart and peripheral tissues, and lowers BP (Sandvik et al., 1993). Moderate alcohol consumption has been associated with significantly lower PWV (Sierksma et al., 2004a; Sierksma et al., 2004b), and consequently it is suggested that it may reduce arterial stiffness (Mahmud & Feely, 2002). However, excess alcohol consumption (more than four drinks daily) has been associated with high BP (Beilin, Puddey, & Burke, 1999; de Lorimier, 2000), and increased large artery stiffness assessed by PWV in middle-aged Japanese men (Nakanishi et al., 2001). However, the mechanisms involved in this are unclear. Research has stated that salt intake may have the most potent effects on arterial stiffness (Zieman et al., 2005). It is suggested that besides changing mean pressure, salt exposure triggers functional and structural pressure-independent alterations in the vascular wall (Zieman et al., 2005). Where, research conducted on salt-sensitive rats with a high salt diet found altered arterial wall composition that precedes BP increases by weeks, and increased vascular stiffness (Limas, Westrum, Limas, & Cohn, 1980). These pressure-independent alterations are due to abnormal endothelial function, intimal medial thickening, increased smooth muscle tone, and increased collagen, hyaluronic acid, fibronectin, and collagen cross-link formation (Levy et al., 1997; Mizutani, Ikeda, Kawai, & Yamori, 1999). Yet, short-term and long-term restriction of salt can improve arterial stiffness (Zieman et al., 2005). The exact mechanisms involved in cigarette smoking related cardiovascular dysfunction are largely unknown (Ambrose & Barua, 2004). However, cigarette smoking has been stated to increase inflammation, oxidation of low density lipoprotein cholesterol, and thrombosis (Ambrose & Barua, 2004). Therefore, research suggests that the potential mechanism of cigarette smoke exposure to cardiovascular dysfunction may be increased oxidative stress (Ambrose & Barua, 2004).

A study by Vlachopoulos, Aznaouridis, and Stefanadis (2010) investigated the predictive value of aortic PWV for future cardiovascular events and all-cause mortality. They found that aortic PWV is a strong predictor of future cardiovascular events and all-cause mortality (Vlachopoulos et al., 2010). Moreover, other studies agree that PWV as an index of aortic

stiffness, is an independent predictor of fatal stroke in patients with uncomplicated essential hypertension (Boutouyrie et al., 1999; Laurent et al., 2003), and an independent predictor of stroke and coronary heart disease in apparently healthy subjects (Mattace-Raso et al., 2006). In particular the study by Laurent et al. (2003) found that PWV was significantly linked with a 72% increase in stroke risk for each 4 ms^{-1} increase in PWV, this 4 ms^{-1} increase in PWV is equivalent to that of 7 years of aging. Additionally, research by Blacher et al. (1998) displayed increased common carotid diameter, via a high-resolution B-mode echo-tracking system, is a significant predictor of all-cause mortality when investigated in patients with end-stage renal disease. Carotid artery distensibility was also shown to be an independent predictor of cardiovascular events post renal transplantation (Barenbrock et al., 2002). Furthermore, Tsivgoulis et al. (2006) showed that when ischaemic stroke subjects are compared to age and sex matched controls, common carotid artery distensibility is significantly lower in stroke patients than that of controls. Additionally, they state that common carotid artery intima-media thickness and distensibility are the only independent predictors of ischaemic stroke (Tsivgoulis et al., 2006). The authors identified that with each 1 standard deviation increase in either common carotid artery intima-media thickness or distensibility, this independently augmented the chance of ischaemic stroke by 167% and 59% respectively (Tsivgoulis et al., 2006). Thus, increased common carotid artery stiffness is associated with ischaemic stroke independent of common carotid artery intima-media thickness or conventional risk factors (Tsivgoulis et al., 2006). A study by Tuttolomondo et al. (2010) evaluated arterial stiffness indexes in participants with acute ischaemic stroke compared to controls matched for sex, age, cardiovascular risk factors and prior cardiovascular morbidity. This study evaluated 209 people and found that when compared to control patients without ischaemic stroke, stroke patients displayed a higher mean Alx ($103 \pm 3.5 \text{ mmHg}$ vs. $99 \pm 4.6 \text{ mmHg}$) and carotid-femoral PWV ($11.8 \pm 3.3 \text{ ms}^{-1}$ vs. $10.02 \pm 2.29 \text{ ms}^{-1}$). Expressing that higher PWV and Alx values in ischaemic stroke patients compared to controls, matched for both cardiovascular risk factors and morbidity, demonstrate that acute ischaemic stroke is associated

with higher arterial stiffness indexes independently from the presence of risk factors such as diabetes and hypertension (Tuttolomondo et al., 2010).

As indicated earlier, arterial stiffness is an independent predictor of fatal stroke in patients with uncomplicated essential hypertension (Boutouyrie et al., 1999; Laurent et al., 2003), and an independent predictor of stroke and coronary heart disease in apparently healthy subjects (Mattace-Raso et al., 2006). As vascular changes are influenced by; hemodynamic forces (shear stress and/or cyclic tensile stress) (London et al., 2003; Wolinsky & Glagov, 1964, 1969); direct injury; atherogenic factors (such as atherosclerosis); and extrinsic factors such as salt, glucose regulation, and hormone regulation (Gibbons & Dzau, 1994; Zarins et al., 1987; Zieman et al., 2005), it is thought that the relationship between arterial stiffness and age, lifestyle, and disease may contribute further to the severity of arterial stiffness through additive effects on the vasculature; as a result these relationships may further impact on stroke.

Chapter 3 – Research Aim and Hypotheses

Chapter 2 provided insights into how individuals with stroke are affected, the risk factors and causes of stroke, and cardiovascular indices that are central to understanding stroke. Additionally, it explored WBV as an exercise regime and identified the potential of WBV as an exercise intervention post-stroke. Consequently, it highlighted noticeable areas requiring further investigation regarding WBV effects on cognition, QOL, and cardiovascular indices such as arterial stiffness, and also WBV as a post-stroke intervention. The literature review illustrated arterial stiffness as a risk factor for atherosclerosis and stroke. Where, atherosclerosis was identified as the most common cause of stroke, along with other risk factors such as; hypertension, hypercholesterolemia, diabetes mellitus, cigarette smoking, and coronary heart disease. Consequently, due to the direct association between arterial stiffness and vascular health, arterial stiffness is an important risk factor to decrease in an attempt to reduce future stroke risk in chronic survivors. Valid measures to assess arterial stiffness in chronic stroke survivors are PWV and carotid arterial stiffness. While PWA is a valid measure of arterial wave reflection in chronic stroke survivors. Furthermore, HRQOL was identified as the most significant effect of a stroke for survivors.

The aim of the present study was to determine what effect multiple sessions of WBV has on indices of arterial stiffness, cognition, and QOL in chronic stroke. It is hypothesised that WBV training will significantly; (1) reduce indices of arterial stiffness (carotid, augmentation index, pulse wave velocity), (2) improve cognitive ability, and (3) QOL in chronic stroke survivors.

Chapter 4 – Methods

4.1 Study Design

Given Palmerston North’s small stroke community, it was envisaged that implementing a repeated measures cross-over design would allow participants to serve as their own matched control (Figure 4.1).

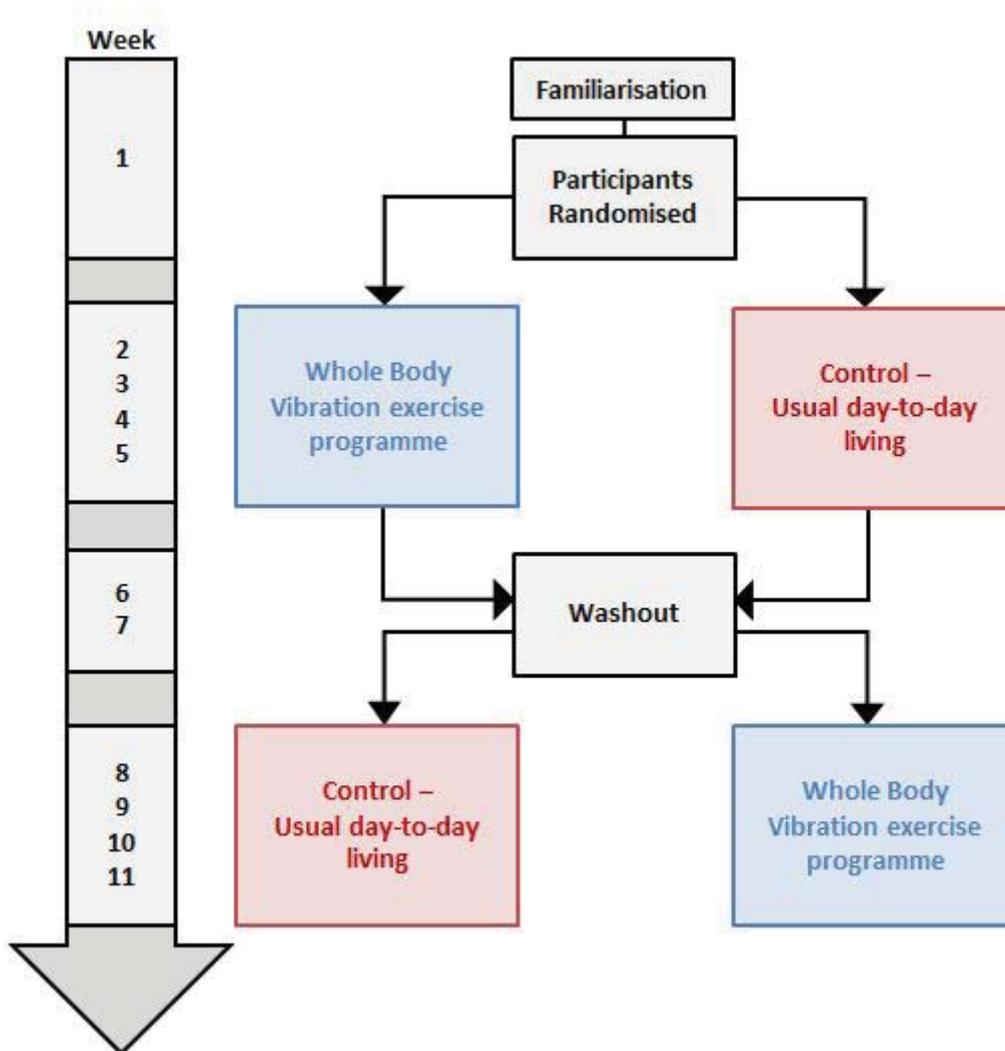


Figure 4.1. General overview of the study design

Statistically, this type of research is efficient and requires fewer participants than non-cross-over designs (Wellek & Blettner, 2012). Previously, it has been noted that 6 weeks of WBV in overweight/obese women improved brachial-ankle PWV by 8% (Figueroa et al., 2012). Using a repeated measures, between factors power analysis (G*Power 3, version 3.1.9.2, Heinrich-Heine University, Dusseldorf, Germany) revealed that a sample size of 8 participants would achieve a power of 0.89 with $\alpha = 0.05$. All testing and WBV sessions were completed at the Manawatu Stewart Centre, where testing was conducted in a first aid room that was fully carpeted and maintained a constant temperature of 21°C. This room was also equipped with its own bed, which allowed participants to be rested before measurements. The WBV sessions took place in another larger room that allowed for mobility difficulties, and maintained a constant temperature of 21°C. After baseline measurements, participants were randomly assigned to 4 weeks of WBV training or control followed by cross-over after a 2 week washout period. During the control and washout periods, participants were instructed to continue their day-to-day activities. The WBV intervention consisted of 3 sessions of WBV per week for 4 weeks, with at least 24 hours of rest between WBV sessions (Figure 4.1). Pre- and post- (4 weeks) WBV and control measurements of PWA and PWV (SphygmoCor, AtCor Medical, Sydney, Australia), local β arterial stiffness of the common carotid artery and DC, CC, and central BPs (commercial B-mode ultrasound, Sonoite Micromaxx), quality of life (Medical Outcomes Study 36-Item Short Form Health Survey, SF-36), and cognition (Addenbrooke's Cognitive Examination-III, also known as ACE-III), were undertaken by all participants. Additionally, rate of perceived exertion (Borg 15-point scale) was also recorded following every WBV session.

Prior to testing participants refrained from consuming caffeine during the preceding 12 hours, refrained from taking drugs with known vascular effects, and only consumed a light meal. Additionally, participants rested in the supine position for 20 minutes prior to testing (Stoner, Lambrick, Faulkner, & Young, 2013; Stoner & Sabatier, 2012). To account for daily biorhythms all testing was conducted at the same time of day. During the course of the study participants were

informed not to engage in any additional physical activity, above of what they were currently performing (Table 4.1). This ensured that their status of being classified as sedentary remained constant during the course of the study. This was monitored by Stewart Centre staff that for five of the six participants had their exercise programme organised and prescribed for them by the Stewart Centre. The one participant that was not part of the Stewart Centre was reminded of this requirement and consequently maintained his level, which included aqua jogging and physiotherapy.

4.2 Participants

The inclusion criteria for the study required the participants to be aged between 35 to 65 years of age and had suffered a clinically diagnosed stroke, regardless of the type, between 6 months to 5 years prior to the study, and there was no exclusion criteria dependant on the type of stroke. To be included participants had to meet the requirements of: (1) the physical activity readiness questionnaire (PARQ) that was customised for this study (Appendix A); (2) had never undertaken whole-body vibration (WBV); (3) were required to be classified as sedentary according to ACSM guidelines; which was defined as not participating in at least 30 minutes of moderate intensity physical activity for at least 3 days per week, for at least 3 months (American College of Sports Medicine, 2010). Four sedentary males (mean and \pm standard deviation [SD], age 50.5 ± 14.5 years; body mass 106.6 ± 25.9 kg; height 179.3 ± 3.8 cm) and two sedentary females (age 39 ± 2 years; body mass 86.5 ± 15.5 kg; height 168.0 ± 4.0 cm) who suffered a stroke between 6 months to 5 years prior to the commencement of the study volunteered for the project. The type of stroke and its extent of disability were classified by the modified Rankin Scale (mRS) (Table 4.1). This 6-point scale ranges from 0 to 5; where no impairment or symptoms receives a score of 0, whilst those with severe disability (bedridden and require constant nursing care) are noted as a 5. Previous studies have shown the mRS is a valid measure that has moderate to excellent inter-rater reliability (Banks & Marotta, 2007; Bonita & Beaglehole, 1988; Broderick et al., 2000).

Furthermore, five participants did partake in weekly-organised activities such as boccia, aqua jogging, and physiotherapy, but these activities did not exceed the aforementioned parameters of a sedentary lifestyle (Table 4.1).

Table 4.1. Participant characteristics

Stroke Type, <i>n</i>				
	Ischaemic			1
	Haemorrhagic			4
	Transient Ischaemic Attack			1
Stroke Laterality, <i>n</i>				
	Left Hemisphere			2
	Right Hemisphere			4
mRS prior to WBV				
	Sub01			3
	Sub02			2
	Sub03			1
	Sub04			3
	Sub05			2
	Sub06			4
	Mean (SD)			2.5 (1.05)
Organised Physical Activity				
	Boccia (seated bowls)	1 x per week	60 min	Sub01 Sub04 Sub05 Sub06
	Aqua Jogging	1 x per week	30-40 min	Sub03 Sub05
	Physiotherapy	1 x per week	30 min	Sub03

mRS: modified Rankin Scale; Sub*: participant identification number; standard deviation, SD.

Participants were recruited through Stroke Foundation Manawatu and the Manawatu Stewart Centre (a centre for brain injury rehabilitation), following permission of both the Manawatu Field

Officer for the Stroke Foundation and the Manager of the Manawatu Stewart Centre. All participants were first approached by either the Manawatu Field Officer for the Stroke Foundation or the Manager of the Manawatu Stewart Centre, and upon reading the information sheet detailing the study (Appendix B) they gave permission for the researcher to contact them with further information. All participants then personally met with the researcher who explained the study in further detail and organised their initial testing date, after the completion of this meeting all participants gave their written consent (Appendix C) to participate in the study. The research was approved by the Massey University Human Ethics Committee: Southern A (Appendix D).

4.3 WBV

WBV was performed on a commercial machine (Galileo Sport, Novotec, Pforzheim, Germany), which had a motorised teeterboard that produced side-alternating vertical sinusoidal vibrations of up to 30 Hz, and maximum amplitude of 12 mm. With this WBV machine, amplitude was dependent upon the participant's foot position; the further the feet were from the central oscillating axis the larger the amplitude and vice versa. Thus, a single axis accelerometer (iMEMS®, ADXL250, Analog Devices, Norwood, MA, USA) was fixed to the edge of the vibrating platform to measure the amplitude of the different foot positions. To guarantee the precise location and identification of the different displacements, longitudinal strips of reflective adhesive tape were applied to the WBV plate (Figure 4.2). Participants could then easily identify with these visual clues where to place their second toe and heel midpoint in line with the tape; this aided the feet to remain in the correct position during each of the sessions. The researcher constantly checked each participant's foot positioning, as any movement of the feet medially or laterally could affect the displacement setting. Over the 12 sessions participants had 3 different foot placements where: foot position 1 (FP1) = 2.1 mm (amplitude), foot position 2 (FP2) = 4.3 mm (amplitude), and foot position 3 (FP3) = 6.5 mm (amplitude).

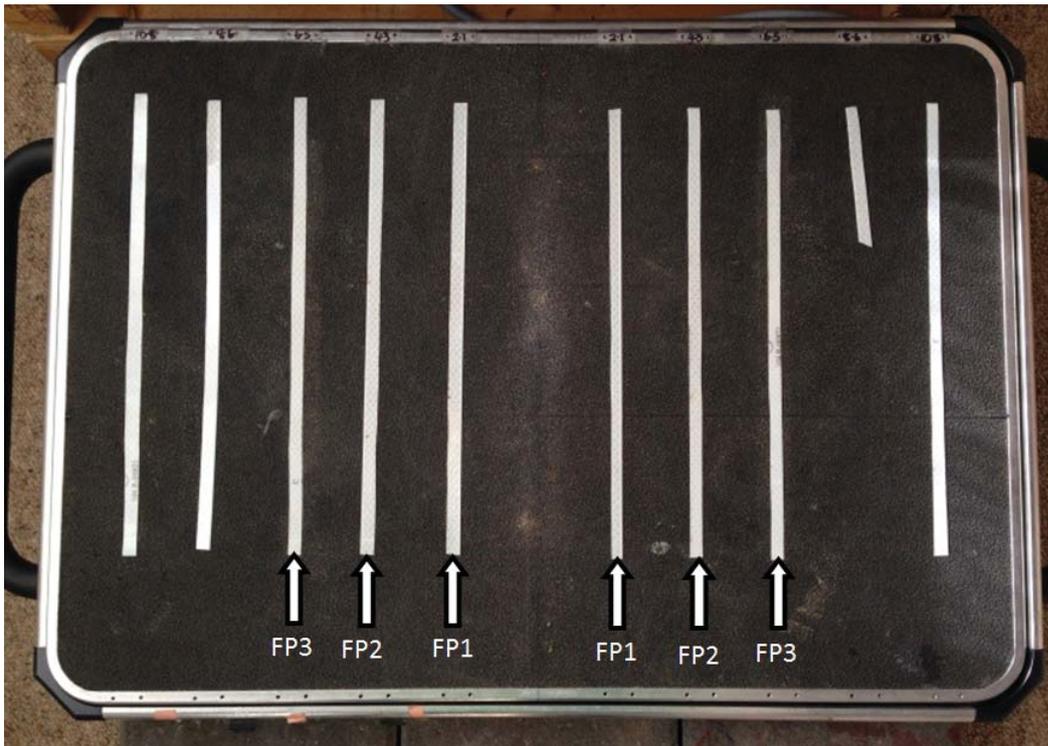


Figure 4.2. WBV Machine indicating foot positions and reflective tape markings

Participants were asked to maintain a static squat stance with 110° knee flexion (where knee fully extended = 0°), this was attained using a manual goniometer. Participants were instructed to use a static squat as opposed to dynamic squat as research by Abercromby et al. (2007b) suggests that a knee angle of 110° minimises the possibility of negative side effects of vibration being transferred through the spinal column to the head. Furthermore, it has been reported that static squatting maximises leg extensor activation (Abercromby et al., 2007a). The participants were instructed to place their feet with shoes on in the protocol-defined positions, maintain an upright torso with their eyes and head facing forward, evenly distribute their body weight through the mid-foot of both feet, and were allowed to use the support bar if required. All participants wore shoes as they had foot braces to help with their foot drop. Immediately following each 1 min bout of WBV (within 5 sec) participants scored their perceived rate of exertion from the 15-point Borg scale. These scores were then averaged to give a representative RPE for each WBV session;

with the overall average RPE for each session being derived from the average of all six participants per session.

4.4 WBV Training Protocol

At present there have been no scientifically tested WBV short-term training protocols for stroke sufferers. A four week training protocol was implemented, which was based on previous acute and chronic WBV protocols having an ability to bring positive improvements in other compromised health populations such as stroke (Chan et al., 2012; Tihanyi, Horváth, Fazekas, Hortobágyi, & Tihanyi, 2007; van Nes et al., 2004), middle-aged and elderly (Lai et al., 2014), and multiple sclerosis (Mason, Cochrane, Denny, Firth, & Stannard, 2012). Previous WBV acute studies involving stroke have elicited positive changes such as, improved gait velocity and reduction of ankle plantarflexion spasticity (Chan et al., 2012), increased voluntary force and muscle activation of the quadriceps muscle (Tihanyi et al., 2007), and enhanced proprioceptive control of posture (van Nes et al., 2004). Additionally, acute WBV on arterial stiffness in healthy and elderly populations have been examined (Figuerola et al., 2011; Lai et al., 2014; Otsuki et al., 2008). However, the aim of the current study was to investigate the effect of cardiovascular indices using short-term WBV in people that suffered from a stroke. Therefore, the current WBV was one based on various WBV protocols, of which had displayed positive changes in both stroke and in cardiovascular indices (Chan et al., 2012; Figuerola et al., 2011; Lai et al., 2014; Otsuki et al., 2008; Tihanyi et al., 2007; van Nes et al., 2004). Further, an appropriate vibration frequency was selected from previous research that 25-26 Hz has shown to enhance muscular performance (Bosco et al., 1999b; Cochrane & Stannard, 2005; Torvinen et al., 2002a). Finally, a duration of 1-minute exposure with 1-minute rest was prescribed due to previous research showing positive reductions in arterial stiffness with these parameters (Figuerola et al., 2011; Otsuki et al., 2008).

The current 4-week WBV protocol was devised from previous WBV research that reported improved standing balance and walking time in multiple sclerosis patients (Mason et al., 2012). In the current study, the vibration parameters of vibration frequency (Hz), amplitude (foot positioning; mm), peak acceleration (ms^{-2}), and session duration (min) were periodised into four blocks (Table 4.2).

Table 4.2. WBV training protocol

Session	Vibration Frequency (Hz)	Amplitude (mm)	Peak Acceleration ms^{-2}	Vibration Duration (min)
1	22	2.1	29.8	5 x 1
2	24	2.1	30.2	5 x 1
3	26	2.1	34.1	5 x 1
4	22	4.3	48.8	5 x 1
5	24	4.3	52.6	5 x 1
6	26	4.3	60.7	5 x 1
7	22	6.5	67.3	5 x 1
8	24	6.5	74.5	5 x 1
9	26	6.5	86.8	5 x 1
10	26	6.5	86.8	7 x 1
11	26	6.5	86.8	7 x 1
12	26	6.5	86.8	7 x 1

Each block consisted of three WBV sessions where the vibration frequency was systematically increased by 2 Hz (22 Hz, 24 Hz, and 26 Hz) and amplitude was increased at the commencement of a new block of training. The duration remained the same during the first three blocks; 5 sets of 1-minute bouts of WBV with 1-minute rest between exposures. To maximise the associated benefits of overload the fourth block of training (session 10-12) was set at 26 Hz, 6.5 mm (amplitude) and seven sets of 1-minute exposes with 1-minute rest. All participants performed

the same exercise protocol and if a new frequency was not tolerated by the participant then the previous frequency was used for the subsequent session and adjustments were recorded. This only occurred in one instance, where the participant opted for a lower frequency due to foot pain that was present before the commencement of the WBV session.

4.5 SphygmoCor

This is a non-invasive tool used in the assessment of the cardiovascular system, which measures systemic and regional arterial stiffness, central blood pressures and autonomic function (Figure 4.3) (Stoner et al., 2013). This was analysed by Pulse Wave Analysis (PWA) of the radial artery and Carotid-Radial Pulse Wave Velocity (PWV). Measurements were obtained at pre- and post-testing.

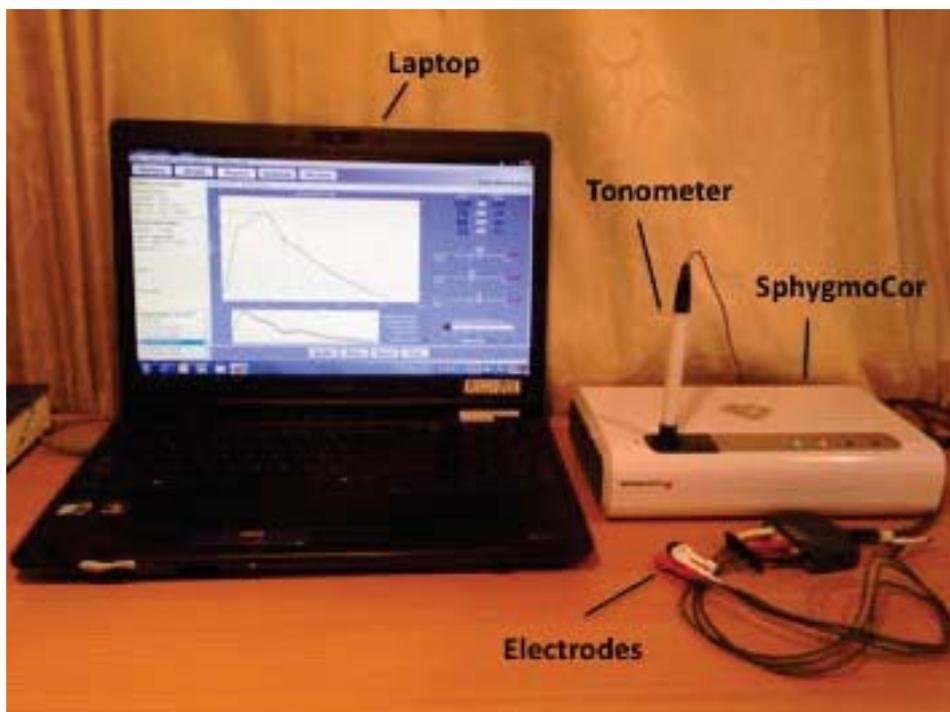


Figure 4.3. SphygmoCor

4.5.1 Pulse Wave Analysis (PWA)

PWA is not strictly an assessment of arterial stiffness, rather it is an assessment of arterial wave reflection; however through this assessment, augmentation index (AIx) can be determined as a representation of both aortic wave reflection and systemic arterial stiffness (Stoner et al., 2012). PWA was performed using the SphygmoCor device (AtCor Medical, Sydney, Australia), as previously described. Brachial BP was recorded using an automated oscillometric device (Nissei DS-157; Mentone Educational Centre, Carnegie, Victoria, Australia). Radial artery waveforms were non-invasively recorded with a high-fidelity micromanometer (SPC-301; Millar Instruments, TX, USA) from the wrist of the non-affected stroke arm by applanation tonometry. These waveforms were calibrated against brachial SBP and DBP due to comparable hemodynamic properties of the upper limb arteries (Karamanoglu, O'Rourke, Avolio, & Kelly, 1993). Data was collected directly via a personal computer (Toshiba, Windows 7 Intel® Core™ i5 operating system). A corresponding aortic pressure waveform was generated using a validated transfer function (Pauca, O'Rourke, & Kon, 2001; Sharman et al., 2006), from which central systolic blood pressure (cSBP), central diastolic blood pressure (cDBP), central pulse pressure (cPP) and augmentation index (AIx) was calculated using the integrated software (SCOR Px 7.1, AtCor Medical, Sydney, Australia). AIx was normalised to a HR of 75 beats/min (AIx@75) as HR has been shown to have a major influence on AIx, displaying an inverse relationship between the two variables as an increase of just 10 bpm can result in a 4% reduction in AIx (Wilkinson et al., 2000). HR was measured from the time between pulse waveforms and participants remained in a supine position for all PWA measurements. If the first two consecutive AIx@75 values differed by more than 4% or blood pressures of greater than 5 mmHg, a third measurement was taken and the mean of the closest two values was recorded. The researcher had an operator index of approximately 80%, indicating that high-quality values were used in the analysis, and is the requirement reported by previous studies (Figuroa et al., 2011; Stoner, Faulkner, Westrupp, & Lambrick, 2015; Stoner et al., 2012).

4.5.2 Carotid-Radial Pulse Wave Velocity (PWV)

The PWV is the speed that the pressure wave is transmitted through the vascular tree, and is calculated by measuring the time taken for the arterial waveform to pass between two points a measured distance apart. Carotid-Radial PWV was conducted using the SphygmoCor device. The pulse pressure wave of the common carotid and radial arteries was recorded non-invasively using applanation tonometry as described above. The recordings were gated using the integrated electrocardiogram (ECG), with the velocity of the pulse wave being calculated using the integrated software. Participants remained in the supine position for blood pressure measurements that were obtained prior to PWV measurements being recorded. Prior to placing the electrodes on the participants, excess hair was removed with a razor and alcohol wipes were used to remove excess dead skin. Three lead electrodes were placed on the participant's chest: 1cm below the suprasternal notch on the sternum, 1 cm above the xiphoid process on the sternum, and finally 3cm above the left iliac crest (Figure 4.4). Distal and proximal measurements were then measured and recorded for each participant. The measurements obtained were PWV and carotid to radial pulse transit time standard deviation (PTT SD).

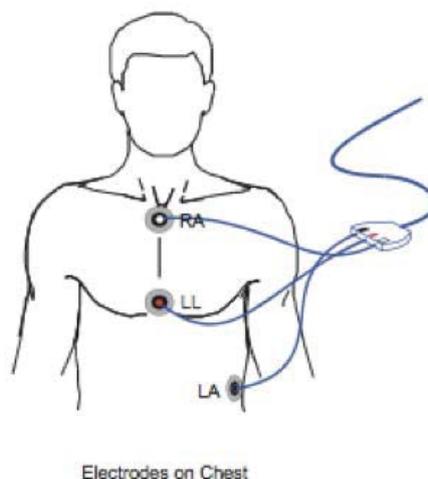


Figure 4.4. Electrode placements for PWV (AtCor Medical, 2008).

4.6 Ultrasound

The common carotid artery was imaged non-invasively using commercial B-mode ultrasound (Sonoite Micromaxx) equipped with a 6-13 MHz linear array transducer. Ultrasound was applied to find local arterial stiffness (β), where $\beta = \ln(\text{SBP}/\text{DBP})/(\Delta D/Dd)$ (Nakatani et al., 1995; Störk et al., 2004). Therefore, β is the change in arterial diameter over the cardiac cycle relative to change in blood pressure (Stoner & Sabatier, 2012). Blood pressure of the common carotid artery was recorded using applanation tonometry as described above. Blood pressure at the brachial artery; systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure (PP) was also recorded and applied to each of the four 6-second video recordings; these were collected at pre-testing and post-testing. For each participant the probe was placed on the opposite common carotid artery to that of the stroke-affected side and at a perpendicular (90°) angle to the vessel, 1 to 2 cm below bifurcation. Ultrasound global and probe-dependent settings were all standardised. Participants held their breath during each of the four 6 second video recordings with the common carotid artery diameters extending across the entire imaging plane. The four 6-second diameter measurements (D_{sys} , D_{dia} , and D_{dist}) were then collected and averaged; where D_{sys} is the systolic diameter, D_{dia} is the diastolic diameter, and D_{dist} is the difference between systolic diameter and diastolic diameter. Additionally, distensibility coefficient (DC) and compliance coefficient (CC) measurements were obtained via ultrasound; where DC is the relative rise of arterial cross-sectional area for a given increase in pressure, and CC is the absolute rise in cross-sectional area for a given increase in arterial pressure, this assumes that the length of the vessel is unaltered by the pulse wave (Hamilton et al., 2007; van der Heijden-Spek et al., 2000).

4.7 Cognition and Quality of Life Measures

4.7.1 Addenbrooke's Cognitive Examination (ACE-III)

The Addenbrooke's Cognitive Examination-III (ACE-III) is a revision of the Mini-Mental State Examination (MMSE) that aims to improve the screening performance and neuropsychological absences of the MMSE (Appendix F). The ACE-III is a short cognitive test that assesses five cognitive domains: memory, attention, language, verbal fluency, and visuospatial abilities. All five domains have allocated scores for each question. The total score for this test is 100, with higher scores indicating better cognitive functioning (Mathuranath et al., 2000). The ACE-III has been proven to be satisfactory to patients and has exceptional performance in identifying cognitive impairment in a variety of clinical situations such as stroke and vascular dementia, brain injury, Alzheimer's disease, parkinsonian syndromes, and frontotemporal lobar degenerations (Davies & Larner, 2012).

4.7.2 Quality of Life (QOL)

The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) United States Version 1.0 was implemented to assess quality of life (Appendix E). The SF-36 is a set of generic, coherent, and self-administered quality of life measures that are divided into eight main health domains: physical functioning, bodily pain, role limitations due to physical health problems, social functioning, vitality, general health, and role limitations due to emotional health problems and mental health (Marosszky & Sansoni, 2005). The SF-36 scores participants using eight multi-item Likert scales comprising of 2 to 10 items each. The results are reported on a scale of 0 to 100, with 100 indicating a high health status. Additionally, the results can be divided into two aggregate summary measures, the Mental Component Summary (MCS) and the Physical Component Summary (PCS) (Marosszky & Sansoni, 2005). The SF-36 has been proven to avoid

the “ceiling effect” of most disability scales and produces a valid measure of physical and mental health after stroke (Anderson et al., 1996).

4.8 Statistical Analysis

A repeated measures Analysis of Variance (ANOVA) was performed to determine differences in dependent variables versus time (time [pre-WBV, post-WBV, pre-control, post-control] x condition). Data gathered was analysed using SPSS software (version 21.0 for windows; SPSS Inc., Chicago, IL, USA). SF-36 scores were calculated according to standardised procedures (Ware, Snow, Kosinski, & Gandek, 1993). A Bonferroni correction post-hoc analysis was performed on any significant values and the level of statistical significance was set at $p < 0.05$. All values are expressed as mean and standard deviation (SD).

Chapter 5 – Results

5.1 Participant Characteristics

All six participants completed the required 12 sessions of WBV, four weeks of control, and the physiological and psychological tests. During the WBV period the protocol was adjusted if a participant missed a session due to personal reasons, such as doctors' appointment, this resulted in participants taking on average 4.5 ± 0.5 weeks (mean \pm SD) to complete the 12 sessions. Following a one-month follow-up, no participant suffered any further strokes, symptoms of stroke, or any other complications associated with WBV during the 12 WBV sessions.

5.2 SphygmoCor - PWA

The following measurements: central blood pressures, HR, and central augmentation index at 75 bpm (Alx@75), were obtained through the use of PWA method, which have previously been described. There was no significant interaction effect of intervention*time, and no main effect of intervention or time for any of the PWA measurements (Table 5.1 and Figure 5.1).

Table 5.1. SphygmoCor values for pre and post WBV and control interventions (mean \pm SD)

		WBV		Control	
		Pre	Post	Pre	Post
PWA	cSBP (mmHg)	110.8 \pm 9.0	112.5 \pm 12.7	111.9 \pm 13.3	110.3 \pm 11.7
	cDBP (mmHg)	76.4 \pm 10.0	77.9 \pm 8.6	77.9 \pm 10.0	76.6 \pm 10.1
	cPP (mmHg)	34.3 \pm 3.7	34.6 \pm 7.5	34.0 \pm 6.7	33.8 \pm 6.4
	HR	60.3 \pm 9.8	63.3 \pm 11.6	62.0 \pm 12.5	64.3 \pm 13.7

PWA, pulse wave analysis; cSBP, central systolic blood pressure; cDBP, central diastolic blood pressure; cPP, central pulse pressure; HR, heart rate.

Figures 5.1 below, illustrates the key measurement obtained via the PWA method. This figure presents central Alx@75 for both WBV and control interventions. A decrease in Alx@75 was

displayed for WBV whilst the control illustrated an increase over time. However, this time effect was not significant ($p=0.225$).

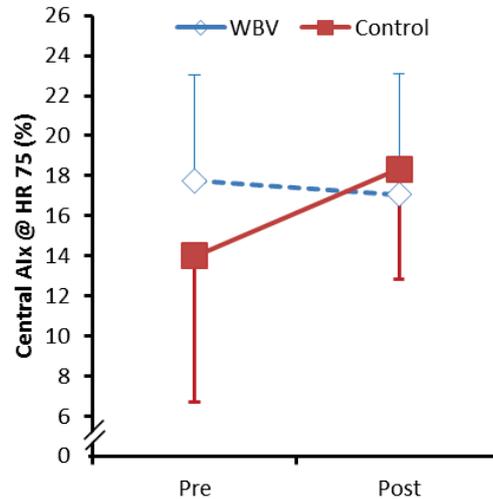


Figure 5.1. Mean (\pm SD) for central augmentation index at 75 bpm

5.3 SphygmoCor - PWV

The resulting measurements were obtained through the use of PWV, which have previously been described. There was no significant interaction effect of intervention*time, and no main effect of intervention or time, for any of the PWV measurements (Figures 5.2 and 5.3).

The subsequent two Figures 5.2 and 5.3, illustrate the key measurements obtained from the PWV method. Figure 5.2 displays the interaction effect of PWV over time, demonstrating a decrease over time for both WBV and control but these measurements were not significant ($p=0.474$). Furthermore, there was no significant difference ($p=0.299$) in carotid to radial pulse transit time standard deviation (PTT SD) between WBV and control interventions (Figure 5.3).

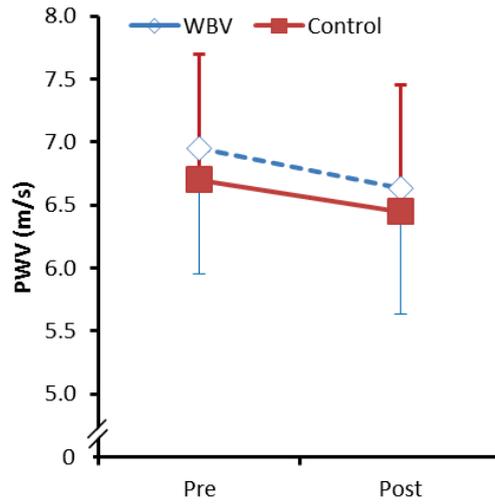


Figure 5.2. Mean (\pm SD) for pulse wave velocity

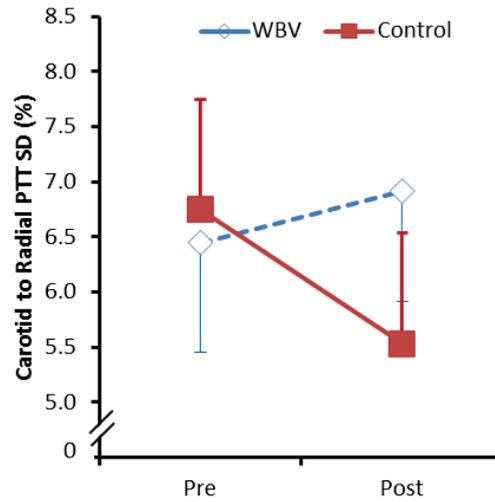


Figure 5.3. Mean (\pm SD) for carotid to radial pulse transit time standard deviation

5.4 Ultrasound

There was no significance found for the main effect of condition or condition*time interaction for any of the following measurements, however, there was a significant time effect post intervention for systolic diameter ($p= 0.039$) and diastolic diameter ($p=0.040$) (Table 5.2).

Table 5.2. Ultrasound values of pre and post WBV and control interventions (mean \pm SD)

		<u>WBV</u>		<u>Control</u>	
		Pre	Post	Pre	Post
US	SBP (mmHg)	120.2 \pm 10.1	123.5 \pm 14.5	122.8 \pm 15.4	120.8 \pm 14.1
	DBP (mmHg)	75.7 \pm 9.7	77.0 \pm 9.7	77.3 \pm 9.4	76.0 \pm 9.8
	PP (mmHg)	44.5 \pm 6.4	46.5 \pm 9.8	45.5 \pm 8.7	44.8 \pm 8.2
	Dsys (mm) *	7.6 \pm 0.9	7.8 \pm 0.8	7.7 \pm 0.6	7.8 \pm 0.7
	Ddia (mm) *	7.3 \pm 0.9	7.5 \pm 0.8	7.3 \pm 0.7	7.5 \pm 0.6
	Dist (mm)	0.3 \pm 0.1	0.4 \pm 0.1	0.4 \pm 0.1	0.3 \pm 0.1

SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure (SBP-DBP); Dsys, systolic diameter; Ddia, diastolic diameter; Dist, difference between Dsys and Ddia.

* Significant time effect post intervention for Dsys ($p= 0.039$) and Ddia ($p=0.040$).

Figures 5.4, 5.5 and 5.6 illustrate three key measurements obtained from ultrasound: arterial stiffness (β), distensibility coefficient (DC) and compliance coefficient (CC). Figure 5.4 displays that arterial stiffness decreased over time for WBV, in contrast, arterial stiffness increased for control over time. However, these measurements and their interaction effect were not found to be significant ($p=0.166$). Figure 5.5 shows distensibility coefficient (DC) where no significance was noted for its interaction effect ($p=0.124$), or main effects between WBV and control interventions ($p=0.431$). Finally, Figure 5.6 illustrates that there was no significant interaction effect ($p=0.237$), or difference in main effect for compliance coefficient (CC) between WBV and control ($p=0.496$).

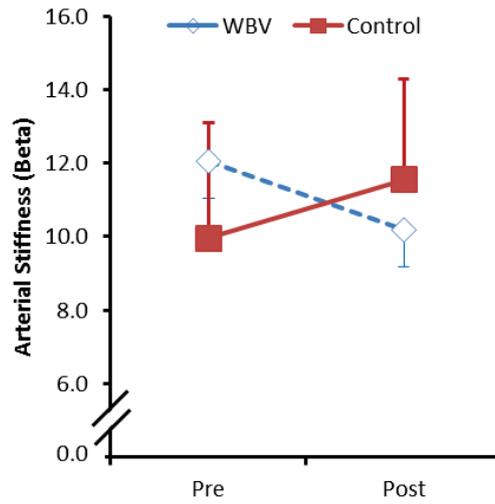


Figure 5.4. Mean (\pm SD) for arterial stiffness

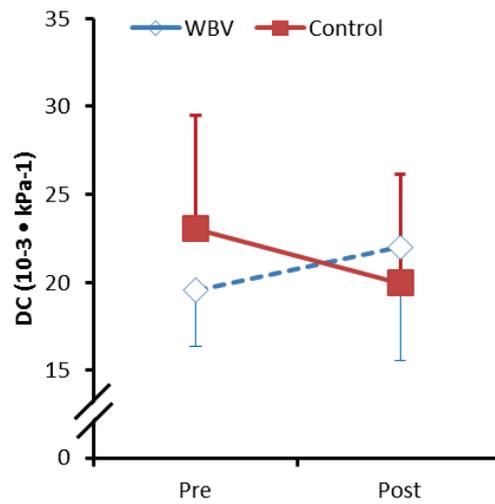


Figure 5.5. Mean (\pm SD) for distensibility coefficient

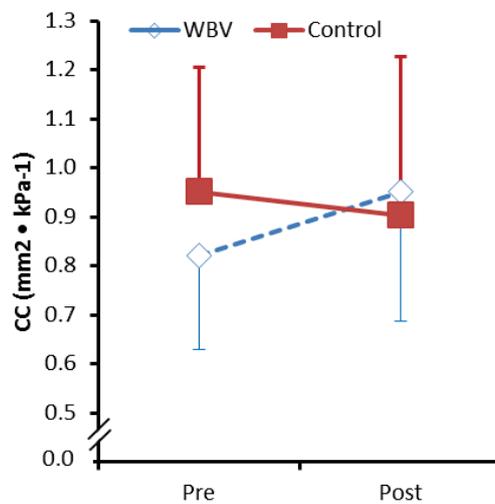


Figure 5.6. Mean (\pm SD) for compliance coefficient

5.5 Quality of Life (SF-36)

Table 5.3 illustrates that there was no significance ($p > 0.05$) of intervention*time interaction or a main effect of condition for any of the following measurements, however, there was a significant time effect for energy/fatigue ($p = 0.023$).

Table 5.3. SF-36 scores for pre and post WBV and control interventions (mean \pm SD)

	<u>WBV</u>		<u>Control</u>	
	Pre	Post	Pre	Post
Physical Functioning	41.7 \pm 9.8	43.3 \pm 8.8	45.0 \pm 6.3	39.2 \pm 11.1
Role limitations due to physical health	33.3 \pm 37.6	33.3 \pm 37.6	20.8 \pm 18.8	45.8 \pm 29.2
Role limitations due to emotional problems	33.3 \pm 42.2	27.8 \pm 44.3	27.8 \pm 32.8	55.5 \pm 40.4
Energy/fatigue *	45.0 \pm 22.8	55.8 \pm 15.9	46.7 \pm 17.8	51.7 \pm 18.1
Emotional well being	60.0 \pm 22.9	72.7 \pm 17.8	66.7 \pm 11.2	70.7 \pm 14.2
Social functioning	45.8 \pm 40.1	62.5 \pm 27.4	62.5 \pm 27.4	58.3 \pm 28.1
Pain	50.4 \pm 29.1	65.0 \pm 29.4	53.8 \pm 21.8	61.7 \pm 25.0
General health	56.7 \pm 21.4	53.3 \pm 20.7	48.3 \pm 14.4	63.3 \pm 15.1

Note: For the SF-36 a score of 100 indicates the highest level of functioning possible, where 0 indicates no level of functioning.

* Significant time effect for energy/fatigue ($p = 0.023$).

5.6 Addenbrooke's Cognitive Examination (ACE-III)

Table 5.4 illustrates that there was no significance ($p > 0.05$) of intervention*time interaction or a main effect of condition for any of the following measurements, however, there was a significant time effect for memory ($p = 0.011$).

Table 5.4. ACE-III scores for pre and post WBV and control interventions (mean \pm SD)

	<u>WBV</u>		<u>Control</u>	
	Pre	Post	Pre	Post
Overall ACE-III	75.5 \pm 13.3	81.2 \pm 10.2	74.3 \pm 16.0	79.7 \pm 14.6
Attention	13.8 \pm 3.8	14.3 \pm 2.5	14.5 \pm 2.7	14.5 \pm 2.4
Memory *	20.5 \pm 4.3	23.3 \pm 2.6	18.8 \pm 5.0	23.5 \pm 2.3
Fluency	7.3 \pm 3.8	8.0 \pm 3.3	7.0 \pm 4.0	7.5 \pm 3.9
Language	22.3 \pm 3.1	23.2 \pm 2.6	22.3 \pm 3.8	23.3 \pm 3.2
Visuospatial	11.5 \pm 4.3	12.3 \pm 3.4	11.7 \pm 3.8	10.8 \pm 4.0

* Significant time effect for memory ($p= 0.011$).

5.7 Rate of Perceived Exertion (RPE)

Figure 5.7 illustrates that there was no significance ($p= >0.05$) of RPE over the 12 WBV sessions.

In addition to RPE, three Participants (2, 3 & 6) commented that WBV warmed their legs, and in particular participant three noted that he felt this warmth in his stroke leg, when normally he has no feeling in (C. Preston, personal communication, April 14, 2014; M. Smith, personal communication, April 26, 2014; A. Luke, personal communication, April 28, 2014). Additionally, participants four and five stated that their stroke legs felt stronger and more mobile (G. Mudikattu, personal communication, July 21, 2014; T. Westwood, personal communication, June 18, 2014). Participant one mentioned that the WBV was better without his ankle brace and he felt that it was stimulating his stroke foot (A. Burne, personal communication, May 14, 2014).

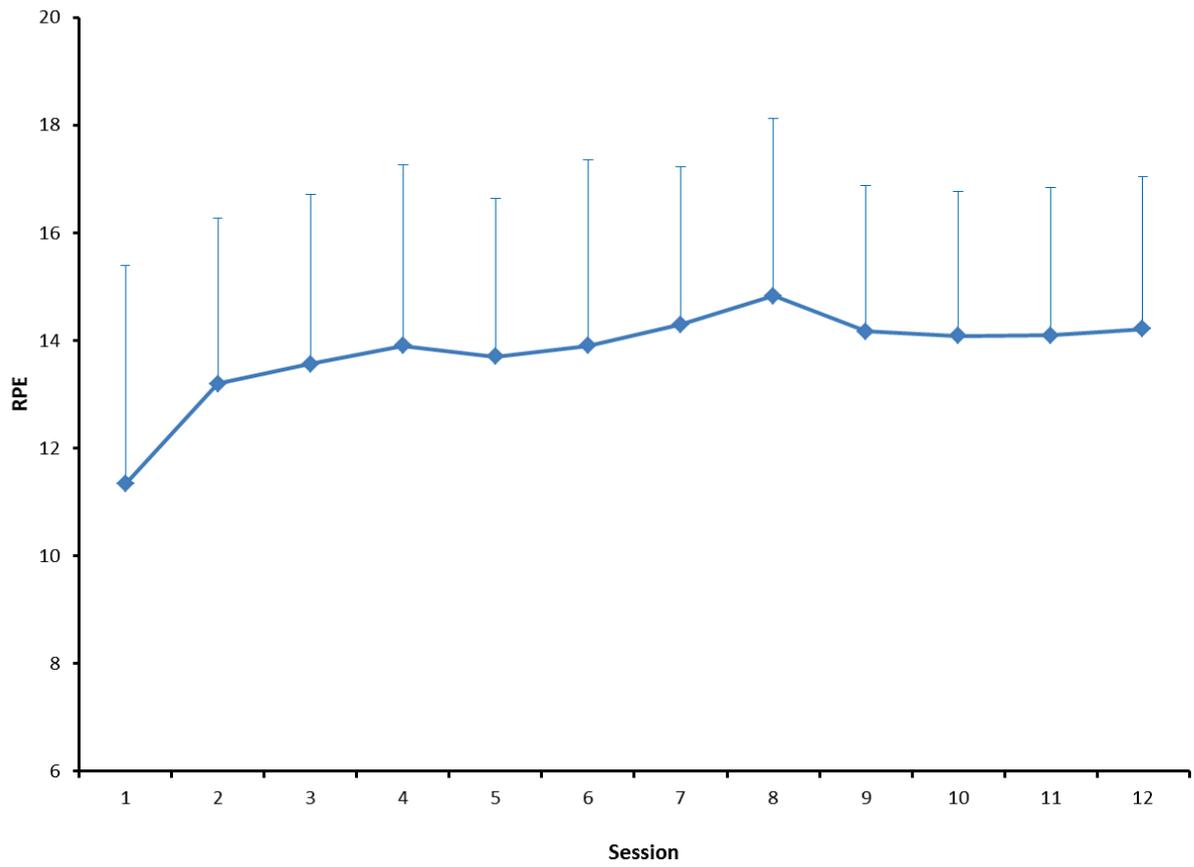


Figure 5.7. Mean (\pm SD) of RPE for all participants across 12 WBV sessions

Chapter 6 – Discussion

The primary aim of this study was to assess the efficacy of 4 weeks of WBV on indices of arterial stiffness, cognition, and QOL in chronic stroke patients. It was hypothesised that WBV training would significantly; (1) reduce indices of arterial stiffness (carotid, augmentation index, pulse wave velocity), (2) improve cognitive ability, and (3) QOL in chronic stroke survivors. However, the current WBV training protocol does not appear to produce any significant positive or negative effects on central BPs, central AIX@75, HR, PWV, carotid arterial stiffness (β), DC, CC, cognitive ability (ACE-III) or QOL (SF-36) in chronic stroke patients. Therefore, the hypotheses cannot be accepted.

6.1 Pulse Wave Analysis (PWA)

The current WBV training protocol does not appear to produce any significant positive or negative effects on central BPs, HR, or central AIX@75 in chronic stroke patients. This is supported by recent research that found no significant changes in blood pressures (SBP and DBP) following 3 months of WBV in middle-aged and older adults (Lai et al., 2014). However, some acute WBV studies have shown significant changes in BP following intervention (Figueroa et al., 2011; Rittweger et al., 2000). Research by Figueroa et al. (2011) and Rittweger et al. (2000) displayed significant increases in SBP after WBV with body-weight squats, where values returned to baseline 15 minutes post intervention; with Rittweger et al. (2000) demonstrating a significant decrease in DBP after WBV compared to control (bicycle ergometry). However, an acute WBV study by Otsuki et al. (2008) found no significant changes in blood pressures (SBP, DBP, and PP) post 60 minutes of WBV or control (no WBV). Additionally, a short-term WBV (6 weeks) study by (Gil, 2011) displayed a significant decrease in SBP at 3 minutes post WBV when compared to control (no exercise). Disparities noted between the results of Gil (2011) and the present study

could be attributed to exercise protocol and participant's health conditions (overweight and obese women vs. chronic stroke). However, unlike the previous studies, the current study similarly prescribes short-term WBV compared to a control intervention, with a small sample size (8 vs. 6). It is possible that significant changes in BP may only occur acutely after WBV as opposed to a short-term WBV training intervention. As noted by Figueroa et al. (2011) and Rittweger et al. (2000), changes in blood pressure dissipate to baseline by 15 minutes post WBV. This may suggest that the possible additive effect of continued WBV training (short-term WBV) may have no continued effect on BP. While no significant changes in blood pressures were detected there was no further deterioration of the blood pressures indicating that it may be of benefit to stroke patients. Therefore, further investigation into the effects on BP from short-term WBV training in chronic stroke is required.

In the present study central Alx at 75 bpm (Alx@75) appeared to decrease post-WBV (0.7 ± 3.1 %), and increase post-Control (4.3 ± 4.8 %). Although it was not significant, a decrease in Alx post-WBV has been reported by Figueroa et al. (2011). They showed Alx was significantly decreased during 15 and 30 minutes of recovery following an acute WBV bout involving a static squat compared to a significant increase in Alx during post recovery of no-WBV (static squat only). According to the authors the decrease in Alx, or decrease in wave magnitude, following WBV was unlikely influenced by HR but rather a result of vasodilation of peripheral arteries (Figueroa et al., 2011), which may explain the decrease in central Alx seen in the present study.

6.2 Pulse Wave Velocity (PWV)

In the present study, there was no significant change in PWV from 4 weeks WBV training. However, there was a non-significant decrease in PWV post-WBV compared to pre-WBV (7.0 ± 0.5 ms⁻¹ vs. 6.6 ± 0.5 ms⁻¹), while Control remained similar between pre and post (6.7 ± 0.5 ms⁻¹ vs. 6.5 ± 0.4 ms⁻¹).

Previously, Otsuki et al. (2008) reported that following acute intermittent WBV (10 x 60s, interspersed with 60s rest) performed by healthy men, brachial-ankle PWV decreased during recovery at 20 and 40 minutes and returned to baseline 60 minutes compared to no WBV (control), indicating that WBV acutely decreased arterial stiffness. In a similar study, the vibration protocol was modified slightly to include a higher frequency (40 Hz) that acquired PWV from carotid-femoral, brachial-ankle, and femoral-ankle sites (Figueroa et al., 2011). Femoral-ankle PWV was significantly reduced at 5 minutes in both WBV and without WBV (control), where it continued to remain low during the 30 minute recovery post-WBV but the control returned to baseline. However, there were no significant changes in carotid-femoral PWV or brachial-ankle PWV after either trial. It should be noted that brachial-ankle PWV involves both central and peripheral arterial stiffness, where aortic and leg PWV are the main independent correlates explaining 58% and 23% of the total variance in brachial-ankle PWV respectively (Sugawara et al., 2005), and as a result any changes in this measure of arterial stiffness should be interpreted carefully (Otsuki et al., 2008). Moreover, various vibration frequencies and amplitudes have been prescribed to healthy participants at a fixed frequency and amplitude for acute WBV (26 Hz and 2-4mm in Otsuki et al., (2008); 40 Hz and 1mm in Figueroa et al., (2011)). However, in the present study a gradual and progressive WBV periodised programme was implemented to increase vibration frequency (22 to 26 Hz), and amplitude (2.1 to 6.5 mm), in a safe manner to allow participants to accustomise and respond to an increasing vibration load. However, a longer duration of weeks with a larger sample size may have elicited the desired changes. This is supported by Gil (2011) who suggested that it may take longer than 6 weeks to detect changes in PWV. Where, Figueroa et al. (2012) displayed a significant 8% decrease in brachial-ankle PWV after 6 weeks of WBV, however this was in 10 young overweight/obese women. Furthermore, studies by Figueroa et al. (2011) and Otsuki et al. (2008) have only examined acute responses performed on healthy participants, thus it is possible that WBV may only acutely reduce PWV after vibration exposure.

Research by Figueroa et al. (2011), suggests that the prolonged reduction in leg PWV after WBV exercise could be linked to a local effect of vibration on the leg arteries. This is supported by several studies which found aerobic exercise (cycling at 65% $\dot{V}O_2$ max for 30 minutes) acutely decreases systemic arterial stiffness (Kingwell et al., 1997), and regional exercise (single-leg cycling or single-leg press) only affects the regional artery (Heffernan et al., 2006; Sugawara et al., 2004). When comparing this theory to passive vibration, defined as the exposure of the limbs (arms and legs) to direct continuous vibration without performing voluntary muscle contractions (Sanchez-Gonzalez et al., 2012), evidence would suggest that there is a local effect on the limbs which increases arm and leg skin blood flow and in turn may evoke local vasodilation of peripheral arteries which may reduce AIX (Koutnik, Wong, Kalfon, Madzima, & Figueroa, 2014). This is supported by an acute passive vibration protocol performed by stroke individuals lying supine placing both legs on a vibrating platform (Koutnik et al., 2014). The results revealed a significant reduction in femoral-ankle PWV (leg PWV) and brachial-ankle PWV in both the paretic and non-paretic sides. This suggests the decrease in aortic wave reflection and systemic arterial stiffness was probably due to a reduction in leg arterial stiffness (Koutnik et al., 2014), and the acute decrease of brachial-ankle PWV is a result of the change in leg PWV (Koutnik et al., 2014; Wong et al., 2011). Therefore, changes in leg arterial stiffness are likely to control central stiffness.

The theory of a local effect may help to explain the current findings. If WBV generates a local effect on PWV it would elicit changes in leg PWV rather than aortic or carotid-radial PWV. This has been demonstrated by changes in femoral-ankle PWV (Figueroa et al., 2011) and brachial-ankle PWV (Otsuki et al., 2008); where brachial-ankle PWV has been independently correlated with leg PWV (Sugawara et al., 2005). However, as mentioned earlier, both aortic and leg PWV can explain 58% and 23% respectively, of the total variance in brachial-ankle PWV (Sugawara et al., 2005). Therefore, the changes seen by Otsuki et al. (2008) may represent

changes in both aortic and leg arterial stiffness. Unfortunately Otsuki et al. (2008) did not measure aortic and leg PWV separately, and it cannot be determined whether leg PWV alone was contributing to the improvement. Likewise, Figueroa et al. (2011) did not display any significant changes in brachial-ankle PWV therefore, it is still possible that a local effect could explain the insignificant findings of the present study.

Interestingly, a study Rubin et al. (2003) may support the idea that aortic PWV can be affected by WBV through transmissibility to the spine. According to the authors during 20 degree knee flexion transmissibility at the hip decreases, as vibration frequency increases, noting that 35 Hz of WBV produces less than 30% transmissibility. However, they identify that spine transmissibility is increased during bent knee posture, where the maximum transmissibility of 80% occurred near 21 Hz (Rubin et al., 2003). Furthermore, they noted that transmissibility then decreases with increased frequency, observing that 35 Hz produced just above 50% transmissibility (Rubin 2003). These findings may offer some insight to why Figueroa et al. (2011) did not find any significant changes in brachial-ankle or carotid-femoral PWV as they prescribed 40 Hz of WBV, whilst also suggesting that WBV-induced oscillation was transmitted to the abdominal aorta in the Otsuki et al. (2008) study. Unfortunately as the present study used carotid-brachial sites for PWV measurements, this may have contributed to the lack of significance seen, as WBV transmissibility may not have affected these sites.

6.3 Local Arterial Stiffness

The findings of present study indicate no significant change in carotid arterial stiffness (β), DC, or CC. Though, a significant time effect was evident for both diastolic diameter ($p=0.040$) and systolic diameter (0.039), these significant time effects did not elicit any significance for the relative stroke change in diameter (Dist). Consequently, none of the carotid diameter measures were significantly different from baseline measurements and as a result no significance for carotid arterial stiffness, distensibility coefficient, or compliance coefficient was found.

Previous studies have reported that low-intensity resistance exercise in healthy individuals (Okamoto, Min, & Sakamaki-Sunaga, 2014) acutely increases carotid arterial compliance, systolic and diastolic diameters, and decreases β stiffness index 30 and 60 minutes post-exercise. But HR and carotid and brachial blood pressures reported no significant changes. The differences between the latter and present study may be attributed to the duration of intervention and consequently when assessments took place after intervention (acute vs. short-term), mode of exercise (bench press vs. WBV), and participants (healthy individuals compared to chronic stroke). However, as highlighted previously, acute WBV has been shown to significantly decrease arterial stiffness in healthy men (Figuerola et al., 2011; Otsuki et al., 2008), and following 3 months of WBV in middle-aged and older sedentary adults (Lai et al., 2014). Furthermore, these studies reported significant decreases in arterial stiffness from leg (femoral-ankle) PWV and brachial-ankle PWV (Figuerola et al., 2011; Lai et al., 2014; Otsuki et al., 2008), which are recognised as regional and systemic arterial stiffness indexes. Whilst two of the aforementioned studies (Figuerola et al., 2011; Otsuki et al., 2008) assessed acute WBV intervention compared to the present study of short-term intervention, these studies were examined due to the lack of research regarding the effects of short-term WBV training on arterial stiffness in chronic stroke. In the present study local carotid arterial stiffness was measured via ultrasound and the differences between the aforementioned and present study may lie in methodology. Significant changes in stiffness can occur locally without changes in systemic arterial stiffness (Figuerola et al., 2011), therefore it is difficult to compare the findings of brachial-ankle and leg PWV methods, indexes of regional and systemic arterial stiffness, to that of the present local carotid stiffness.

Other research has examined the effect of acute WBV dosage (5-30 Hz, 2.5 - 4.5 mm amplitude) in young healthy males and found that common femoral diameter measures were not affected by WBV frequency and amplitude (Lythgo et al., 2009). Likewise, no change in systolic arterial

diameter of the popliteal artery following acute WBV has also been reported (Kerschman-Schindl et al., 2001). Due to the various methodological differences it is difficult to make appropriate comparisons to establish the effect of WBV on carotid arterial stiffness, and warrants further research.

6.4 Cognition and Quality of Life

The present study found quality life measures of energy/fatigue and memory produced a significant time post-WBV. However, no other effect was found for the remaining seven health domains for quality of life (SF-36) and Addenbrooke's Cognitive Examination (ACE-III). This is supported by a recent acute WBV study that found no improvement in the functional levels of stroke patients (Silva et al., 2014). Furthermore, after 5 weeks of WBV (12 sessions) in Parkinson's patients compared to placebo group, no difference in the quality of life was found (Arias et al., 2009). However, Studenski et al. (2005) reported improved SF-36 social function, emotion, social participation, and physical function in subacute stroke survivors who took part in therapeutic exercise. Nonetheless, it has been recommended that exercise interventions are probably best tested in acute and subacute stroke and less in chronic stroke, as these populations are still in the recovery phase and large improvements would be expected (Studenski et al., 2005). This may explain why WBV of the current study had little effect on quality of life.

In the present study social functioning improved more in WBV compared to the control. This would support the idea that a consistent training programme, of 4 weeks WBV, provides participants with social support and consequently improves quality of life. A study by Gordon, Wilks, and McCaw-Binns (2013) showed that there was a trend toward increased improvement over time for the physical component of the SF-36. This improvement was seen in healthy participants that performed a walking programme (30 mins, 3x/week for 12 weeks) compared to those that engaged in light massage (25 mins, 3x/week for 12 weeks); however, there were no group differences displayed for the mental component of the SF-36.

In the current study the overall ACE-III improved in both WBV and control interventions (5.7 ± 4.0 and 5.3 ± 4.0 , respectively) indicating that WBV training is no more effective than the control. Previous research has stated that PWV predicts cognitive decline, with PWV being significantly inversely correlated with Mini-Mental State Examination (MMSE) (Hanon et al., 2005; Scuteri, Brancati, Gianni, Assisi, & Volpe, 2005; Waldstein et al., 2008). Consequently, ACE-III is a revision of MMSE, suggesting that PWV may be significantly inversely correlated with ACE-III. This indicates that individuals with increased PWV have decreased cognitive function (Hanon et al., 2005). Therefore, as stroke is associated with an increased PWV (Tuttolomondo et al., 2010), it could therefore be assumed that stroke survivors have a decreased cognitive function.

Moreover, Waldstein et al. (2008) states that aggressive treatment of risk factors that are associated with increased arterial stiffness may help preserve cognitive function with individuals increasing age. This may suggest that WBV is not an aggressive enough treatment to elicit changes in arterial stiffness and consequently produce a change in cognitive function. However, due to research mentioned previously we know this is not the case as arterial stiffness has shown to significantly decrease due to acute WBV (Figuroa et al., 2011; Otsuki et al., 2008). Additionally, research suggests WBV may augment neurotransmission in the prefrontal cortex and in other surrounding regions by sensory stimulation (Regterschot et al., 2014). However, no significant improvements in cognitive functioning were seen in the present study. Consequently, more research into the effects of WBV on cognition in chronic stroke patients is needed.

6.5 Rating of Perceived Exertion

The rating of perceived exertion (RPE) scale is a beneficial tool in offering subjective reflection of physiological responses during physical exercise, allowing individuals to regulate effort to gain maximum benefit (American College of Sports Medicine, 2015). Additionally, it is beneficial for monitoring and prescribing exercise intensity during physical exercise (American College of

Sports Medicine, 2015). Consequently, this scale indicates whether adjustments in exercise intensity are needed as to gain maximal benefit. Therefore, the RPE scale was important in the present study as to assess chronic stroke participants' feelings of effort, discomfort, strain, and/or fatigue experienced throughout the entire WBV intervention. There was no significance of RPE over the 4 weeks of WBV, with the highest RPE noted at session 8 (24 Hz and 6.5 mm). Thereafter, the RPE plateaued for the remaining 4 sessions. The participants in the present study went beyond subjectively rating their perceived exertion, and communicated that they felt the WBV sessions resulted in stroke-affected legs feeling warmed, strong and more mobile (A. Luke, personal communication, April 28, 2014; G. Mudikattu, personal communication, July 21, 2014; C. Preston, personal communication, April 14, 2014; M. Smith, personal communication, April 26, 2014; T. Westwood, personal communication, June 18, 2014). This suggests that chronic stroke survivors can tolerate WBV training and there are no adverse effects from WBV. This is supported by previous research that investigated the effects of WBV on postural control in chronic stroke patients (van Nes et al., 2004).

6.6 Limitations

This study was novel in that it is the first study to investigate the effects of short-term WBV training on arterial stiffness, QOL and cognition in chronic stroke survivors

As a result, the first limitation was the lack of a scientifically proven WBV training protocols to elicit significant reductions in arterial stiffness, or one that produces positive effects on QOL or cognition. Even with research displaying significant decreases in arterial stiffness as a result of acute or long term (3 months) WBV, methodologies differed, which makes implementation of the best protocol challenging and inconsistency when comparing results.

The study aimed to recruit 8 participants, however due to the small stroke community in Palmerston North only 6 participants were assessed. Whilst the study design (cross-over) aided this, a greater sample size would have allowed for more accurate interpretations of the findings

and consequently improved the significance. However, the findings are still useful in illustrating possible effects on this population especially due to the novelty of the study.

Finally, the washout period between the interventions may have been too short (2 weeks). Consequently, the effects from the WBV intervention may have carried over to the control intervention, which could have affected the overall results. However, the washout duration was chosen based on previous WBV research.

6.7 Future Research

In terms of the present study, as it was novel in investigating the effects of multiple WBV sessions in chronic stroke survivors' QOL, cognition, and arterial stiffness, a future study would need to repeat the present study's protocol and assessments but with a larger sample size. Moreover, to investigate the present studies aims further, future research could include longer WBV intervention (more than 12 sessions), different exercises on the vibration platform such as dynamic squats or an added fixed load. Ideally this would be with a large number of age- and sex-matched chronic stroke survivors of matched stroke subtype. However, as stated earlier, there are difficulties in recruiting stroke survivors, especially with such a varying type and effect of stroke.

Chapter 7 – Conclusion

Limited studies have investigated the effects of multiple sessions of WBV (short-term training) in stroke, with no study examining the effects of WBV on arterial stiffness, QOL or cognition. Consequently, the aim of the present study was to investigate the effect of whole-body vibration (WBV) on arterial stiffness, QOL and cognitive ability in chronic stroke survivors. The present study prescribed a gradual and progressive WBV periodised programme which increased vibration frequency (22 to 26 Hz), amplitude (2.1 to 6.5 mm), and duration (5 repetitions of 1 minute to 7 repetitions of 1 minute) in a safe manner to allow participants to accustomise and respond to an increasing vibration load, all whilst significantly: (1) reducing arterial stiffness, (2) improving QOL, and (3) cognitive ability in chronic stroke survivors. Although the same protocol has been reported to improve standing balance and walking time in multiple sclerosis patients, it did not initiate any significant positive changes to arterial stiffness, QOL and cognitive ability in the present study.

However, whilst there was no significant findings the study did identify a non-significant decrease in PWV post-WBV compared to pre-WBV ($7.0 \pm 0.5 \text{ ms}^{-1}$ vs. $6.6 \pm 0.5 \text{ ms}^{-1}$), while Control remained similar between pre and post ($6.7 \pm 0.5 \text{ ms}^{-1}$ vs. $6.5 \pm 0.4 \text{ ms}^{-1}$). Moreover, social functioning improved more in WBV compared to the control, and RPE plateaued for the final 4 sessions. This suggests that chronic stroke survivors can tolerate WBV training with no adverse effects, and a consistent training programme, of 4 weeks WBV, can provide participants with social support and consequently may improve their QOL. Therefore, proposing that positive improvements may occur as a result of WBV training, however, a larger sample size and further adjustments of the limitations stated below is necessary to further investigate the aims of this study.

References

- Abercromby, A. F. J., Amonette, W. E., Layne, C. S., McFarlin, B. K., Hinman, M. R., & Paloski, W. (2007a). Variation in neuromuscular responses during acute whole-body vibration exercise. *Medicine & Science in Sports & Exercise*, *39*(9), 1642.
- Abercromby, A. F. J., Amonette, W. E., Layne, C. S., McFarlin, B. K., Hinman, M. R., & Paloski, W. H. (2007b). Vibration exposure and biodynamic responses during whole-body vibration training. *Medicine & Science in Sports & Exercise*, *39*(10), 1794.
- Acampa, M., Guideri, F., Di Donato, I., Tassi, R., Marotta, G., Lo Giudice, G., D'Andrea, P., & Martini, G. (2014). Arterial Stiffness in patients with deep and lobar intracerebral hemorrhage. *Journal of Stroke*, *16*(3), 184-188.
- Ada, L., Dean, C. M., Hall, J. M., Bampton, J., & Crompton, S. (2003). A treadmill and overground walking program improves walking in persons residing in the community after stroke: a placebo-controlled, randomized trial. *Archives of Physical Medicine and Rehabilitation*, *84*(10), 1486-1491.
- Ada, L., Dorsch, S., & Canning, C. G. (2006). Strengthening interventions increase strength and improve activity after stroke: a systematic review. *Australian Journal of Physiotherapy*, *52*(4), 241-248.
- Adams, H. P., Bendixen, B. H., Kappelle, L. J., Biller, J., Love, B. B., Gordon, D. L., & Marsh, E. E. (1993). Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke*, *24*(1), 35-41. doi: 10.1161/01.str.24.1.35
- Adams, J. B., Edwards, D., Serviette, D., Bedient, A. M., Huntsman, E., Jacobs, K. A., Del Rossi, G., Roos, B. A., & Signorile, J. F. (2009). Optimal frequency, displacement, duration, and recovery patterns to maximize power output following acute whole-body vibration. *The Journal of Strength & Conditioning Research*, *23*(1), 237-245.
- Ahlsjö, B., Britton, M., Murray, V., & Theorell, T. (1984). Disablement and quality of life after stroke. *Stroke*, *15*(5), 886-890.
- Albansini, A., Krause, M., & Rembitzki, I. (2010). *Using whole body vibration in physical therapy and sport: clinical practice and treatment exercises*. London: Churchill Livingstone Elsevier.
- Allen, C. L., & Bayraktutan, U. (2008). Risk factors for ischaemic stroke. *International Journal of Stroke*, *3*(2), 105-116.
- Almkvist Muren, M., Hütler, M., & Hooper, J. (2008). Functional capacity and health-related quality of life in individuals post stroke. *Topics in Stroke Rehabilitation*, *15*(1), 51-58.
- Ambrose, J. A., & Barua, R. S. (2004). The pathophysiology of cigarette smoking and cardiovascular disease: an update. *Journal of the American College of Cardiology*, *43*(10), 1731-1737.
- American College of Sports Medicine. (2010). *ACSM's health-related physical fitness assessment manual*. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins Health.
- American College of Sports Medicine. (2015). *Perceived exertion*. Retrieved from <https://www.acsm.org/docs/current-comments/perceivedexertion.pdf>.

- American Heart Association. (2012a). Aphasia vs. apraxia from http://www.strokeassociation.org/STROKEORG/LifeAfterStroke/RegainingIndependence/CommunicationChallenges/Aphasia-vs-Apraxia_UCM_310079_Article.jsp
- American Heart Association. (2012b). Effects of stroke, from http://www.strokeassociation.org/STROKEORG/AboutStroke/EffectsofStroke/Effects-of-Stroke_UCM_308534_SubHomePage.jsp
- American Heart Association. (2012c). Types of stroke, from http://www.strokeassociation.org/STROKEORG/AboutStroke/TypesofStroke/Types-of-Stroke_UCM_308531_SubHomePage.jsp
- American Heart Association. (2013). Heart disease and stroke statistics- 2013 update: a report from the American Heart Association. [Review]. *Circulation*, 127(1), e6-e245. doi: 10.1161/CIR.0b013e31828124ad
- Andersen, K. K., Olsen, T. S., Dehlendorff, C., & Kammergaard, L. P. (2009). Hemorrhagic and ischemic strokes compared stroke severity, mortality, and risk factors. *Stroke*, 40(6), 2068-2072.
- Anderson, C., Laubscher, S., & Burns, R. (1996). Validation of the Short Form 36 (SF-36) health survey questionnaire among stroke patients. *Stroke*, 27(10), 1812-1816.
- Anderson, T. J. (2006). Arterial stiffness or endothelial dysfunction as a surrogate marker of vascular risk. *Canadian Journal of Cardiology*, 22, 72B-80B.
- Anderssen, S., Haaland, A., Hjermand, I., Urdal, P., Gjesdal, K., & Holme, I. (1995). Oslo diet and exercise study- a one-year randomized intervention trial-effect on hemostatic variables and other coronary risk factors. *Nutrition Metabolism and Cardiovascular Diseases*, 5(3), 189-200.
- Aprile, I., Piazzini, D., Bertolini, C., Caliandro, P., Pazzaglia, C., Tonali, P., & Padua, L. (2006). Predictive variables on disability and quality of life in stroke outpatients undergoing rehabilitation. *Neurological Sciences*, 27(1), 40-46.
- Arias, P., Chouza, M., Vivas, J., & Cudeiro, J. (2009). Effect of whole body vibration in Parkinson's disease: a controlled study. *Movement Disorders*, 24(6), 891-898.
- Arrick, D. M., Sharpe, G. M., Sun, H., & Mayhan, W. G. (2007). nNOS-dependent reactivity of cerebral arterioles in type 1 diabetes. *Brain Research*, 1184, 365-371.
- Arzt, M., Young, T., Finn, L., Skatrud, J. B., & Bradley, T. D. (2005). Association of sleep-disordered breathing and the occurrence of stroke. *American Journal of Respiratory and Critical Care Medicine*, 172(11), 1447-1451.
- Assmann, G., Cullen, P., Evers, T., Petzinna, D., & Schulte, H. (2005). Importance of arterial pulse pressure as a predictor of coronary heart disease risk in PROCAM. *European Heart Journal*, 26(20), 2120-2126.
- Aström, M., Asplund, K., & Aström, T. (1992). Psychosocial function and life satisfaction after stroke. *Stroke*, 23(4), 527-531.
- Avolio, A., Chen, S.-G., Wang, R.-P., Zhang, C.-L., Li, M.-F., & O'Rourke, M. (1983). Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community. *Circulation*, 68(1), 50-58.
- Ballard, C., Rowan, E., Stephens, S., Kalaria, R., & Kenny, R. A. (2003). Prospective follow-up study between 3 and 15 months after stroke improvements and decline in cognitive function among dementia-free stroke survivors > 75 years of age. *Stroke*, 34(10), 2440-2444.

- Bamford, J., Sandercock, P., Dennis, M., Warlow, C., & Burn, J. (1991). Classification and natural history of clinically identifiable subtypes of cerebral infarction. *The Lancet*, 337(8756), 1521-1526.
- Bank, A. J., & Kaiser, D. R. (1998). Smooth muscle relaxation effects on arterial compliance, distensibility, elastic modulus, and pulse wave velocity. *Hypertension*, 32(2), 356-359.
- Banks, J. L., & Marotta, C. A. (2007). Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials a literature review and synthesis. *Stroke*, 38(3), 1091-1096.
- Barber, M., Fail, M., Shields, M., Stott, D. J., & Langhorne, P. (2003). Validity and reliability of estimating the scandinavian stroke scale score from medical records. *Cerebrovascular Diseases (Basel, Switzerland)*, 17(2-3), 224-227.
- Barenbrock, M., Kosch, M., Jöster, E., Kisters, K., Rahn, K.-H., & Hausberg, M. (2002). Reduced arterial distensibility is a predictor of cardiovascular disease in patients after renal transplantation. *Journal of Hypertension*, 20(1), 79-84.
- Barker-Collo, S., & Feigin, V. (2006). The impact of neuropsychological deficits on functional stroke outcomes. *Neuropsychology Review*, 16(2), 53-64.
- Barker-Collo, S., Feigin, V., Parag, V., Lawes, C., & Senior, H. (2010). Auckland Stroke Outcomes Study Part 2: cognition and functional outcomes 5 years poststroke. *Neurology*, 75(18), 1608-1616.
- Bassiouny, H. S., Zarins, C. K., Kadowaki, M. H., & Glagov, S. (1994). Hemodynamic stress and experimental aortoiliac atherosclerosis. *Journal of Vascular Surgery*, 19(3), 426-434.
- Bateman, A., Culpan, F. J., Pickering, A. D., Powell, J. H., Scott, O. M., & Greenwood, R. J. (2001). The effect of aerobic training on rehabilitation outcomes after recent severe brain injury: a randomized controlled evaluation. *Archives of Physical Medicine and Rehabilitation*, 82(2), 174-182.
- Baumbach, G. L., & Heistad, D. D. (1988). Cerebral circulation in chronic arterial hypertension. *Hypertension*, 12(2), 89-95.
- Baumbach, G. L., & Heistad, D. D. (1989). Remodeling of cerebral arterioles in chronic hypertension. *Hypertension*, 13(6), 968-972.
- Baumbach, G. L., & Heistad, D. D. (1991). Adaptive changes in cerebral blood vessels during chronic hypertension. *Journal of Hypertension*, 9(11), 987-991.
- Bazett-Jones, D. M., Finch, H. W., & Dugan, E. L. (2008). Comparing the effects of various whole-body vibration accelerations on counter-movement jump performance. *Journal of Sports Science & Medicine*, 7(1), 144.
- Bean, J. F., Vora, A., & Frontera, W. R. (2004). Benefits of exercise for community-dwelling older adults. *Archives of Physical Medicine and Rehabilitation*, 85(0), 31-42. doi: <http://dx.doi.org/10.1016/j.apmr.2004.03.010>
- Beattie, D., Xu, C., Vito, R., Glagov, S., & Whang, M. (1998). Mechanical analysis of heterogeneous, atherosclerotic human aorta. *Journal of Biomechanical Engineering*, 120(5), 602-607.
- Beilin, L., Puddey, I., & Burke, V. (1999). Lifestyle and hypertension. *American Journal of Hypertension*, 12(9), 934-945.
- Benetos, A., Laurent, S., Hoeks, A., Boutouyrie, P., & Safar, M. (1993). Arterial alterations with aging and high blood pressure. A noninvasive study of carotid and femoral arteries. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 13(1), 90-97.

- Benetos, A., Rudnichi, A., Thomas, F., Safar, M., & Guize, L. (1999). Influence of heart rate on mortality in a French population role of age, gender, and blood pressure. *Hypertension*, *33*(1), 44-52.
- Benetos, A., Topouchian, J., Ricard, S., Gautier, S., Bonnardeaux, A., Asmar, R., Poirier, O., Soubrier, F., Safar, M., & Cambien, F. (1995). Influence of angiotensin II type 1 receptor polymorphism on aortic stiffness in never-treated hypertensive patients. *Hypertension*, *26*(1), 44-47.
- Blacher, J., Pannier, B., Guerin, A. P., Marchais, S. J., Safar, M. E., & London, G. M. (1998). Carotid arterial stiffness as a predictor of cardiovascular and all-cause mortality in end-stage renal disease. *Hypertension*, *32*(3), 570-574.
- Blacher, J., Staessen, J. A., Girerd, X., Gasowski, J., Thijs, L., Liu, L., Wang, J. G., Fagard, R. H., & Safar, M. E. (2000). Pulse pressure not mean pressure determines cardiovascular risk in older hypertensive patients. *Archives of Internal Medicine*, *160*(8), 1085-1089.
- Blake, H., McKinney, M., Treece, K., Lee, E., & Lincoln, N. B. (2002). An evaluation of screening measures for cognitive impairment after stroke. *Age and Ageing*, *31*(6), 451-456.
- Bloch, R. (1988). Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*, *19*(11), 1448-1448.
- Bogousslavsky, J. (Ed.). (2002). *Long term effects of stroke*. New York, NY: Marcel Dekker.
- Bohannon, R. W. (2007). Muscle strength and muscle training after stroke. *Journal of Rehabilitation Medicine*, *39*(1), 14-20.
- Boman, K., Hellsten, G., Bruce, Å., Hallmans, G., & Nilsson, T. K. (1994). Endurance physical activity, diet and fibrinolysis. *Atherosclerosis*, *106*(1), 65-74.
- Bonita, R., & Beaglehole, R. (1988). Recovery of motor function after stroke. *Stroke*, *19*(12), 1497-1500.
- Bonita, R., Duncan, J., Truelsen, T., Jackson, R. T., & Beaglehole, R. (1999). Passive smoking as well as active smoking increases the risk of acute stroke. *Tobacco Control*, *8*(2), 156-160.
- Boreham, C. A., Ferreira, I., Twisk, J. W., Gallagher, A. M., Savage, M. J., & Murray, L. J. (2004). Cardiorespiratory fitness, physical activity, and arterial stiffness: the Northern Ireland Young Hearts Project. *Hypertension*, *44*(5), 721-726.
- Bosco, C., Cardinale, M., & Tsarpela, O. (1999a). Influence of vibration on mechanical power and electromyogram activity in human arm flexor muscles. *European Journal of Applied Physiology and Occupational Physiology*, *79*(4), 306-311.
- Bosco, C., Cardinale, M., Tsarpela, O., Colli, R., Tihanyi, J., von Duvillard, S. P., & Viru, A. (1998). The influence of whole body vibration on jumping performance. *Biology of Sport*, *15*(3), 157-164.
- Bosco, C., Colli, R., Intorini, E., Cardinale, M., Tsarpela, O., Madella, A., Tihanyi, J., & Viru, A. (1999b). Adaptive responses of human skeletal muscle to vibration exposure. *Clinical Physiology*, *19*, 183-187.
- Bosco, C., Iacovelli, M., Tsarpela, O., Cardinale, M., Bonifazi, M., Tihanyi, J., Viru, M., De Lorenzo, A., & Viru, A. (2000). Hormonal responses to whole-body vibration in men. *European Journal of Applied Physiology*, *81*(6), 449-454.
- Boutouyrie, P., Bussy, C., Lacolley, P., Girerd, X., Laloux, B., & Laurent, S. (1999). Association between local pulse pressure, mean blood pressure, and large-artery remodeling. *Circulation*, *100*(13), 1387-1393.

- Boutouyrie, P., Laurent, S., Benetos, A., Girerd, X. J., Hoeks, A. P., & Safar, M. E. (1992). Opposing effects of ageing on distal and proximal large arteries in hypertensives. *Journal of Hypertension, 10*, S87-S92.
- Braak, H., Braak, E., Yilmazer, D., & Bohl, J. (1996). Topical review: functional anatomy of human hippocampal formation and related structures. *Journal of Child Neurology, 11*(4), 265-275.
- Broderick, J. P., Lu, M., Kothari, R., Levine, S. R., Lyden, P. D., Haley, E. C., Brott, T. G., Grotta, J., Tilley, B. C., & Marler, J. R. (2000). Finding the most powerful measures of the effectiveness of tissue plasminogen activator in the NINDS tPA stroke trial. *Stroke, 31*(10), 2335-2341.
- Bronner, L. L., Kanter, D. S., & Manson, J. E. (1995). Primary prevention of stroke. *New England Journal of Medicine, 333*(21), 1392-1400.
- Brott, T., Adams, H., Olinger, C. P., Marler, J. R., Barsan, W. G., Biller, J., Spilker, J., Holleran, R., Eberle, R., & Hertzberg, V. (1989). Measurements of acute cerebral infarction: a clinical examination scale. *Stroke, 20*(7), 864-870.
- Brown, R., Whisnant, J. P., Sicks, J., O'Fallon, W. M., & Wiebers, D. O. (1996). Stroke incidence, prevalence, and survival: secular trends in Rochester, Minnesota, through 1989. *Stroke, 27*(3), 373-380.
- Bruyere, O., Wuidart, M.-A., Di Palma, E., Gourlay, M., Ethgen, O., Richy, F., & Reginster, J.-Y. (2005). Controlled whole body vibration to decrease fall risk and improve health-related quality of life of nursing home residents. *Archives of Physical Medicine and Rehabilitation, 86*(2), 303-307.
- Burn, J. (1992). Reliability of the modified Rankin Scale. *Stroke, 23*(3), 438-438.
- Calvert, R. N. (2002). *The history of massage: an illustrated survey from around the world*. Rochester, VT: Healing Arts Press.
- Cameron, J. D., & Dart, A. M. (1994). Exercise training increases total systemic arterial compliance in humans. *American Journal of Physiology Heart and Circulatory Physiology, 266*(2), H693-H701.
- Campbell, A., Converse, P. E., & Rodgers, W. L. (1976). *The quality of American life: perceptions, evaluations, and satisfactions*. New York, NY: Russell Sage Foundation.
- Cardinale, M., & Bosco, C. (2003). The use of vibration as an exercise intervention. *Exercise and Sport Sciences Reviews, 31*(1), 3-7.
- Cardinale, M., Leiper, J., Erskine, J., Milroy, M., & Bell, S. (2006). The acute effects of different whole body vibration amplitudes on the endocrine system of young healthy men: a preliminary study. *Clinical Physiology and Functional Imaging, 26*(6), 380-384.
- Cardinale, M., & Lim, J. (2003). Electromyography activity of vastus lateralis muscle during whole-body vibrations of different frequencies. *The Journal of Strength & Conditioning Research, 17*(3), 621-624.
- Cardinale, M., & Wakeling, J. (2005). Whole body vibration exercise: are vibrations good for you? *British Journal of Sports Medicine, 39*(9), 585-589. doi: 10.1136/bjism.2005.016857
- Cavanagh, S. J., & Gordon, V. L. (2002). Grading scales used in the management of aneurysmal subarachnoid hemorrhage: a critical review. *Journal of Neuroscience Nursing, 34*(6), 288-295.
- Cecelja, M., & Chowienzyk, P. (2012). Role of arterial stiffness in cardiovascular disease. *JRSM Cardiovascular Disease, 1*(4), 11.

- Cecelja, M., Jiang, B., Bevan, L., Frost, M. L., Spector, T. D., & Chowienczyk, P. J. (2011). Arterial stiffening relates to arterial calcification but not to noncalcified atheroma in women: a twin study. *Journal of the American College of Cardiology*, *57*(13), 1480-1486.
- Chae, C. U., Lee, R. T., Rifai, N., & Ridker, P. M. (2001). Blood pressure and inflammation in apparently healthy men. *Hypertension*, *38*(3), 399-403. doi: 10.1161/01.hyp.38.3.399
- Chan, K. S., Liu, C. W., Chen, T. W., Weng, M. C., Huang, M. H., & Chen, C. H. (2012). Effects of a single session of whole body vibration on ankle plantarflexion spasticity and gait performance in patients with chronic stroke: a randomized controlled trial. *Clinical Rehabilitation*, *26*(12), 1087-1095.
- Chapman, J. H., & Elliott, P. (1988). Cardiovascular effects of static and dynamic exercise. *European Journal of Applied Physiology and Occupational Physiology*, *58*(1-2), 152-157.
- Charakida, M., Tousoulis, D., Skoumas, I., Pitsavos, C., Vasiliadou, C., Stefanadi, E., Antoniadou, C., Latsios, G., Siasos, G., & Stefanadis, C. (2009). Inflammatory and thrombotic processes are associated with vascular dysfunction in children with familial hypercholesterolemia. *Atherosclerosis*, *204*(2), 532-537.
- Chen, M., & Rimmer, J. H. (2011). Effects of exercise on quality of life in stroke survivors: a meta-analysis. *Stroke*, *42*(3), 832-837.
- Chirinos, J. A., Zambrano, J. P., Chakko, S., Veerani, A., Schob, A., Willens, H. J., Perez, G., & Mendez, A. J. (2005). Aortic pressure augmentation predicts adverse cardiovascular events in patients with established coronary artery disease. *Hypertension*, *45*(5), 980-985.
- Chiu, Y. C., Arand, P. W., Shroff, S. G., Feldman, T., & Carroll, J. D. (1991). Determination of pulse wave velocities with computerized algorithms. *American Heart Journal*, *121*(5), 1460-1470.
- Chobanian, A. V. (1983). The influence of hypertension and other hemodynamic factors in atherogenesis. *Progress in Cardiovascular Diseases*, *26*(3), 177-196.
- Choi-Kwon, S., Choi, J. M., Kwon, S. U., Kang, D.-W., & Kim, J. S. (2006). Factors that affect the quality of life at 3 years post-stroke. *Journal of Clinical Neurology*, *2*(1), 34-41.
- Cholesterol Treatment Trialists. (2005). Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins. *The Lancet*, *366*(9493), 1267-1278.
- Chu, K. S., Eng, J. J., Dawson, A. S., Harris, J. E., Ozkaplan, A., & Gylfadóttir, S. (2004). Water-based exercise for cardiovascular fitness in people with chronic stroke: a randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*, *85*(6), 870-874.
- Claesson, L., Lindén, T., Skoog, I., & Blomstrand, C. (2004). Cognitive impairment after stroke-impact on activities of daily living and costs of care for elderly people. The Goteborg 70+ Stroke Study. *Cerebrovascular Diseases (Basel, Switzerland)*, *19*(2), 102-109.
- Cleaver, O., & Melton, D. A. (2003). Endothelial signaling during development. *Nature Medicine*, *9*(6), 661-668.
- Cochrane, D. J. (2010). *The effect of vibration exercise on aspects of muscle physiology and muscular performance*. Doctoral dissertation, Massey University, Palmerston North, New Zealand. Retrieved from <http://mro.massey.ac.nz/handle/10179/1831>
- Cochrane, D. J., & Hawke, E. J. (2007). Effects of acute upper-body vibration on strength and power variables in climbers. *The Journal of Strength & Conditioning Research*, *21*(2), 527-531.

- Cochrane, D. J., & Stannard, S. R. (2005). Acute whole body vibration training increases vertical jump and flexibility performance in elite female field hockey players. *British Journal of Sports Medicine*, *39*(11), 860-865. doi: 10.1136/bjism.2005.019950
- Cockcroft, J. R., Wilkinson, I. B., Evans, M., McEwan, P., Peters, J. R., Davies, S., Scanlon, M. F., & Currie, C. J. (2005). Pulse pressure predicts cardiovascular risk in patients with type 2 diabetes mellitus. *American Journal of Hypertension*, *18*(11), 1463-1467.
- Cohn, J. N., Quyyumi, A. A., Hollenberg, N. K., & Jamerson, K. A. (2004). Surrogate markers for cardiovascular disease functional markers. *Circulation*, *109*(25), 31-46.
- Collin, C., Wade, D., Davies, S., & Horne, V. (1988). The Barthel ADL Index: a reliability study. *Disability and Rehabilitation*, *10*(2), 61-63.
- Collins, R., Peto, R., MacMahon, S., Godwin, J., Qizilbash, N., Hebert, P., Eberlein, K., Taylor, J., Hennekens, C., & Fiebach, N. (1990). Blood pressure, stroke, and coronary heart disease: part 2, short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *The Lancet*, *335*(8693), 827-838.
- Compton, F., Wittrock, M., Schaefer, J.-H., Zidek, W., Tepel, M., & Scholze, A. (2008). Noninvasive cardiac output determination using applanation tonometry-derived radial artery pulse contour analysis in critically ill patients. *Anesthesia & Analgesia*, *106*(1), 171-174.
- Cormie, P., Deane, R. S., Triplett, N. T., & McBride, J. M. (2006). Acute effects of whole-body vibration on muscle activity, strength, and power. *The Journal of Strength & Conditioning Research*, *20*(2), 257-261.
- Cote, R., Battista, R., Wolfson, C., Boucher, J., Adam, J., & Hachinski, V. (1989). The Canadian neurological scale validation and reliability assessment. *Neurology*, *39*(5), 638-638.
- Cote, R., Hachinski, V., Shurvell, B., Norris, J., & Wolfson, C. (1986). The Canadian Neurological Scale: a preliminary study in acute stroke. *Stroke*, *17*(4), 731-737.
- Coulshed, N., Epstein, E., McKendrick, C., Galloway, R., & Walker, E. (1970). Systemic embolism in mitral valve disease. *British Heart Journal*, *32*(1), 26.
- Cramp, M. C., Greenwood, R. J., Gill, M., Rothwell, J. C., & Scott, O. M. (2006). Low intensity strength training for ambulatory stroke patients. *Disability and Rehabilitation*, *28*(13-14), 883-889.
- Crewther, B., Cronin, J., & Keogh, J. (2004). Gravitational forces and whole body vibration: implications for prescription of vibratory stimulation. *Physical Therapy in Sport*, *5*(1), 37-43.
- Cronin, J. B., Oliver, M., & McNair, P. J. (2004). Muscle stiffness and injury effects of whole body vibration. *Physical Therapy in Sport*, *5*(2), 68-74.
- Curb, J. D., Abbott, R. D., Rodriguez, B. L., Masaki, K. H., Chen, R., Popper, J. S., Petrovitch, H., Ross, G. W., Schatz, I. J., & Belleau, G. C. (2004). High density lipoprotein cholesterol and the risk of stroke in elderly men: the Honolulu Heart Program. *American Journal of Epidemiology*, *160*(2), 150-157.
- Custodis, F., Schirmer, S. H., Baumhäkel, M., Heusch, G., Böhm, M., & Laufs, U. (2010). Vascular pathophysiology in response to increased heart rate. *Journal of the American College of Cardiology*, *56*(24), 1973-1983.
- D'Olhaberriague, L., Litvan, I., Mitsias, P., & Mansbach, H. H. (1996). A reappraisal of reliability and validity studies in stroke. *Stroke*, *27*(12), 2331-2336.

- da Cunha Filho, I. T., Lim, P. A. C., Qureshy, H., Henson, H., Monga, T., & Protas, E. J. (2001). A comparison of regular rehabilitation and regular rehabilitation with supported treadmill ambulation training for acute stroke patients. *Journal of Rehabilitation Research and Development*, *38*(2), 245-256.
- da Cunha, I. N., Lim, P. A., Qureshy, H., Henson, H., Monga, T., & Protas, E. J. (2002). Gait outcomes after acute stroke rehabilitation with supported treadmill ambulation training: a randomized controlled pilot study. *Archives of Physical Medicine and Rehabilitation*, *83*(9), 1258-1265.
- Da Silva, M. E., Nunez, V. M., Vaamonde, D., Fernandez, J. M., Poblador, M. S., Garcia-Manso, J. M., & Lancho, J. L. (2006). Effects of different frequencies of whole body vibration on muscular performance. *Biology of Sport*, *23*(3), 267.
- Daniels, S. R. (2012). Obesity, vascular changes, and elevated blood pressure. *Journal of the American College of Cardiology*, *60*(25), 2651-2652.
- Darlington, A., Dippel, D., Ribbers, G., van Balen, R., Passchier, J., & van Busschbach, J. (2007). Coping strategies as determinants of quality of life in stroke patients: a longitudinal study. *Cerebrovascular Diseases*, *23*(5-6), 401-407.
- Dart, A. M., & Kingwell, B. A. (2001). Pulse pressure—a review of mechanisms and clinical relevance. *Journal of the American College of Cardiology*, *37*(4), 975-984.
- Dauchet, L., Amouyel, P., Hercberg, S., & Dallongeville, J. (2006). Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies. *The Journal of Nutrition*, *136*(10), 2588-2593.
- Davies, R. R., & Larner, A. J. (Eds.). (2012). *Addenbrooke's Cognitive Examination (ACE) and its Revision (ACE-R)*. London: Springer-Verlag.
- Davies, T., Frenneaux, M., Campbell, R., & White, M. (2007). Human arterial responses to isometric exercise: the role of the muscle metaboreflex. *Clinical Science*, *112*, 441-447.
- Davignon, J., & Ganz, P. (2004). Role of endothelial dysfunction in atherosclerosis. *Circulation*, *109*(23), 27-32.
- de Haan, R., Horn, J., Limburg, M., Van Der Meulen, J., & Bossuyt, P. (1993a). A comparison of five stroke scales with measures of disability, handicap, and quality of life. *Stroke*, *24*(8), 1178-1181.
- de Haan, R., Limburg, M., Schuling, J., Broeshart, J., Jonkers, L., & Van Zuylen, P. (1993b). Clinimetric evaluation of the Barthel Index, a measure of limitations in daily activities. *Nederlands Tijdschrift Voor Geneeskunde*, *137*(18), 917-921.
- de Lorimier, A. A. (2000). Alcohol, wine, and health. *The American Journal of Surgery*, *180*(5), 357-361.
- de Ruiter, C., Van Der Linden, R., Van der Zijden, M., Hollander, A., & De Haan, A. (2003). Short-term effects of whole-body vibration on maximal voluntary isometric knee extensor force and rate of force rise. *European Journal of Applied Physiology*, *88*(4-5), 472-475.
- De Silva, D., Woon, F., Chen, C., Chang, H., Kingwell, B., Cameron, J., & Wong, M. (2008). Profile and associations of central pulse wave velocity and central pulse pressure among ischemic stroke patients. *European Journal of Neurology*, *15*(2), 196-198.
- de Simone, G., Roman, M. J., Koren, M. J., Mensah, G. A., Ganau, A., & Devereux, R. B. (1999). Stroke volume/pulse pressure ratio and cardiovascular risk in arterial hypertension. *Hypertension*, *33*(3), 800-805.

- Delecluse, C., Roelants, M., & Verschueren, S. (2003). Strength increase after whole-body vibration compared with resistance training. *Medicine & Science in Sports & Exercise*, 35(6), 1033-1041. doi: 10.1249/01.MSS.0000069752.96438.B0
- Dennis, M. S., Burn, J., Sandercock, P., Bamford, J. M., Wade, D. T., & Warlow, C. P. (1993). Long-term survival after first-ever stroke: the Oxfordshire Community Stroke Project. *Stroke*, 24(6), 796-800.
- Dereix, L., Nighoghossian, N., Hermier, M., Adeleine, P., Berthezène, Y., Philippeau, F., Honnorat, J., Froment, J.-C., & Trouillas, P. (2004). Influence of pretreatment MRI parameters on clinical outcome, recanalization and infarct size in 49 stroke patients treated by intravenous tissue plasminogen activator. *Journal of the Neurological Sciences*, 225(1), 3-9.
- Desmond, D. W., Moroney, J. T., Sano, M., & Stern, Y. (1996). Recovery of cognitive function after stroke. *Stroke*, 27(10), 1798-1803.
- Dhamoon, M. S., Moon, Y. P., Paik, M. C., Boden-Albala, B., Rundek, T., Sacco, R. L., & Elkind, M. S. (2009). Long-term functional recovery after first ischemic stroke: the Northern Manhattan Study. *Stroke*, 40(8), 2805-2811.
- Di Gimniani, R., Tihanyi, J., Safar, S., & Scrimaglio, R. (2009). The effects of vibration on explosive and reactive strength when applying individualized vibration frequencies. *Journal of Sports Sciences*, 27(2), 169-177. doi: 10.1080/02640410802495344
- Di Iorio, B. R., Cucciniello, E., Alinei, P., & Torraca, S. (2010). Reproducibility of regional pulse - wave velocity in uremic subjects. *Hemodialysis International*, 14(4), 441-446.
- Di Napoli, M., Schwaninger, M., Cappelli, R., Ceccarelli, E., Di Gianfilippo, G., Donati, C., Emsley, H. C., Forconi, S., Hopkins, S. J., & Masotti, L. (2005). Evaluation of C-reactive protein measurement for assessing the risk and prognosis in ischemic stroke: a statement for health care professionals from the CRP Pooling Project Members. *Stroke*, 36(6), 1316-1329.
- Di Tullio, M., Sacco, R. L., Gopal, A., Mohr, J., & Homma, S. (1992). Patent foramen ovale as a risk factor for cryptogenic stroke. *Annals of Internal Medicine*, 117(6), 461-465.
- Diaz, A., Bourassa, M. G., Guertin, M.-C., & Tardif, J.-C. (2005). Long-term prognostic value of resting heart rate in patients with suspected or proven coronary artery disease. *European Heart Journal*, 26(10), 967-974.
- Dlin, R. A., Hanne, N., Silverberg, D. S., & Bar-Or, O. (1983). Follow-up of normotensive men with exaggerated blood pressure response to exercise. *American Heart Journal*, 106(2), 316-320.
- Do Lee, C., Folsom, A. R., & Blair, S. N. (2003). Physical activity and stroke risk: a meta-analysis. *Stroke*, 34(10), 2475-2481.
- Domanski, M. J., Davis, B. R., Pfeffer, M. A., Kastantin, M., & Mitchell, G. F. (1999). Isolated systolic hypertension prognostic information provided by pulse pressure. *Journal of Hypertension*, 34(3), 375-380.
- Donnan, G., Adena, M., O'Malley, H., Mcneil, J., Doyle, A., & Neill, G. (1989). Smoking as a risk factor for cerebral ischaemia. *The Lancet*, 334(8664), 643-647.
- Donnan, G. A., Fisher, M., Macleod, M., & Davis, S. M. (2008). Stroke. *The Lancet*, 371(9624), 1612-1623. doi: 10.1016/s0140-6736(08)60694-7
- Douiri, A., McKeivitt, C., Emmett, E. S., Rudd, A. G., & Wolfe, C. D. (2013). Long-term effects of secondary prevention on cognitive function in stroke patients. *Circulation*, CIRCULATIONAHA. 113.002236.

- Douiri, A., Rudd, A. G., & Wolfe, C. D. (2013). Prevalence of poststroke cognitive impairment South London stroke register 1995–2010. *Stroke*, *44*(1), 138-145.
- Doyle, P. J. (2002). Measuring health outcomes in stroke survivors. *Archives of Physical Medicine and Rehabilitation*, *83*, S39-S43.
- Duncan, P., Richards, L., Wallace, D., Stoker-Yates, J., Pohl, P., Luchies, C., Ogle, A., & Studenski, S. (1998). A randomized, controlled pilot study of a home-based exercise program for individuals with mild and moderate stroke. *Stroke*, *29*(10), 2055-2060.
- Duncan, P., Studenski, S., Richards, L., Gollub, S., Lai, S. M., Reker, D., Perera, S., Yates, J., Koch, V., & Rigler, S. (2003). Randomized clinical trial of therapeutic exercise in subacute stroke. *Stroke*, *34*(9), 2173-2180.
- Durstine, J. L., Moore, G. E., Painter, P. L., & Roberts, S. O. (Eds.). (2009). *ACSM's exercise management for persons with chronic disabilities* (3rd ed.): Human Kinetics.
- Dykes, R. W. (1983). Parallel processing of somatosensory information: a theory. *Brain Research Reviews*, *6*(1), 47-115.
- Elkayam, U., Khan, S., Mehboob, A., & Ahsan, N. (2002). Impaired endothelium-mediated vasodilation in heart failure: clinical evidence and the potential for therapy. *Journal of Cardiac Failure*, *8*(1), 15-20.
- Eng, J. J., Chu, K. S., Kim, C. M., Dawson, A. S., Carswell, A., & Hepburn, K. E. (2003). A community-based group exercise program for persons with chronic stroke. *Medicine & Science in Sports & Exercise*, *35*(8), 1271.
- Ernst, E. (1993). Regular exercise reduces fibrinogen levels: a review of longitudinal studies. *British Journal of Sports Medicine*, *27*(3), 175-176.
- Ezzati, M., Lopez, A. D., Rodgers, A., Vander Hoorn, S., & Murray, C. J. (2002). Selected major risk factors and global and regional burden of disease. *The Lancet*, *360*(9343), 1347-1360.
- Ezzati, M., Vander Hoorn, S., Rodgers, A., Lopez, A. D., Mathers, C. D., & Murray, C. J. (2003). Estimates of global and regional potential health gains from reducing multiple major risk factors. *The Lancet*, *362*(9380), 271-280.
- Fagard, R. (2006). Exercise is good for your blood pressure: effects of endurance training and resistance training. *Clinical and Experimental Pharmacology and Physiology*, *33*(9), 853-856.
- Falzone, R., & Brown, M. J. (2004). Determinants of arterial stiffness in offspring of families with essential hypertension. *American Journal of Hypertension*, *17*(4), 292-298.
- Fang, J., Madhavan, S., Cohen, H., & Alderman, M. H. (1995). Measures of blood pressure and myocardial infarction in treated hypertensive patients. *Journal of Hypertension*, *13*(4), 413-420.
- Faulkner, J., McGonigal, G., Woolley, B., Stoner, L., Wong, L., & Lambrick, D. (2013). The effect of a short-term exercise programme on haemodynamic adaptability; a randomised controlled trial with newly diagnosed transient ischaemic attack patients. *Journal of Human Hypertension*, *27*(12), 736-743.
- Feigin, V., Carter, K., Hackett, M., Barber, P. A., McNaughton, H., Dyal, L., Chen, M.-h., Anderson, C., & Auckland Regional Community Stroke Study Group. (2006). Ethnic disparities in incidence of stroke subtypes: Auckland Regional Community Stroke Study, 2002–2003. *The Lancet Neurology*, *5*(2), 130-139.

- Feigin, V. L., Barker-Collo, S., Parag, V., Senior, H., Lawes, C. M., Ratnasabapathy, Y., & Glen, E. (2010). Auckland Stroke Outcomes Study Part 1: gender, stroke types, ethnicity, and functional outcomes 5 years poststroke. *Neurology*, *75*(18), 1597-1607.
- Feigin, V. L., Rinkel, G. J., Lawes, C. M., Algra, A., Bennett, D. A., van Gijn, J., & Anderson, C. S. (2005). Risk factors for subarachnoid hemorrhage an updated systematic review of epidemiological studies. *Stroke*, *36*(12), 2773-2780.
- Figuroa, A., Gil, R., Wong, A., Hooshmand, S., Park, S. Y., Vicil, F., & Sanchez-Gonzalez, M. A. (2012). Whole-body vibration training reduces arterial stiffness, blood pressure and sympathovagal balance in young overweight/obese women. *Hypertension Research*, *35*(6), 667-672.
- Figuroa, A., Kalfon, R., Madzima, T. A., & Wong, A. (2014). Whole-body vibration exercise training reduces arterial stiffness in postmenopausal women with prehypertension and hypertension. *Menopause*, *21*(2), 131-136.
- Figuroa, A., Vicil, F., & Sanchez-Gonzalez, M. A. (2011). Acute exercise with whole-body vibration decreases wave reflection and leg arterial stiffness. *American Journal of Cardiovascular Disease*, *1*(1), 60.
- Fitzpatric, R., Davey, C., Buxton, M. J., & Jones, D. R. (1998). Evaluating patient based outcome measures for use in clinical trials. *Health Technology Assessment*, *2*, 1-74.
- Flansbjerg, U.-B., Miller, M., Downham, D., & Lexell, J. (2008). Progressive resistance training after stroke: effects on muscle strength, muscle tone, gait performance and perceived participation. *Journal of Rehabilitation Medicine*, *40*(1), 42-48.
- Frangos, J. A., Eskin, S. G., McIntire, L. V., & Ives, C. (1985). Flow effects on prostacyclin production by cultured human endothelial cells. *Science*, *227*(4693), 1477-1479.
- Franklin, S. S., Khan, S. A., Wong, N. D., Larson, M. G., & Levy, D. (1999). Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham Heart Study. *Circulation*, *100*(4), 354-360.
- Franklin, S. S., Sutton-Tyrrell, K., Belle, S. H., Weber, M. A., & Kuller, L. H. (1997). The importance of pulsatile components of hypertension in predicting carotid stenosis in older adults. *Journal of Hypertension*, *15*(10), 1143-1150.
- Fujime, M., Tomimatsu, T., Okaue, Y., Koyama, S., Kanagawa, T., Taniguchi, T., & Kimura, T. (2012). Central aortic blood pressure and augmentation index during normal pregnancy. *Hypertension Research*, *35*(6), 633-638.
- Furie, K. L., Kasner, S. E., Adams, R. J., Albers, G. W., Bush, R. L., Fagan, S. C., Halperin, J. L., Johnston, S. C., Katzan, I., & Kernan, W. N. (2011). Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, *42*(1), 227-276.
- Furness, T. (2007). *Effects of whole body vibration on neuromuscular performance of community dwelling older adults furness*. Masters dissertation, Australian Catholic University, Victoria, Australia. Retrieved from <http://dlibrary.acu.edu.au/digitaltheses/public/adt-acuvp153.29052008/02whole.pdf>
- Gaber, T. A.-Z. (2008). Evaluation of the Addenbrooke's Cognitive Examination's validity in a brain injury rehabilitation setting. *Brain Injury*, *22*(7-8), 589-593.

- Gadidi, V., Katz-Leurer, M., Carmeli, E., & Bornstein, N. M. (2011). Long-term outcome poststroke: predictors of activity limitation and participation restriction. *Archives of Physical Medicine and Rehabilitation, 92*(11), 1802-1808.
- Gandevia, S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews, 81*(4), 1725-1789.
- Gao, Y. (2010). The multiple actions of NO. *Pflügers Archiv- European Journal of Physiology, 459*(6), 829-839.
- García-Palmieri, M. R., Crespo, C. J., Mc Gee, D., Sempos, C., Smit, E., & Sorlie, P. D. (2005). Wide pulse pressure is an independent predictor of cardiovascular mortality in Puerto Rican men. *Nutrition, Metabolism & Cardiovascular Diseases, 15*(1), 71-78.
- Ge, D., Young, T. W., Wang, X., Kapuku, G. K., Treiber, F. A., & Snieder, H. (2007). Heritability of arterial stiffness in black and white American youth and young adults. *American Journal of Hypertension, 20*(10), 1065-1072.
- Ghiadoni, L., Taddei, S., & Viridis, A. (2012). Hypertension and endothelial dysfunction: therapeutic approach. *Current Vascular Pharmacology, 10*(1), 42-60.
- Gibbons, G. H., & Dzau, V. J. (1994). The emerging concept of vascular remodeling. *New England Journal of Medicine, 330*(20), 1431-1438.
- Gil, R. (2011). *The effects of whole-body vibration on cardiovascular and autonomic function in overweight-obese premenopausal women*. Masters thesis, Florida State University, Florida, United States of America. Retrieved from <http://diginole.lib.fsu.edu/etd/4303/>
- Glasser, S. P., Arnett, D. K., McVeigh, G. E., Finkelstein, S. M., Bank, A. J., Morgan, D. J., & Cohn, J. N. (1997). Vascular compliance and cardiovascular disease: a risk factor or a marker? *American Journal of Hypertension, 10*(10), 1175-1189.
- Goldstein, L. B., Bushnell, C. D., Adams, R. J., Appel, L. J., Braun, L. T., Chaturvedi, S., Creager, M. A., Culebras, A., Eckel, R. H., Hart, R. G., Hinchey, J. A., Howard, V. J., Jauch, E. C., Levine, S. R., Meschia, J. F., Moore, W. S., Nixon, J. V., & Pearson, T. A. (2011). Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke, 42*(2), 517-584. doi: 10.1161/STR.0b013e3181fcb238
- González-Camarena, R., Carrasco-Sosa, S., Román-Ramos, R., Gaitán-González, M. J., Medina-Bañuelos, V., & Azpiroz-Leehan, J. (2000). Effect of static and dynamic exercise on heart rate and blood pressure variabilities. *Medicine & Science in Sports & Exercise, 32*(10), 1719-1728.
- Gordon, C. D., Wilks, R., & McCaw-Binns, A. (2013). Effect of aerobic exercise (walking) training on functional status and health-related quality of life in chronic stroke survivors: a randomized controlled trial. *Stroke, 44*(4), 1179-1181.
- Gordon, N. F., Gulanick, M., Costa, F., Fletcher, G., Franklin, B. A., Roth, E. J., & Shephard, T. (2004). Physical activity and exercise recommendations for stroke survivors: an American Heart Association scientific statement from the Council on Clinical Cardiology, Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention; the Council on Cardiovascular Nursing; the Council on Nutrition, Physical Activity, and Metabolism; and the Stroke Council. *Stroke, 35*(5), 1230-1240. doi: 10.1161/01.STR.0000127303.19261.19
- Gordon, N. F., Kohl, H. W., Pollock, M. L., Vaandrager, H., Gibbons, L. W., & Blair, S. N. (1995). Cardiovascular safety of maximal strength testing in healthy adults. *The American Journal of Cardiology, 76*(11), 851-853.

- Gorelick, P. B., Sacco, R. L., Smith, D. B., Alberts, M., Mustone-Alexander, L., Rader, D., Ross, J. L., Raps, E., Ozer, M. N., & Brass, L. M. (1999). Prevention of a first stroke: a review of guidelines and a multidisciplinary consensus statement from the National Stroke Association. *JAMA*, *281*(12), 1112-1120.
- Gottesman, R. F., & Hillis, A. E. (2010). Predictors and assessment of cognitive dysfunction resulting from ischaemic stroke. *The Lancet Neurology*, *9*(9), 895-905.
- Granger, C. V., Albrecht, G. L., & Hamilton, B. B. (1979). Outcome of comprehensive medical rehabilitation: measurement by PULSES profile and the Barthel Index. *Archives of Physical Medicine and Rehabilitation*, *60*(4), 145-154.
- Green, D. J., O'Driscoll, G., Blanksby, B. A., & Taylor, R. R. (1996). Control of skeletal muscle blood flow during dynamic exercise. *Sports Medicine*, *21*(2), 119-146.
- Gresham, G. E., Phillips, T., Wolf, P., McNamara, P., Kannel, W., & Dawber, T. (1979). Epidemiologic profile of long-term stroke disability: the Framingham study. *Archives of Physical Medicine and Rehabilitation*, *60*(11), 487-491.
- Gris, J. C., Schved, J. F., Feugeas, O., Aguilar-Martinez, P., Arnaud, A., Sanchez, N., & Sarlat, C. (1990). Impact of smoking, physical training and weight reduction on FVII, PAI-1 and hemostatic markers in sedentary men. *Thrombosis and Haemostasis*, *64*(4), 516-520.
- Gunaydin, R., Karatepe, A. G., Kaya, T., & Ulutas, O. (2011). Determinants of quality of life (QoL) in elderly stroke patients: a short-term follow-up study. *Archives of Gerontology and Geriatrics*, *53*(1), 19-23.
- Haacke, C., Althaus, A., Spottke, A., Siebert, U., Back, T., & Dodel, R. (2006). Long-term outcome after stroke evaluating health-related quality of life using utility measurements. *Stroke*, *37*(1), 193-198.
- Hackett, M. L., & Anderson, C. S. (2005). Predictors of depression after stroke: a systematic review of observational studies. *Stroke*, *36*(10), 2296-2301.
- Hackett, M. L., Duncan, J. R., Anderson, C. S., Broad, J. B., & Bonita, R. (2000). Health-related quality of life among long-term survivors of stroke results from the Auckland stroke study, 1991–1992. *Stroke*, *31*(2), 440-447.
- Hackett, M. L., Yapa, C., Parag, V., & Anderson, C. S. (2005). Frequency of depression after stroke: a systematic review of observational studies. *Stroke*, *36*(6), 1330-1340. doi: 10.1161/01.STR.0000165928.19135.35
- Hadi, H. A., & Al Suwaidi, J. (2007). Endothelial dysfunction in diabetes mellitus. *Vascular Health and Risk Management*, *3*(6), 853–876.
- Hamilton, P., Lockhart, C., Quinn, C., & Mcveigh, G. (2007). Arterial stiffness: clinical relevance, measurement and treatment. *Clinical Science*, *113*, 157-170.
- Hankey, G. J. (2006). Potential new risk factors for ischemic stroke: what is their potential? *Stroke*, *37*(8), 2181-2188.
- Hankey, G. J., & Blacker, D. J. (2015). Is it a stroke? *British Medical Journal*, *350*, 1-6.
- Hankey, G. J., Jamrozik, K., Broadhurst, R. J., Forbes, S., & Anderson, C. S. (2002). Long-term disability after first-ever stroke and related prognostic factors in the Perth Community Stroke Study, 1989–1990. *Stroke*, *33*(4), 1034-1040.

- Hanon, O., Haulon, S., Lenoir, H., Seux, M.-L., Rigaud, A.-S., Safar, M., Girerd, X., & Forette, F. (2005). Relationship between arterial stiffness and cognitive function in elderly subjects with complaints of memory loss. *Stroke*, *36*(10), 2193-2197.
- Harazin, B., & Grzesik, J. (1998). The transmission of vertical whole-body vibration to the body segments of standing subjects. *Journal of Sound and Vibration*, *215*(4), 775-787.
- Hart, R. G., Benavente, O., McBride, R., & Pearce, L. A. (1999). Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. *Annals of Internal Medicine*, *131*(7), 492-501.
- Hart, R. G., Pearce, L. A., McBride, R., Rothbart, R. M., & Asinger, R. W. (1999). Factors associated with ischemic stroke during aspirin therapy in atrial fibrillation: analysis of 2012 participants in the SPAF I-III clinical trials. *Stroke*, *30*(6), 1223-1229.
- Hart, R. G., Pearce, L. A., Rothbart, R. M., McAnulty, J. H., Asinger, R. W., & Halperin, J. L. (2000). Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. *Journal of the American College of Cardiology*, *35*(1), 183-187.
- Haslam, D. R., McCartney, N., McKelvie, R. S., & MacDougall, J. D. (1988). Direct measurements of arterial blood pressure during formal weightlifting in cardiac patients. *Journal of Cardiopulmonary Rehabilitation and Prevention*, *8*(6), 213-225.
- Hazell, T. J., Thomas, G. W., DeGuire, J. R., & Lemon, P. W. (2008). Vertical whole-body vibration does not increase cardiovascular stress to static semi-squat exercise. *European Journal of Applied Physiology*, *104*(5), 903-908.
- He, F. J., Nowson, C. A., & MacGregor, G. A. (2006). Fruit and vegetable consumption and stroke: meta-analysis of cohort studies. *The Lancet*, *367*(9507), 320-326.
- He, J., Klag, M. J., Wu, Z., & Whelton, P. K. (1995). Stroke in the People's Republic of China I. Geographic variations in incidence and risk factors. *Stroke*, *26*(12), 2222-2227.
- Heffernan, K. S., Rossow, L., Jae, S. Y., Shokunbi, H. G., Gibson, E. M., & Fernhall, B. (2006). Effect of single-leg resistance exercise on regional arterial stiffness. *European Journal of Applied Physiology*, *98*(2), 185-190.
- Heidland, U. E., & Strauer, B. E. (2001). Left ventricular muscle mass and elevated heart rate are associated with coronary plaque disruption. *Circulation*, *104*(13), 1477-1482.
- Hochstenbach, J. B., den Otter, R., & Mulder, T. W. (2003). Cognitive recovery after stroke: a 2-year follow-up. *Archives of Physical Medicine and Rehabilitation*, *84*(10), 1499-1504.
- Holme, I., Aastveit, A., Hammar, N., Jungner, I., & Walldius, G. (2009). Relationships between lipoprotein components and risk of ischaemic and haemorrhagic stroke in the Apolipoprotein Mortality RISK study (AMORIS). *Journal of Internal Medicine*, *265*(2), 275-287.
- Howard, G., Anderson, R., Sorlie, P., Andrews, V., Backlund, E., & Burke, G. L. (1994a). Ethnic differences in stroke mortality between non-Hispanic whites, Hispanic whites, and blacks. The National Longitudinal Mortality Study. *Stroke*, *25*(11), 2120-2125.
- Howard, G., Evans, G. W., Crouse, J., Toole, J. F., Ryu, J. E., Tegeler, C., Frye-Pierson, J., Mitchell, E., & Sanders, L. (1994b). A prospective reevaluation of transient ischemic attacks as a risk factor for death and fatal or nonfatal cardiovascular events. *Stroke*, *25*(2), 342-345.
- Hsieh, S., Schubert, S., Hoon, C., Mioshi, E., & Hodges, J. R. (2013). Validation of the Addenbrooke's Cognitive Examination III in frontotemporal dementia and alzheimer's disease. *Dementia and Geriatric Cognitive Disorders*(36), 242-250.

- Hu, G., Sarti, C., Jousilahti, P., Silventoinen, K., Barengo, N. C., & Tuomilehto, J. (2005). Leisure time, occupational, and commuting physical activity and the risk of stroke. *Stroke*, *36*(9), 1994-1999.
- Hu, G., Tuomilehto, J., Silventoinen, K., Sarti, C., Männistö, S., & Jousilahti, P. (2007). Body mass index, waist circumference, and waist-hip ratio on the risk of total and type-specific stroke. *Archives of Internal Medicine*, *167*(13), 1420-1427.
- Hubner, N., Yagil, C., & Yagil, Y. (2006). Novel integrative approaches to the identification of candidate genes in hypertension. *Hypertension*, *47*(1), 1-5.
- Hughes, M., & Lip, G. (2008). Stroke and thromboembolism in atrial fibrillation: a systematic review of stroke risk factors, risk stratification schema and cost effectiveness data. *Thrombosis and Haemostasis*, *99*(2), 295-304.
- Hunt, K. J., Duggirala, R., Göring, H. H., Williams, J. T., Almasy, L., Blangero, J., O'Leary, D. H., & Stern, M. P. (2002). Genetic basis of variation in carotid artery plaque in the San Antonio Family Heart Study. *Stroke*, *33*(12), 2775-2780.
- Hurairah, H., & Ferro, A. (2004). The role of the endothelium in the control of vascular function. *International Journal of Clinical Practice*, *58*(2), 173-183.
- Iadecola, C., & Davisson, R. L. (2008). Hypertension and cerebrovascular dysfunction. *Cell Metabolism*, *7*(6), 476-484.
- Iadecola, C., Park, L., & Capone, C. (2009). Threats to the mind: aging, amyloid, and hypertension. *Stroke*, *40*(3), S40-S44.
- Iellamo, F., Pizzinelli, P., Massaro, M., Raimondi, G., Peruzzi, G., & Legramante, J. M. (1999). Muscle metaboreflex contribution to sinus node regulation during static exercise Insights from spectral analysis of heart rate variability. *Circulation*, *100*(1), 27-32.
- Immink, R. V., van den Born, B.-J. H., van Montfrans, G. A., Koopmans, R. P., Karemaker, J. M., & Van Lieshout, J. J. (2004). Impaired cerebral autoregulation in patients with malignant hypertension. *Circulation*, *110*(15), 2241-2245.
- Issurin, V. (2005). Vibrations and their applications in sport. *Journal of Sports Medicine and Physical Fitness*, *45*, 324-336.
- Issurin, V., & Tenenbaum, G. (1999). Acute and residual effects of vibratory stimulation on explosive strength in elite and amateur athletes. *Journal of Sports Sciences*, *17*(3), 177-182.
- Ivey, F. M., Ryan, A. S., Hafer-Macko, C. E., Goldberg, A. P., & Macko, R. F. (2007). Treadmill aerobic training improves glucose tolerance and indices of insulin sensitivity in disabled stroke survivors: a preliminary report. *Stroke*, *38*(10), 2752-2758.
- Jackson, S. W., & Turner, D. L. (2003). Prolonged muscle vibration reduces maximal voluntary knee extension performance in both the ipsilateral and the contralateral limb in man. *European Journal of Applied Physiology*, *88*(4-5), 380-386.
- Jagoda, A., Myers, J. N., Kaminsky, L. A., & Whaley, M. H. (2014). Heart rate response at the onset of exercise in an apparently healthy cohort. *European Journal of Applied Physiology*, *114*(7), 1367-1375.
- James, A. H., Bushnell, C. D., Jamison, M. G., & Myers, E. R. (2005). Incidence and risk factors for stroke in pregnancy and the puerperium. *Obstetrics & Gynecology*, *106*(3), 509-516.

- Jennett, B., & Bond, M. (1975). Assessment of outcome after severe brain damage: a practical scale. *The Lancet*, 305(7905), 480-484.
- Johansson, R. S., & Vallbo, Å. B. (1983). Tactile sensory coding in the glabrous skin of the human hand. *Trends in Neurosciences*, 6, 27-32.
- Johnson, C., Baugh, R., Wilson, C., & Burns, J. (2001). Age related changes in the tunica media of the vertebral artery: implications for the assessment of vessels injured by trauma. *Journal of Clinical Pathology*, 54(2), 139-145.
- Johnston, S. C., Mendis, S., & Mathers, C. D. (2009). Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *The Lancet Neurology*, 8(4), 345-354.
- Jordan, M. J., Norris, S. R., Smith, D. J., & Herzog, W. (2005). Vibration training: an overview of the area, training consequences, and future considerations. *The Journal of Strength & Conditioning Research*, 19(2), 459-466.
- Jouven, X., Empana, J.-P., Schwartz, P. J., Desnos, M., Courbon, D., & Ducimetière, P. (2005). Heart-rate profile during exercise as a predictor of sudden death. *New England Journal of Medicine*, 352(19), 1951-1958.
- Kaess, B. M., Rong, J., Larson, M. G., Hamburg, N. M., Vita, J. A., Levy, D., Benjamin, E. J., Vasan, R. S., & Mitchell, G. F. (2012). Aortic stiffness, blood pressure progression, and incident hypertension. *JAMA*, 308(9), 875-881.
- Kamiya, A., & Togawa, T. (1980). Adaptive regulation of wall shear stress to flow change in the canine carotid artery. *American Journal of Physiology-Heart and Circulatory Physiology*, 239(1), H14-H21.
- Kannel, W. B. (2009). Hypertension: reflections on risks and prognostication. *Medical Clinics of North America*, 93(3), 541-558.
- Kannel, W. B., Kannel, C., Paffenbarger, R. S., & Cupples, L. A. (1987a). Heart rate and cardiovascular mortality: the Framingham Study. *American Heart Journal*, 113(6), 1489-1494.
- Kannel, W. B., Wolf, P. A., Castelli, W. P., & D'Agostino, R. B. (1987b). Fibrinogen and risk of cardiovascular disease: the Framingham Study. *JAMA*, 258(9), 1183-1186.
- Karamanoglu, M., O'Rourke, M., Avolio, A., & Kelly, R. (1993). An analysis of the relationship between central aortic and peripheral upper limb pressure waves in man. *European Heart Journal*, 14(2), 160-167.
- Katch, V. L., McArdle, W. D., & Katch, F. I. (2011). *Essentials of exercise physiology* (4th ed.). Baltimore, MD: Wolters Kluwer Health/Lippincott Williams & Wilkins Health.
- Katz-Leurer, M., Carmeli, E., & Shochina, M. (2003a). The effect of early aerobic training on independence six months post stroke. *Clinical Rehabilitation*, 17(7), 735-741.
- Katz-Leurer, M., Shochina, M., Carmeli, E., & Friedlander, Y. (2003b). The influence of early aerobic training on the functional capacity in patients with cerebrovascular accident at the subacute stage. *Archives of Physical Medicine and Rehabilitation*, 84(11), 1609-1614.
- Kawasaki, T., Sasayama, S., Yagi, S., Asakawa, T., & Hirai, T. (1987). Non-invasive assessment of the age related changes in stiffness of major branches of the human arteries. *Cardiovascular Research*, 21(9), 678-687.
- Kelly, R., Daley, J., Avolio, A., & O'Rourke, M. (1989). Arterial dilation and reduced wave reflection. Benefit of diltiazem in hypertension. *Hypertension*, 14(1), 14-21.

- Kelly, R., Hayward, C., Avolio, A., & O'rourke, M. (1989). Noninvasive determination of age-related changes in the human arterial pulse. *Circulation*, *80*(6), 1652-1659.
- Kelly, R., Millasseau, S., Ritter, J., & Chowienczyk, P. (2001). Vasoactive drugs influence aortic augmentation index independently of pulse-wave velocity in healthy men. *Hypertension*, *37*(6), 1429-1433.
- Kerschlan-Schindl, K., Grampp, S., Henk, C., Resch, H., Preisinger, E., Fialka-Moser, V., & Imhof, H. (2001). Whole-body vibration exercise leads to alterations in muscle blood volume. *Clinical Physiology*, *21*(3), 377-382.
- Kiely, D. K., Wolf, P. A., Cupples, L. A., Beiser, A., & Myers, R. (1993). Familial aggregation of stroke. The Framingham Study. *Stroke*, *24*(9), 1366-1371.
- Kim, J., Song, T.-J., Song, D., Lee, K. J., Kim, E. H., Lee, H. S., Nam, C. M., Nam, H. S., Kim, Y. D., & Heo, J. H. (2014). Brachial-ankle pulse wave velocity is a strong predictor for mortality in patients with acute stroke. *Hypertension*, *64*(2), 240-246.
- Kim, P., Warren, S., Madill, H., & Hadley, M. (1999). Quality of life of stroke survivors. *Quality of Life Research*, *8*(4), 293-301.
- Kim, Y., Immink, R., Stok, W., Karemaker, J., Secher, N., & van Lieshout, J. (2008). Dynamic cerebral autoregulatory capacity is affected early in type 2 diabetes. *Clinical Science*, *115*, 255-262.
- King, R. B. (1996). Quality of life after stroke. *Stroke*, *27*(9), 1467-1472.
- Kingwell, B. A., Berry, K. L., Cameron, J. D., Jennings, G. L., & Dart, A. M. (1997). Arterial compliance increases after moderate-intensity cycling. *American Journal of Physiology-Heart and Circulatory Physiology*, *273*(5), H2186-H2191.
- Kinlay, S., Creager, M. A., Fukumoto, M., Hikita, H., Fang, J. C., Selwyn, A. P., & Ganz, P. (2001). Endothelium-derived nitric oxide regulates arterial elasticity in human arteries in vivo. *Hypertension*, *38*(5), 1049-1053.
- Kinsler, A. M., Ramsey, M. W., O'Bryant, H. S., Ayres, C. A., Sands, W. A., & Stone, M. H. (2008). Vibration and stretching effects on flexibility and explosive strength in young gymnasts. *Medicine & Science in Sports & Exercise*, *40*(1), 133.
- Kirkevold, M. (2002). The unfolding illness trajectory of stroke. *Disability & Rehabilitation*, *24*(17), 887-898.
- Kissela, B. M., Khoury, J., Kleindorfer, D., Woo, D., Schneider, A., Alwell, K., Miller, R., Ewing, I., Moomaw, C. J., & Szaflarski, J. P. (2005). Epidemiology of ischemic stroke in patients with diabetes: the Greater Cincinnati/Northern Kentucky Stroke Study. *Diabetes Care*, *28*(2), 355-359.
- Kissela, B. M., Sauerbeck, L., Woo, D., Khoury, J., Carrozzella, J., Pancioli, A., Jauch, E., Moomaw, C. J., Shukla, R., & Gebel, J. (2002). Subarachnoid hemorrhage a preventable disease with a heritable component. *Stroke*, *33*(5), 1321-1326.
- Kitayama, J., Faraci, F. M., Lentz, S. R., & Heistad, D. D. (2007). Cerebral vascular dysfunction during hypercholesterolemia. *Stroke*, *38*(7), 2136-2141.
- Kittner, S. J., Stern, B. J., Feaser, B. R., Hebel, J. R., Nagey, D. A., Buchholz, D. W., Earley, C. J., Johnson, C. J., Macko, R. F., & Sloan, M. A. (1996). Pregnancy and the risk of stroke. *New England Journal of Medicine*, *335*(11), 768-774.
- Kizer, J. R., Wiebers, D. O., Whisnant, J. P., Galloway, J. M., Welty, T. K., Lee, E. T., Best, L. G., Resnick, H. E., Roman, M. J., & Devereux, R. B. (2005). Mitral annular calcification, aortic valve sclerosis, and

- incident stroke in adults free of clinical cardiovascular disease: the strong heart study. *Stroke*, 36(12), 2533-2537.
- Koenig, W., Sund, M., Do, A., & Ernst, E. (1997). Leisure-time physical activity but not work-related physical activity is associated with decreased plasma viscosity results from a large population sample. *Circulation*, 95(2), 335-341.
- Koutnik, A. P., Wong, A., Kalfon, R., Madzima, T. A., & Figueroa, A. (2014). Acute passive vibration reduces arterial stiffness and aortic wave reflection in stroke survivors. *European Journal of Applied Physiology*, 114(1), 105-111.
- Kullo, I. J., & Malik, A. R. (2007). Arterial ultrasonography and tonometry as adjuncts to cardiovascular risk stratification. *Journal of the American College of Cardiology*, 49(13), 1413-1426.
- Kwakkel, G., van Peppen, R., Wagenaar, R. C., Dauphinee, S. W., Richards, C., Ashburn, A., Miller, K., Lincoln, N., Partridge, C., & Wellwood, I. (2004). Effects of augmented exercise therapy time after stroke a meta-analysis. *Stroke*, 35(11), 2529-2539.
- Lai, C., Chen, H., Tseng, S., Liao, W., Liu, B., Lee, M., & Chen, H. (2014). Effect of whole-body vibration for 3 months on arterial stiffness in the middle-aged and elderly. *Clinical Interventions in Aging*, 9, 821-828.
- Lai, S., Studenski, S., Richards, L., Perera, S., Reker, D., Rigler, S., & Duncan, P. W. (2006). Therapeutic exercise and depressive symptoms after stroke. *Journal of the American Geriatrics Society*, 54(2), 240-247.
- Laird, W. P., Fixler, D. E., & Huffines, F. D. (1979). Cardiovascular response to isometric exercise in normal adolescents. *Circulation*, 59(4), 651-654.
- Lajemi, M., Labat, C., Gautier, S., Lacolley, P., Safar, M., Asmar, R., Cambien, F., & Benetos, A. (2001). Angiotensin II type 1 receptor- 153A/G and 1166A/C gene polymorphisms and increase in aortic stiffness with age in hypertensive subjects. *Journal of Hypertension*, 19(3), 407-413.
- Lakatta, E. G. (2003). Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises part III: cellular and molecular clues to heart and arterial aging. *Circulation*, 107(3), 490-497.
- Lammie, G. A. (2000). Pathology of small vessel stroke. *British Medical Bulletin*, 56(2), 296-306.
- Langille, B. L., & O'Donnell, F. (1986). Reductions in arterial diameter produced by chronic decreases in blood flow are endothelium-dependent. *Science*, 231(4736), 405-407.
- Larner, A. (2007). Addenbrooke's Cognitive Examination-Revised (ACE-R) in day-to-day clinical practice. *Age and Ageing*, 36(6), 685-686.
- Lauer, M. S., Okin, P. M., Larson, M. G., Evans, J. C., & Levy, D. (1996). Impaired heart rate response to graded exercise prognostic implications of chronotropic incompetence in the Framingham Heart Study. *Circulation*, 93(8), 1520-1526.
- Laughlin, M. H. (2000). Cardiovascular response to exercise. *The American Journal of Physiology*(277), S244-259.
- Laughlin, M. H., Oltman, C. L., & Bowles, D. K. (1998). Exercise training-induced adaptations in the coronary circulation. *Medicine and Science in Sports and Exercise*, 30(3), 352-360.
- Laurent, S., Boutouyrie, P., Asmar, R., Gautier, I., Laloux, B., Guize, L., Ducimetiere, P., & Benetos, A. (2001). Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension*, 37(5), 1236-1241.

- Laurent, S., Boutouyrie, P., & Lacolley, P. (2005). Structural and genetic bases of arterial stiffness. *Hypertension*, *45*(6), 1050-1055.
- Laurent, S., Cockcroft, J., Van Bortel, L., Boutouyrie, P., Giannattasio, C., Hayoz, D., Pannier, B., Vlachopoulos, C., Wilkinson, I., & Struijker-Boudier, H. (2006a). Expert consensus document on arterial stiffness: methodological issues and clinical applications. *European Heart Journal*, *27*(21), 2588-2605.
- Laurent, S., Girerd, X., Mourad, J.-J., Lacolley, P., Beck, L., Boutouyrie, P., Mignot, J.-P., & Safar, M. (1994). Elastic modulus of the radial artery wall material is not increased in patients with essential hypertension. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *14*(7), 1223-1231.
- Laurent, S., Hayoz, D., Trazzi, S., Boutouyrie, P., Waeber, B., Omboni, S., Brunner, H. R., Mancia, G., & Safar, M. (1993). Isobaric compliance of the radial artery is increased in patients with essential hypertension. *Journal of Hypertension*, *11*(1), 89-98.
- Laurent, S., Katsahian, S., Fassot, C., Tropeano, A.-I., Gautier, I., Laloux, B., & Boutouyrie, P. (2003). Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. *Stroke*, *34*(5), 1203-1206.
- Laurent, S., Tropeano, A.-I., & Boutouyrie, P. (2006b). Pulse pressure reduction and cardiovascular protection. *Journal of Hypertension*, *24*, S13-S18.
- Lawes, C., Parag, V., Bennett, D., Suh, I., Whitlock, G., Barzi, F., Pan, W., Rodgers, A., Lin, R., & Woodward, M. (2004a). Blood glucose and risk of cardiovascular disease in the Asia Pacific region. *Diabetes Care*, *27*(12), 2836-2842.
- Lawes, C. M., Bennett, D. A., Feigin, V. L., & Rodgers, A. (2004b). Blood pressure and stroke an overview of published reviews. *Stroke*, *35*(3), 776-785.
- Lechat, P., Mas, J., Lascault, G., Loron, P., Theard, M., Klimczac, M., Drobinski, G., Thomas, D., & Grosogoeat, Y. (1988). Prevalence of patent foramen ovale in patients with stroke. *New England Journal of Medicine*, *318*(18), 1148-1152.
- Lee, M., Saver, J. L., Chang, K.-H., Liao, H.-W., Chang, S.-C., & Ovbiagele, B. (2010). Low glomerular filtration rate and risk of stroke: meta-analysis. *BMJ*, *341*.
- Lee, P. N., & Forey, B. A. (2006). Environmental tobacco smoke exposure and risk of stroke in nonsmokers: a review with meta-analysis. *Journal of Stroke and Cerebrovascular Diseases*, *15*(5), 190-201.
- Leicht, A. S., Sinclair, W. H., & Spinks, W. L. (2008). Effect of exercise mode on heart rate variability during steady state exercise. *European Journal of Applied Physiology*, *102*(2), 195-204.
- Lemogoum, D., Flores, G., Van den Abeele, W., Ciarka, A., Leeman, M., Degaute, J. P., Van De Borne, P., & Van Bortel, L. (2004). Validity of pulse pressure and augmentation index as surrogate measures of arterial stiffness during beta-adrenergic stimulation. *Journal of Hypertension*, *22*(3), 511-517.
- Levine, S. R., Barsan, W. G., Biller, J., Clark, W., Hecht, J., Hobson II, R. W., Mayberg, M., & Shuaib, A. (2006). *Stroke scales: an update*. National Stroke Association.
- Levy, B. I., Poitevin, P., Duriez, M., Guez, D. C., Schiavi, P. D., & Safar, M. E. (1997). Sodium, survival, and the mechanical properties of the carotid artery in stroke-prone hypertensive rats. *Journal of Hypertension*, *15*(3), 251-258.
- Levy, D., DeStefano, A. L., Larson, M. G., O'Donnell, C. J., Lifton, R. P., Gavras, H., Cupples, L. A., & Myers, R. H. (2000). Evidence for a gene influencing blood pressure on chromosome 17 genome scan

linkage results for longitudinal blood pressure phenotypes in subjects from the framingham heart study. *Hypertension*, 36(4), 477-483.

- Lewis, S. F., Snell, P. G., Taylor, W. F., Hamra, M., Graham, R. M., Pettinger, W. A., & Blomqvist, C. G. (1985). Role of muscle mass and mode of contraction in circulatory responses to exercise. *Journal of Applied Physiology*, 58(1), 146-151.
- Liao, D., Cooper, L., Cai, J., Toole, J., Bryan, N., Burke, G., Shahar, E., Nieto, J., Mosley, T., & Heiss, G. (1997a). The prevalence and severity of white matter lesions, their relationship with age, ethnicity, gender, and cardiovascular disease risk factors: the ARIC Study. *Neuroepidemiology*, 16(3), 149-162.
- Liao, D., Myers, R., Hunt, S., Shahar, E., Paton, C., Burke, G., Province, M., & Heiss, G. (1997b). Familial history of stroke and stroke risk: the Family Heart Study. *Stroke*, 28(10), 1908-1912.
- Limas, C., Westrum, B., Limas, C., & Cohn, J. (1980). Effect of salt on the vascular lesions of spontaneously hypertensive rats. *Hypertension*, 2(4), 477-489.
- Lind, A., & McNicol, G. (1967). Muscular factors which determine the cardiovascular responses to sustained and rhythmic exercise. *Canadian Medical Association Journal*, 96(12), 706.
- Lind, L., Andrén, B., & Sundström, J. (2004). The stroke volume/pulse pressure ratio predicts coronary heart disease mortality in a population of elderly men. *Journal of Hypertension*, 22(5), 899-905.
- Lindquist, V. A., Spangler, R. D., & Blount, S. G. (1973). A comparison between the effects of dynamic and isometric exercise as evaluated by the systolic time intervals in normal man. *American Heart Journal*, 85(2), 227-236.
- Lisabeth, L. D., Beiser, A. S., Brown, D. L., Murabito, J. M., Kelly-Hayes, M., & Wolf, P. A. (2009). Age at natural menopause and risk of ischemic stroke: the Framingham Heart Study. *Stroke*, 40(4), 1044-1049.
- Liu, A.-B., Hsu, P.-C., Chen, Z.-L., & Wu, H.-T. (2011). Measuring pulse wave velocity using ECG and photoplethysmography. *Journal of Medical Systems*, 35(5), 771-777.
- Loh, E., Sutton, M. S. J., Wun, C.-C. C., Rouleau, J. L., Flaker, G. C., Gottlieb, S. S., Lamas, G. A., Moyé, L. A., Goldhaber, S. Z., & Pfeffer, M. A. (1997). Ventricular dysfunction and the risk of stroke after myocardial infarction. *New England Journal of Medicine*, 336(4), 251-257.
- Lohman, E. B., Petrofsky, J. S., Maloney-Hinds, C., Betts-Schwab, H., & Thorpe, D. (2007). The effect of whole body vibration on lower extremity skin blood flow in normal subjects. *Medical Science Monitor Basic Research*, 13(2), CR71-CR76.
- London, G. M., Blacher, J., Pannier, B., Guérin, A. P., Marchais, S. J., & Safar, M. E. (2001). Arterial wave reflections and survival in end-stage renal failure. *Hypertension*, 38(3), 434-438.
- London, G. M., Guerin, A. P., Pannier, B., Marchais, S. J., & Stimpel, M. (1995). Influence of sex on arterial hemodynamics and blood pressure role of body height. *Hypertension*, 26(3), 514-519.
- London, G. M., Marchais, S. J., Guerin, A. P., & Pannier, B. (2003). Arterial stiffness: pathophysiology and clinical impact. *Clinical and Experimental Hypertension (New York, NY: 1993)*, 26(7-8), 689-699.
- Longstreth, W., Nelson, L. M., Koepsell, T. D., & Van Belle, G. (1992). Cigarette smoking, alcohol use, and subarachnoid hemorrhage. *Stroke*, 23(9), 1242-1249.
- Lorenzen, C., Maschette, W., Koh, M., & Wilson, C. (2009). Inconsistent use of terminology in whole body vibration exercise research. *Journal of Science and Medicine in Sport*, 12(6), 676-678.

- Lovett, J. K., Howard, S. C., & Rothwell, P. M. (2003). Pulse pressure is independently associated with carotid plaque ulceration. *Journal of Hypertension*, *21*(9), 1669-1676.
- Luescher, T. F., & Barton, M. (1997). Biology of the endothelium. *Clinical Cardiology*, 3-10.
- Lupattelli, G., Lombardini, R., Schillaci, G., Ciuffetti, G., Marchesi, S., Siepi, D., & Mannarino, E. (2000). Flow-mediated vasoactivity and circulating adhesion molecules in hypertriglyceridemia: association with small, dense LDL cholesterol particles. *American Heart Journal*, *140*(3), 521-526.
- Luscher, T. F., & Barton, M. (1997). Biology of the endothelium. *Clinical Cardiology*, 3-10.
- Lyden, P., Broderick, J., Mascha, E., & Investigators, N. t.-P. S. T. (1995). Reliability of the Barthel Index outcome measure selected for the NINDS t-PA Stroke Trial *Thrombolytic Therapy in Acute Ischemic Stroke III* (pp. 327-334). Japan: Springer.
- Lyden, P., Shuaib, A., Ng, K., Levin, K., Atkinson, R., Rajput, A., Wechsler, L., Ashwood, T., Claesson, L., & Odergren, T. (2002). Clomethiazole acute stroke study in ischemic stroke (CLASS-I) final results. *Stroke*, *33*(1), 122-129.
- Lyden, P. D., & Lau, G. T. (1991). A critical appraisal of stroke evaluation and rating scales. *Stroke*, *22*(11), 1345-1352.
- Lyon, R. T., Runyon-Hass, A., Davis, H. R., Glagov, S., & Zarins, C. K. (1987). Protection from atherosclerotic lesion formation by reduction of artery wall motion. *Journal of Vascular Surgery*, *5*(1), 59-67.
- Lythgo, N., Eser, P., de Groot, P., & Galea, M. (2009). Whole-body vibration dosage alters leg blood flow. *Clinical Physiology and Functional Imaging*, *29*(1), 53-59. doi: 10.1111/j.1475-097X.2008.00834.x
- Macciocchi, S. N., Diamond, P. T., Alves, W. M., & Mertz, T. (1998). Ischemic stroke: relation of age, lesion location, and initial neurologic deficit to functional outcome. *Archives of Physical Medicine and Rehabilitation*, *79*(10), 1255-1257.
- MacDougall, J., Tuxen, D., Sale, D., Moroz, J., & Sutton, J. (1985). Arterial blood pressure response to heavy resistance exercise. *Journal of Applied Physiology*, *58*(3), 785-790.
- MacKay-Lyons, M. J., & Makrides, L. (2004). Longitudinal changes in exercise capacity after stroke. *Archives of Physical Medicine and Rehabilitation*, *85*(10), 1608-1612.
- Mahmud, A., & Feely, J. (2002). Divergent effect of acute and chronic alcohol on arterial stiffness. *American Journal of Hypertension*, *15*(3), 240-243.
- Mahmud, A., & Feely, J. (2005). Arterial stiffness is related to systemic inflammation in essential hypertension. *Hypertension*, *46*(5), 1118-1122.
- Maizels, D. J., & Akademisk, G. (2011). Atherosclerosis, from <http://www.scientific-art.com/portfolio%20medicine%20pages/atherosclerosis.htm>
- Mannucci, E., Lambertucci, L., Monami, M., Fedeli, A., Chiasserini, V., Marchionni, N., Masotti, G., & Ungar, A. (2006). Pulse pressure and mortality in hypertensive type 2 diabetic patients. A cohort study. *Diabetes/Metabolism Research and Reviews*, *22*(3), 172-175.
- Marosszeky, N., & Sansoni, J. (2005). Instrument review- SF-36® health survey (version 1.0) for use in Australia, from <http://ro.uow.edu.au/cgi/viewcontent.cgi?article=1001&context=ahoc>
- Martin, J. H. (2003). *Neuroanatomy: text and atlas*. New York, NY: McGraw-Hill.

- Mason, R. R., Cochrane, D. J., Denny, G. J., Firth, E. C., & Stannard, S. R. (2012). Is 8 weeks of side-alternating whole-body vibration a safe and acceptable modality to improve functional performance in multiple sclerosis? *Disability and Rehabilitation*, *34*(8), 647-654.
- Mathuranath, P., Nestor, P., Berrios, G., Rakowicz, W., & Hodges, J. (2000). A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology*, *55*(11), 1613-1620.
- Matsuoka, O., Otsuka, K., Murakami, S., Hotta, N., Yamanaka, G., Kubo, Y., Yamanaka, T., Shinagawa, M., Nunoda, S., & Nishimura, Y. (2005). Arterial stiffness independently predicts cardiovascular events in an elderly community- Longitudinal Investigation for the Longevity and Aging in Hokkaido County (LILAC) study. *Biomedicine & Pharmacotherapy*, *59*, S40-S44.
- Mattace-Raso, F. U., van der Cammen, T. J., Hofman, A., van Popele, N. M., Bos, M. L., Schalekamp, M. A., Asmar, R., Reneman, R. S., Hoeks, A. P., & Breteler, M. M. (2006). Arterial stiffness and risk of coronary heart disease and stroke the rotterdam study. *Circulation*, *113*(5), 657-663.
- McCall, D. O., McGartland, C. P., Woodside, J. V., Sharpe, P., McCance, D. R., & Young, I. S. (2010). The relationship between microvascular endothelial function and carotid-radial pulse wave velocity in patients with mild hypertension. *Clinical and Experimental Hypertension*, *32*(7), 474-479.
- McEniery, C. M., Hall, I. R., Qasem, A., Wilkinson, I. B., & Cockcroft, J. R. (2005). Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo-Cardiff Collaborative Trial (ACCT). *Journal of the American College of Cardiology*, *46*(9), 1753-1760.
- McEniery, C. M., Wallace, S., Mackenzie, I. S., McDonnell, B., Newby, D. E., Cockcroft, J. R., & Wilkinson, I. B. (2006). Endothelial function is associated with pulse pressure, pulse wave velocity, and augmentation index in healthy humans. *Hypertension*, *48*(4), 602-608.
- McQueen, M. J., Hawken, S., Wang, X., Ounpuu, S., Sniderman, A., Probstfield, J., Steyn, K., Sanderson, J. E., Hasani, M., & Volkova, E. (2008). Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. *The Lancet*, *372*(9634), 224-233.
- Mead, G., Lewis, S., Wardlaw, J., Dennis, M., & Warlow, C. (2000). How well does the Oxfordshire Community Stroke Project classification predict the site and size of the infarct on brain imaging? *Journal of Neurology, Neurosurgery & Psychiatry*, *68*(5), 558-562.
- Mead, G. E., Greig, C. A., Cunningham, I., Lewis, S. J., Dinan, S., Saunders, D. H., Fitzsimons, C., & Young, A. (2007). Stroke: a randomized trial of exercise or relaxation. *Journal of the American Geriatrics Society*, *55*(6), 892-899.
- Meek, C., Pollock, A., Potter, J., & Langhorne, P. (2003). A systematic review of exercise trials post stroke. *Clinical rehabilitation*, *17*(1), 6-13.
- Mellon, L., Brewer, L., Hall, P., Horgan, F., Williams, D., & Hickey, A. (2015). Cognitive impairment six months after ischaemic stroke: a profile from the ASPIRE-S study. *BMC Neurology*(1), 31.
- Merillon, J., Lebras, Y., Chastre, J., Lerallut, J., Motte, G., Fontenier, G., Huet, Y., Jaffrin, M., & Gourgon, R. (1983). Forward and backward waves in the arterial system, their relationship to pressure waves form. *European Heart Journal*, *4*(Suppl G), 13-20.
- Mester, J., Spitzenfeil, P., Schwarzer, J., & Seifriz, F. (1999). Biological reaction to vibration-implications for sport. *Journal of Science and Medicine in Sport*, *2*(3), 211-226.
- Meyers, M. R., & Gokce, N. (2007). Endothelial dysfunction in obesity: etiological role in atherosclerosis. *Current Opinion in Endocrinology, Diabetes and Obesity*, *14*(5), 365-369.

- Michel, T., & Vanhoutte, P. M. (2010). Cellular signaling and NO production. *Pflügers Archiv- European Journal of Physiology*, 459(6), 807-816.
- Millar, J. A., Lever, A. F., & Burke, V. (1999). Pulse pressure as a risk factor for cardiovascular events in the MRC Mild Hypertension Trial. *Journal of hypertension*, 17(8), 1065-1072.
- Mitchell, J., Payne, F., Saltin, B., & Schibye, B. (1980). The role of muscle mass in the cardiovascular response to static contractions. *The Journal of physiology*, 309(1), 45-54.
- Miyachi, M. (2013). Effects of resistance training on arterial stiffness: a meta-analysis. *British Journal of Sports Medicine*, 47(6), 393-396.
- Mizutani, K., Ikeda, K., Kawai, Y., & Yamori, Y. (1999). Biomechanical properties and chemical composition of the aorta in genetic hypertensive rats. *Journal of Hypertension*, 17(4), 481-487.
- Mohr, J. P., Albers, G. W., Amarenco, P., Babikian, V. L., Biller, J., Brey, R. L., Coull, B., Easton, J. D., Gomez, C. R., & Helgason, C. M. (1997). Etiology of stroke. *Stroke*, 28(7), 1501-1506.
- Moncada, S., & Higgs, A. (1993). The L-arginine-nitric oxide pathway. *The New England Journal of Medicine*, 329(27), 2002-2012.
- Moncada, S., & Higgs, E. (2006). Nitric oxide and the vascular endothelium. *Handbook of Experimental Pharmacology*(176), 213.
- Morris, K., Hacker, V., & Lincoln, N. B. (2012). The validity of the Addenbrooke's Cognitive Examination-Revised (ACE-R) in acute stroke. *Disability and Rehabilitation*, 34(3), 189-195.
- Morris, S. L., Dodd, K. J., & Morris, M. E. (2004). Outcomes of progressive resistance strength training following stroke: a systematic review. *Clinical rehabilitation*, 18(1), 27-39.
- Morrison, V., Pollard, B., Johnston, M., & MacWalter, R. (2005). Anxiety and depression 3 years following stroke: demographic, clinical, and psychological predictors. *Journal of Psychosomatic Research*, 59(4), 209-213.
- Moskau, S., Golla, A., Grothe, C., Boes, M., Pohl, C., & Klockgether, T. (2005). Heritability of Carotid Artery Atherosclerotic Lesions An Ultrasound Study in 154 Families. *Stroke*, 36(1), 5-8.
- Moskowitz, M. A., Lo, E. H., & Iadecola, C. (2010). The science of stroke: mechanisms in search of treatments. *Neuron*, 67(2), 181-198.
- MRC Asymptomatic Carotid Surgery Trial Collaborative Group. (2004). Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *The Lancet*, 363(9420), 1491-1502.
- Muir, K. W., Weir, C. J., Murray, G. D., Povey, C., & Lees, K. R. (1996). Comparison of neurological scales and scoring systems for acute stroke prognosis. *Stroke*, 27(10), 1817-1820.
- Mundal, R., Kjeldsen, S. E., Sandvik, L., Erikssen, G., Thaulow, E., & Erikssen, J. (1994). Exercise blood pressure predicts cardiovascular mortality in middle-aged men. *Hypertension*, 24(1), 56-62.
- Munro, J., & Cotran, R. (1988). The pathogenesis of atherosclerosis: atherogenesis and inflammation. *Laboratory investigation; a journal of technical methods and pathology*, 58(3), 249-261.
- Myers, G. L., Christenson, R. H., Cushman, M., Ballantyne, C. M., Cooper, G. R., Pfeiffer, C. M., Grundy, S. M., Labarthe, D. R., Levy, D., & Rifai, N. (2009). National Academy of Clinical Biochemistry Laboratory Medicine Practice guidelines: emerging biomarkers for primary prevention of cardiovascular disease. *Clinical chemistry*, 55(2), 378-384.

- Naidu, M., Reddy, B. M., Yashmaina, S., Patnaik, A. N., & Rani, P. U. (2005). Validity and reproducibility of arterial pulse wave velocity measurement using new device with oscillometric technique: a pilot study. *Biomed Eng Online*, 4(49), 1-14.
- Nakanishi, N., Kawashimo, H., Nakamura, K., SUZUKI, K., YOSHIDA, H., UZURA, S., & TATARA, K. (2001). Association of alcohol consumption with increase in aortic stiffness: a 9-year longitudinal study in middle-aged Japanese men. *Industrial Health*, 39(1), 24-28.
- Nakatani, S., Yamagishi, M., Tamai, J., Goto, Y., Umeno, T., Kawaguchi, A., Yutani, C., & Miyatake, K. (1995). Assessment of coronary artery distensibility by intravascular ultrasound application of simultaneous measurements of luminal area and pressure. *Circulation*, 91(12), 2904-2910.
- Nakayama, R., & Azuma, T. (1977). Noninvasive measurements of digital arterial pressure and compliance in man. *American Journal of Physiology Heart and Circulatory Physiology*, 233(1), H168-H179.
- Napoli, C., de Nigris, F., Williams-Ignarro, S., Pignalosa, O., Sica, V., & Ignarro, L. J. (2006). Nitric oxide and atherosclerosis: an update. *Nitric Oxide*, 15(4), 265-279.
- National Health Committee. (2013). *Strategic overview: Cardiovascular disease in New Zealand*. Wellington: National Health Committee. Retrieved from <http://nhc.health.govt.nz/strategic-overview-cardiovascular-disease-new-zealand>.
- National Stroke Association. (2009). Stroke & vision loss, from www.stroke.org/site/DocServer/Vision09WEB.pdf
- Nedeltchev, K., Wiedmer, S., Schwerzmann, M., Windecker, S., Haefeli, T., Meier, B., Mattle, H. P., & Arnold, M. (2008). Sex differences in cryptogenic stroke with patent foramen ovale. *American heart journal*, 156(3), 461-465.
- Nelson, A. J., Worthley, S. G., Cameron, J. D., Willoughby, S. R., Piantadosi, C., Carbone, A., Dundon, B. K., Leung, M. C., Hope, S. A., & Meredith, I. T. (2009). Cardiovascular magnetic resonance-derived aortic distensibility: validation and observed regional differences in the elderly. *Journal of hypertension*, 27(3), 535-542.
- Nesbitt, E., Schmidt-Trucksäss, A., Il'yasov, K., Weber, H., Huonker, M., Laubenberger, J., Keul, J., Hennig, J., & Langer, M. (2000). Assessment of arterial blood flow characteristics in normal and atherosclerotic vessels with the fast Fourier flow method. *Magnetic Resonance Materials in Physics, Biology and Medicine*, 10(1), 27-34.
- NHLBI. (2014). Types of stroke, from <http://www.nhlbi.nih.gov/health/health-topics/topics/stroke/types>
- Niemi, M.-L., Laaksonen, R., Kotila, M., & Waltimo, O. (1988). Quality of life 4 years after stroke. *Stroke*, 19(9), 1101-1107.
- Nigg, B. M. (1997). Impact forces in running. *Current Opinion in Orthopaedics*, 8(6), 43-47.
- North Central London Cardiac and Stroke Network. (2012). *Recommendations for screening for cognitive difficulties post-stroke*. Retrieved from <http://improvementsystem.nhs.uk/ImprovementSystem/ViewDocument.aspx?path=Stroke/National/website/Psychology/screening/NCL+Stroke+project.Guidance+on+cognitive+screening.february+2012.pdf>.
- Nys, G., Van Zandvoort, M., De Kort, P., Jansen, B., De Haan, E., & Kappelle, L. (2006). Cognitive disorders in acute stroke: prevalence and clinical determinants. *Cerebrovascular Diseases (Basel, Switzerland)*, 23(5-6), 408-416.

- Nys, G., van Zandvoort, M., de Kort, P., Jansen, B., Kappelle, L., & de Haan, E. (2005a). Restrictions of the Mini-Mental State Examination in acute stroke. *Archives of Clinical Neuropsychology: the Official Journal of the National Academy of Neuropsychologists*, 20(5), 623.
- Nys, G., Van Zandvoort, M., De Kort, P., Van der Worp, H., Jansen, B., Algra, A., De Haan, E., & Kappelle, L. (2005b). The prognostic value of domain-specific cognitive abilities in acute first-ever stroke. *Neurology*, 64(5), 821-827.
- O'Donnell, C. J., Chazaro, I., Wilson, P. W., Fox, C., Hannan, M. T., Kiel, D. P., & Cupples, L. A. (2002). Evidence for heritability of abdominal aortic calcific deposits in the Framingham Heart Study. *Circulation*, 106(3), 337-341.
- O'Donnell, M. J., Xavier, D., Liu, L., Zhang, H., Chin, S. L., Rao-Melacini, P., Rangarajan, S., Islam, S., Pais, P., & McQueen, M. J. (2010). Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *The Lancet*, 376(9735), 112-123.
- O'Rourke, M. (1990). Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. *Hypertension*, 15(4), 339-347.
- O'Rourke, M. F., & Kelly, R. P. (1993). Wave reflection in the systemic circulation and its implications in ventricular function. *Journal of Hypertension*, 11(4), 327-337.
- O'Rourke, M. F., Pauca, A., & Jiang, X.-J. (2001). Pulse wave analysis. *British Journal of Clinical Pharmacology*, 51(6), 507-522.
- O'Sullivan, C., & Chard, G. (2010). An exploration of participation in leisure activities post-stroke. *Australian Occupational Therapy Journal*, 57(3), 159-166.
- Oberoi, S., Schoepf, U. J., Meyer, M., Henzler, T., Rowe, G. W., Costello, P., & Nance, J. W. (2013). Progression of arterial stiffness and coronary atherosclerosis: longitudinal evaluation by cardiac CT. *American Journal of Roentgenology*, 200(4), 798-804.
- Ochfeld, E., Newhart, M., Molitoris, J., Leigh, R., Cloutman, L., Davis, C., Crinion, J., & Hillis, A. E. (2010). Ischemia in broca area is associated with broca aphasia more reliably in acute than in chronic stroke. *Stroke*, 41(2), 325-330.
- Ohayon, J., Gharib, A. M., Garcia, A., Heroux, J., Yazdani, S. K., Malvè, M., Tracqui, P., Martinez, M.-A., Doblare, M., & Finet, G. (2011). Is arterial wall-strain stiffening an additional process responsible for atherosclerosis in coronary bifurcations?: an in vivo study based on dynamic CT and MRI. *American Journal of Physiology-Heart and Circulatory Physiology*, 301(3), H1097-H1106.
- Okamoto, T., Min, S., & Sakamaki-Sunaga, M. (2014). Arterial compliance and stiffness following low-intensity resistance exercise. *European Journal of Applied Physiology*, 114(2), 235-241.
- Oliver, J. J., & Webb, D. J. (2003). Noninvasive assessment of arterial stiffness and risk of atherosclerotic events. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 23(4), 554-566.
- Oono, I., Mackay, D., & Pell, J. (2011). Meta-analysis of the association between secondhand smoke exposure and stroke. *Journal of Public Health*, 33(4), 496-502.
- Otsuki, T., Takanami, Y., Aoi, W., Kawai, Y., Ichikawa, H., & Yoshikawa, T. (2008). Arterial stiffness acutely decreases after whole-body vibration in humans. *Acta Physiologica*, 194(3), 189-194.
- Otten, M. W., Teutsch, S. M., Williamson, D. F., & Marks, J. S. (1990). The effect of known risk factors on the excess mortality of black adults in the United States. *JAMA*, 263(6), 845-850.

- Ouellette, M. M., LeBrasseur, N. K., Bean, J. F., Phillips, E., Stein, J., Frontera, W. R., & Fielding, R. A. (2004). High-intensity resistance training improves muscle strength, self-reported function, and disability in long-term stroke survivors. *Stroke*, *35*(6), 1404-1409.
- Paini, A., Boutouyrie, P., Calvet, D., Tropeano, A.-I., Laloux, B., & Laurent, S. (2006). Carotid and aortic stiffness determinants of discrepancies. *Hypertension*, *47*(3), 371-376.
- Pak, S., & Patten, C. (2008). Strengthening to promote functional recovery poststroke: an evidence-based review. *Topics in Stroke Rehabilitation*, *15*(3), 177.
- Panagiotakos, D. B., Kromhout, D., Menotti, A., Chrysohoou, C., Dontas, A., Pitsavos, C., Adachi, H., Blackburn, H., Nedeljkovic, S., & Nissinen, A. (2005). The relation between pulse pressure and cardiovascular mortality in 12 763 middle-aged men from various parts of the world: a 25-year follow-up of the seven countries study. *Archives of Internal Medicine*, *165*(18), 2142-2147.
- Pang, M., Lau, R., & Yip, S. (2013a). The effects of whole-body vibration therapy on bone turnover, muscle strength, motor function, and spasticity in chronic stroke: a randomized controlled trial. *European Journal of Physical and Rehabilitation Medicine*, *49*(4), 439-450.
- Pang, M. Y., Eng, J. J., Dawson, A. S., & Gylfadóttir, S. (2006). The use of aerobic exercise training in improving aerobic capacity in individuals with stroke: a meta-analysis. *Clinical Rehabilitation*, *20*(2), 97-111.
- Pang, M. Y. C., Charlesworth, S. A., Lau, R. W. K., & Chung, R. C. K. (2013b). Using aerobic exercise to improve health outcomes and quality of life in stroke: evidence-based exercise prescription recommendations. *Cerebrovascular Diseases*, *35*(1), 7-22.
- Pang, M. Y. C., Eng, J. J., Dawson, A. S., McKay, H. A., & Harris, J. E. (2005). A community based fitness and mobility exercise program for older adults with chronic stroke: a randomized, controlled trial. *Journal of the American Geriatrics Society*, *53*(10), 1667-1674.
- Pannier, B. M., Avolio, A. P., Hoeks, A., Manca, G., & Takazawa, K. (2002). Methods and devices for measuring arterial compliance in humans. *American Journal of Hypertension*, *15*(8), 743-753.
- Paoletti, R., Gotto, A. M., & Hajjar, D. P. (2004). Inflammation in atherosclerosis and implications for therapy. *Circulation*, *109*(23 suppl 1), III-20-III-26.
- Pappas, E., & Salem, Y. (2009). Overground physical therapy gait training for chronic stroke patients with mobility deficits. *Stroke*, *40*(11), e627-e628.
- Parati, G., & Bernardi, L. (2006). How to assess arterial compliance in humans. *Journal of Hypertension*, *24*(6), 1009-1012.
- Patel, M., Tilling, K., Lawrence, E., Rudd, A., Wolfe, C., & McKeivitt, C. (2006). Relationships between long-term stroke disability, handicap and health-related quality of life. *Age and Ageing*, *35*(3), 273-279.
- Patel, M. D., Coshall, C., Rudd, A. G., & Wolfe, C. D. (2002). Cognitive impairment after stroke: clinical determinants and its associations with long-term stroke outcomes. *Journal of the American Geriatrics Society*, *50*(4), 700-706.
- Pauca, A. L., O'Rourke, M. F., & Kon, N. D. (2001). Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform. *Hypertension*, *38*(4), 932-937.
- Pearson, T. A., Blair, S. N., Daniels, S. R., Eckel, R. H., Fair, J. M., Fortmann, S. P., Franklin, B. A., Goldstein, L. B., Greenland, P., & Grundy, S. M. (2002). AHA guidelines for primary prevention of cardiovascular

disease and stroke: 2002 update consensus panel guide to comprehensive risk reduction for adult patients without coronary or other atherosclerotic vascular diseases. *Circulation*, 106(3), 388-391.

- Pohjasvaara, T., Vataja, R., Leppävuori, A., Kaste, M., & Erkinjuntti, T. (2001). Depression is an independent predictor of poor long-term functional outcome post-stroke. *European Journal of Neurology*, 8(4), 315-319.
- Pollock, R. D., Woledge, R. C., Mills, K. R., Martin, F. C., & Newham, D. J. (2010). Muscle activity and acceleration during whole body vibration: effect of frequency and amplitude. *Clinical Biomechanics*, 25(8), 840-846. doi: 10.1016/j.clinbiomech.2010.05.004
- Potempa, K., Lopez, M., Braun, L. T., Szidon, J. P., Fogg, L., & Tincknell, T. (1995). Physiological outcomes of aerobic exercise training in hemiparetic stroke patients. *Stroke*, 26(1), 101-105.
- Powers, S. K., & Howley, E. T. (2015). *Exercise physiology: theory and application to fitness and performance* (9th ed.). New York, NY: McGraw-Hill Education.
- Rankin, J. (1957). Cerebral vascular accidents in patients over the age of 60. II. Prognosis. *Scottish Medical Journal*, 2(5), 200.
- Ranoux, D., Cohen, A., Cabanes, L., Amarenco, P., Bousser, M., & Mas, J. (1993). Patent foramen ovale: is stroke due to paradoxical embolism? *Stroke*, 24(1), 31-34.
- Rasquin, S., Lodder, J., Ponds, R., Winkens, I., Jolles, J., & Verhey, F. (2003). Cognitive functioning after stroke: a one-year follow-up study. *Dementia and Geriatric Cognitive Disorders*, 18(2), 138-144.
- Rauramaa, R., Salonen, J. T., Seppänen, K., Salonen, R., Venäläinen, J. M., Ihanainen, M., & Rissanen, V. (1986). Inhibition of platelet aggregability by moderate-intensity physical exercise: a randomized clinical trial in overweight men. *Circulation*, 74(5), 939-944.
- Redline, S., Yenokyan, G., Gottlieb, D. J., Shahar, E., O'Connor, G. T., Resnick, H. E., Diener-West, M., Sanders, M. H., Wolf, P. A., & Geraghty, E. M. (2010). Obstructive sleep apnea-hypopnea and incident stroke: the sleep heart health study. *American Journal of Respiratory and Critical Care Medicine*, 182(2), 269-277.
- Regterschot, G. R. H., Van Heuvelen, M. J., Zeinstra, E. B., Fuermaier, A. B., Tucha, L., Koerts, J., Tucha, O., & Van Der Zee, E. A. (2014). Whole body vibration improves cognition in healthy young adults. *PLoS ONE*, 9(6).
- Reneman, R., Van Merode, T., Hick, P., & Hoeks, A. (1985). Flow velocity patterns in and distensibility of the carotid artery bulb in subjects of various ages. *Circulation*, 71(3), 500-509.
- Reneman, R. S., van Merode, T., Brands, P. J., & Hoeks, A. P. (1992). Inhomogeneities in arterial wall properties under normal and pathological conditions. *Journal of Hypertension*, 10, S35-S40.
- Reneman, R. S., Van Merode, T., Hick, P., Muijtjens, A. M., & Hoeks, A. P. (1986). Age-related changes in carotid artery wall properties in men. *Ultrasound in Medicine & Biology*, 12(6), 465-471.
- Reynolds, K., Lewis, B., Nolen, J. D. L., Kinney, G. L., Sathya, B., & He, J. (2003). Alcohol consumption and risk of stroke: a meta-analysis. *JAMA*, 289(5), 579-588.
- Ridker, P. M., Hennekens, C. H., Manson, J., Vaughan, D., & Stampfer, M. (1994). Prospective study of endogenous tissue plasminogen activator and risk of stroke. *The Lancet*, 343(8903), 940-943.
- Riley, W., Freedman, D., Higgs, N., Barnes, R., Zinkgraf, S., & Berenson, G. (1986). Decreased arterial elasticity associated with cardiovascular disease risk factors in the young. Bogalusa Heart Study. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 6(4), 378-386.

- Rimmer, J. H., Rauworth, A. E., Wang, E. C., Nicola, T. L., & Hill, B. (2009). A preliminary study to examine the effects of aerobic and therapeutic (nonaerobic) exercise on cardiorespiratory fitness and coronary risk reduction in stroke survivors. *Archives of Physical Medicine and Rehabilitation, 90*(3), 407-412.
- Rittweger, J., Beller, G., & Felsenberg, D. (2000). Acute physiological effects of exhaustive whole-body vibration exercise in man. *Clinical Physiology, 20*(2), 134-142.
- Rittweger, J., Ehrig, J., Just, K., Mutschelknauss, M., Kirsch, K., & Felsenberg, D. (2002a). Oxygen uptake in whole-body vibration exercise: influence of vibration frequency, amplitude, and external load. *International Journal of Sports Medicine, 23*(6), 428-432.
- Rittweger, J., Just, K., Kautzsch, K., Reeg, P., & Felsenberg, D. (2002b). Treatment of chronic lower back pain with lumbar extension and whole-body vibration exercise: a randomized controlled trial. *Spine, 27*(17), 1829-1834.
- Rittweger, J., Mutschelknauss, M., & Felsenberg, D. (2003). Acute changes in neuromuscular excitability after exhaustive whole body vibration exercise as compared to exhaustion by squatting exercise. *Clinical Physiology and Functional Imaging, 23*(2), 81-86.
- Rittweger, J., Schiessl, H., & Felsenberg, D. (2001). Oxygen uptake during whole-body vibration exercise: comparison with squatting as a slow voluntary movement. *European Journal of Applied Physiology, 86*(2), 169-173.
- Ritzmann, R., Gollhofer, A., & Kramer, A. (2013). The influence of vibration type, frequency, body position and additional load on the neuromuscular activity during whole body vibration. *European Journal of Applied Physiology, 113*(1), 1-11. doi: 10.1007/s00421-012-2402-0
- Robinson, R. G., & Spalletta, G. (2010). Poststroke depression: a review. *Canadian Journal of Psychiatry, 55*(6), 341.
- Robison, J., Wiles, R., Ellis-Hill, C., McPherson, K., Hyndman, D., & Ashburn, A. (2009). Resuming previously valued activities post-stroke: who or what helps? *Disability & Rehabilitation, 31*(19), 1555-1566.
- Rödén-Jülig, Å., Britton, M., Gustafsson, C., & Fugl-Meyer, A. (1994). Validation of four scales for the acute stage of stroke. *Journal of Internal Medicine, 236*(2), 125-136.
- Rödén-Jülig, Å., Britton, M., Malmkvist, K., & Leijd, B. (2003). Aspirin in the prevention of progressing stroke: a randomized controlled study. *Journal of Internal Medicine, 254*(6), 584-590.
- Rodgers, H., Greenaway, J., Davies, T., Wood, R., Steen, N., & Thomson, R. (2004). Risk factors for first-ever stroke in older people in the north east of England a population-based study. *Stroke, 35*(1), 7-11.
- Roelants, M., Delecluse, C., Goris, M., & Verschueren, S. (2004). Effects of 24 weeks of whole body vibration training on body composition and muscle strength in untrained females. *International Journal of Sports Medicine, 25*(1), 1-5.
- Roelants, M., Verschueren, S., Delecluse, C., Levin, O., & Stijnen, V. (2006). Whole-body-vibration-induced increase in leg muscle activity during different squat exercises. *The Journal of Strength & Conditioning Research, 20*(1), 124.
- Rogowski, O., Shapira, I., Shirom, A., Melamed, S., Toker, S., & Berliner, S. (2007). Heart rate and microinflammation in men: a relevant atherothrombotic link. *Heart, 93*(8), 940-944.
- Rosengren, A., Hawken, S., Ôunpuu, S., Sliwa, K., Zubaid, M., Almahmeed, W. A., Blackett, K. N., Sitthiamorn, C., Sato, H., & Yusuf, S. (2004). Association of psychosocial risk factors with risk of acute

- myocardial infarction in 11 119 cases and 13 648 controls from 52 countries (the INTERHEART study): case-control study. *The Lancet*, 364(9438), 953-962.
- Ross, R. (1993). The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature*, 362, 801-809. doi: 10.1038/362801a0
- Ross, R. (1995). Cell biology of atherosclerosis. *Annual Review of Physiology*, 57(1), 791-804.
- Ross, R. (1999). Atherosclerosis- an inflammatory disease. *New England Journal of Medicine*, 340(2), 115-126.
- Rothwell, P., Eliasziw, M., Gutnikov, S., Fox, A., Taylor, D., Mayberg, M., Warlow, C., Barnett, H., & Collaboration, C. E. T. (2003). Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *The Lancet*, 361(9352), 107-116.
- Rothwell, P. M., Howard, S. C., Power, D. A., Gutnikov, S. A., Algra, A., van Gijn, J., Clark, T. G., Murphy, M. F., & Warlow, C. P. (2004). Fibrinogen concentration and risk of ischemic stroke and acute coronary events in 5113 patients with transient ischemic attack and minor ischemic stroke. *Stroke*, 35(10), 2300-2305.
- Rowell, L. B. (1986). *Human circulation: regulation during physical stress*. New York, NY: Oxford University Press.
- Rowell, L. B., & O'Leary, D. S. (1990). Reflex control of the circulation during exercise: chemoreflexes and mechanoreflexes. *Journal of Applied Physiology*, 69(2), 407-418.
- Rubanyi, G. M., Romero, J. C., & Vanhoutte, P. M. (1986). Flow-induced release of endothelium-derived relaxing factor. *American Journal of Physiology- Heart and Circulatory Physiology*, 250(6), H1145-H1149.
- Rubin, C., Pope, M., Fritton, J. C., Magnusson, M., Hansson, T., & McLeod, K. (2003). Transmissibility of 15-hertz to 35-hertz vibrations to the human hip and lumbar spine: determining the physiologic feasibility of delivering low-level anabolic mechanical stimuli to skeletal regions at greatest risk of fracture because of osteoporosis. *Spine*, 28(23), 2621-2627.
- Russo, G., Leopold, J. A., & Loscalzo, J. (2002). Vasoactive substances: nitric oxide and endothelial dysfunction in atherosclerosis. *Vascular Pharmacology*, 38(5), 259-269.
- Sabaté, E., & Wimalaratna, S. (2004). Acute Stroke. *Background paper for "priority medicines for Europe and the world, a public health approach to innovation*.
- Sacco, R. L., Benjamin, E. J., Broderick, J. P., Dyken, M., Easton, J. D., Feinberg, W. M., Goldstein, L. B., Gorelick, P. B., Howard, G., & Kittner, S. J. (1997). Risk factors. *Stroke*, 28(7), 1507-1517.
- Safar, M., Simon, A. C., & Levenson, J. (1984). Structural changes of large arteries in sustained essential hypertension. *Hypertension*, 6(6), III117.
- Safar, M. E. (1989). Pulse pressure in essential hypertension: clinical and therapeutical implications. *Journal of Hypertension*, 7(10), 769-776.
- Safar, M. E., Czernichow, S., & Blacher, J. (2006). Obesity, arterial stiffness, and cardiovascular risk. *Journal of the American Society of Nephrology*, 17(4), S109-S111.
- Sajadieh, A., Nielsen, O. W., Rasmussen, V., Hein, H. O., Abedini, S., & Hansen, J. F. (2004). Increased heart rate and reduced heart-rate variability are associated with subclinical inflammation in middle-aged and elderly subjects with no apparent heart disease. *European Heart Journal*, 25(5), 363-370.

- Salter, K. L., Moses, M. B., Foley, N. C., & Teasell, R. W. (2008). Health-related quality of life after stroke: what are we measuring? *International Journal of Rehabilitation Research*, 31(2), 111-117.
- Salvi, P., Lio, G., Labat, C., Ricci, E., Pannier, B., & Benetos, A. (2004). Validation of a new non-invasive portable tonometer for determining arterial pressure wave and pulse wave velocity: the PulsePen device. *Journal of Hypertension*, 22(12), 2285-2293.
- Samijo, S. K., Willigers, J. M., Barkhuysen, R., Kitslaar, P., Reneman, R. S., Brands, P. J., & Hoeks, A. (1998). Wall shear stress in the human common carotid artery as function of age and gender. *Cardiovascular Research*, 39(2), 515-522.
- Samuelson, B., Jorfeldt, L., & Ahlborg, B. (1989). Influence of vibration on work performance during ergometer cycling. *Uppsala Journal of Medical Sciences*, 94(1), 73-79.
- Sanchez-Gonzalez, M., Wong, A., Vicil, F., Gil, R., Park, S., & Figueroa, A. (2012). Impact of passive vibration on pressure pulse wave characteristics. *Journal of human hypertension*, 26(10), 610-615.
- Sands, W. A., McNeal, J. R., Stone, M. H., Haff, G. G., & Kinser, A. M. (2008). Effect of vibration on forward split flexibility and pain perception in young male gymnasts. *International Journal of Sports Physiology and Performance*, 3, 469-481.
- Sands, W. A., McNeal, J. R., Stone, M. H., Russell, E. M., & Jemni, M. (2006). Flexibility enhancement with vibration: acute and long-term. *Medicine & Science in Sports & Exercise*, 38(4), 720.
- Sandvik, L., Erikssen, J., Thaulow, E., Erikssen, G., Mundal, R., & Rodahl, K. (1993). Physical fitness as a predictor of mortality among healthy, middle-aged Norwegian men. *New England Journal of Medicine*, 328(8), 533-537.
- Saunders, D. H., Greig, C. A., Young, A., & Mead, G. E. (2004). Physical fitness training for stroke patients. *Stroke*, 35(9), 2235-2235.
- Sayed-Tabatabaei, F., Van Rijn, M., Schut, A., Aulchenko, Y., Croes, E., Zillikens, M., Pols, H., Witteman, J., Oostra, B., & Van Duijn, C. (2005). Heritability of the function and structure of the arterial wall: findings of the Erasmus Rucphen Family (ERF) study. *Stroke*, 36(11), 2351-2356.
- Schillaci, G., & Parati, G. (2008). Ambulatory arterial stiffness index: merits and limitations of a simple surrogate measure of arterial compliance. *Journal of Hypertension*, 26(2), 182-185.
- Schillaci, G., Pirro, M., Mannarino, M. R., Pucci, G., Savarese, G., Franklin, S. S., & Mannarino, E. (2006). Relation between renal function within the normal range and central and peripheral arterial stiffness in hypertension. *Hypertension*, 48(4), 616-621.
- Schlegel, D., Kolb, S. J., Luciano, J. M., Tovar, J. M., Cucchiara, B. L., Liebeskind, D. S., & Kasner, S. E. (2003). Utility of the NIH Stroke Scale as a predictor of hospital disposition. *Stroke*, 34(1), 134-137.
- Schlegel, D. J., Tanne, D., Demchuk, A. M., Levine, S. R., & Kasner, S. E. (2004). Prediction of hospital disposition after thrombolysis for acute ischemic stroke using the National Institutes of Health Stroke Scale. *Archives of Neurology*, 61(7), 1061-1064.
- Schmidt, R., Mechtler, L., Kinkel, P. R., Fazekas, F., Kinkel, W. R., & Freidl, W. (1993). Cognitive impairment after acute supratentorial stroke: a 6-month follow-up clinical and computed tomographic study. *European Archives of Psychiatry and Clinical Neuroscience*, 243(1), 11-15.
- Scuteri, A., Brancati, A. M., Gianni, W., Assisi, A., & Volpe, M. (2005). Arterial stiffness is an independent risk factor for cognitive impairment in the elderly: a pilot study. *Journal of Hypertension*, 23(6), 1211-1216.

- Shah, R. S., & Cole, J. W. (2010). Smoking and stroke: the more you smoke the more you stroke. *Expert Review of Cardiovascular Therapy*, 8(7), 917-932.
- Sharman, J. E., Lim, R., Qasem, A. M., Coombes, J. S., Burgess, M. I., Franco, J., Garrahy, P., Wilkinson, I. B., & Marwick, T. H. (2006). Validation of a generalized transfer function to noninvasively derive central blood pressure during exercise. *Hypertension*, 47(6), 1203-1208.
- Sherman, D. L. (2000). Exercise and endothelial function. *Coronary Artery Disease*, 11(2), 117-122.
- Shulman, K. I., Herrmann, N., Brodaty, H., Chiu, H., Lawlor, B., Ritchie, K., & Scanlan, J. M. (2006). IPA survey of brief cognitive screening instruments. *International Psychogeriatrics*, 18(02), 281-294.
- Sierksma, A., Lebrun, C. E., van der Schouw, Y. T., Grobbee, D. E., Lamberts, S. W., Hendriks, H. F., & Bots, M. L. (2004a). Alcohol consumption in relation to aortic stiffness and aortic wave reflections: a cross-sectional study in healthy postmenopausal women. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 24(2), 342-348.
- Sierksma, A., Muller, M., van der Schouw, Y. T., Grobbee, D. E., Hendriks, H. F., & Bots, M. L. (2004b). Alcohol consumption and arterial stiffness in men. *Journal of Hypertension*, 22(2), 357-362.
- Silva, A. T., Dias, M. P. F., Calixto Jr, R., Carone, A. L., Martinez, B. B., Silva, A. M., & Honorato, D. C. (2014). Acute effects of whole-body vibration on the motor function of patients with stroke: a randomized clinical trial. *American Journal of Physical Medicine & Rehabilitation*, 93(4), 310-319.
- Simons, L. A., McCallum, J., Friedlander, Y., & Simons, J. (1998). Risk factors for ischemic stroke Dubbo Study of the elderly. *Stroke*, 29(7), 1341-1346.
- Sims, J., Galea, M., Taylor, N., Dodd, K., Jespersen, S., Joubert, L., & Joubert, J. (2009). Regenerate: assessing the feasibility of a strength - training program to enhance the physical and mental health of chronic post stroke patients with depression. *International Journal of Geriatric Psychiatry*, 24(1), 76-83.
- Singhal, A., Farooqi, I. S., Cole, T. J., O'Rahilly, S., Fewtrell, M., Kattahorn, M., Lucas, A., & Deanfield, J. (2002). Influence of leptin on arterial distensibility a novel link between obesity and cardiovascular disease? *Circulation*, 106(15), 1919-1924.
- Soga, J., Nakamura, S., Nishioka, K., Umemura, T., Jitsuiki, D., Hidaka, T., Teragawa, H., Takemoto, H., Goto, C., & Yoshizumi, M. (2008). Relationship between augmentation index and flow-mediated vasodilation in the brachial artery. *Hypertension Research*, 31(7), 1293-1298.
- Stavem, K., Lossius, M., & Ronning, O. (2002). Reliability and validity of the Canadian Neurological Scale in retrospective assessment of initial stroke severity. *Cerebrovascular Diseases (Basel, Switzerland)*, 16(3), 286-291.
- Stewart, J. A., Cochrane, D. J., & Morton, R. H. (2009). Differential effects of whole body vibration durations on knee extensor strength. *Journal of Science and Medicine in Sport / Sports Medicine Australia*, 12(1), 50-53. doi: 10.1016/j.jsams.2007.09.005
- Stoner, L., Faulkner, J., Westrupp, N., & Lambrick, D. (2015). Sexual differences in central arterial wave reflection are evident in prepubescent children. *Journal of Hypertension*, 33(2), 304-307.
- Stoner, L., Lambrick, D. M., Faulkner, J., & Young, J. (2013). Guidelines for the use of pulse wave analysis in adults and children. *Journal of Atherosclerosis and Thrombosis*, 20(4), 404.
- Stoner, L., Lambrick, D. M., Westrupp, N., Young, J., & Faulkner, J. (2014). Validation of oscillometric pulse wave analysis measurements in children. *American Journal of Hypertension*, 27(6), 865-872.

- Stoner, L., & Sabatier, M. J. (2012). Use of ultrasound for non-invasive assessment of flow-mediated dilation. *Journal of Atherosclerosis and Thrombosis*, *19*(5), 407-421.
- Stoner, L., Young, J. M., & Fryer, S. (2012). Assessments of arterial stiffness and endothelial function using pulse wave analysis. *International Journal of Vascular Medicine*, *2012*.
- Störk, S., van den Beld, A. W., von Schacky, C., Angermann, C. E., Lamberts, S. W., Grobbee, D. E., & Bots, M. L. (2004). Carotid artery plaque burden, stiffness, and mortality risk in elderly men a prospective, population-based cohort study. *Circulation*, *110*(3), 344-348.
- Studenski, S., Duncan, P. W., Perera, S., Reker, D., Lai, S. M., & Richards, L. (2005). Daily functioning and quality of life in a randomized controlled trial of therapeutic exercise for subacute stroke survivors. *Stroke*, *36*(8), 1764-1770.
- Sugawara, J., Hayashi, K., Yokoi, T., Cortez-Cooper, M. Y., DeVan, A. E., Anton, M. A., & Tanaka, H. (2005). Brachial-ankle pulse wave velocity: an index of central arterial stiffness? *Journal of Human Hypertension*, *19*(5), 401-406.
- Sugawara, J., Maeda, S., Otsuki, T., Tanabe, T., Ajisaka, R., & Matsuda, M. (2004). Effects of nitric oxide synthase inhibitor on decrease in peripheral arterial stiffness with acute low-intensity aerobic exercise. *American Journal of Physiology-Heart and Circulatory Physiology*, *287*(6), H2666-H2669.
- Sugawara, J., Otsuki, T., Tanabe, T., Maeda, S., Kuno, S., Ajisaka, R., & Matsuda, M. (2003). The effects of low-intensity single-leg exercise on regional arterial stiffness. *The Japanese Journal of Physiology*, *53*(3), 239-241.
- Sugioka, K., Hozumi, T., Sciacca, R. R., Miyake, Y., Titova, I., Gaspard, G., Sacco, R. L., Homma, S., & Di Tullio, M. R. (2002). Impact of aortic stiffness on ischemic stroke in elderly patients. *Stroke*, *33*(8), 2077-2081.
- Sulter, G., Steen, C., & De Keyser, J. (1999). Use of the Barthel index and modified Rankin scale in acute stroke trials. *Stroke*, *30*(8), 1538-1541.
- Svindland, A. (1983). The localization of sudanophilic and fibrous plaques in the main left coronary bifurcation. *Atherosclerosis*, *48*(2), 139-145.
- Tanaka, H., Dinunno, F. A., Monahan, K. D., Clevenger, C. M., DeSouza, C. A., & Seals, D. R. (2000). Aging, habitual exercise, and dynamic arterial compliance. *Circulation*, *102*(11), 1270-1275.
- Tanaka, H., Munakata, M., Kawano, Y., Ohishi, M., Shoji, T., Sugawara, J., Tomiyama, H., Yamashina, A., Yasuda, H., & Sawayama, T. (2009). Comparison between carotid-femoral and brachial-ankle pulse wave velocity as measures of arterial stiffness. *Journal of Hypertension*, *27*(10), 2022-2027.
- Tanaka, H., & Safar, M. E. (2005). Influence of lifestyle modification on arterial stiffness and wave reflections. *American Journal of Hypertension*, *18*(1), 137-144.
- Teixeira-Salmela, L. F., Olney, S. J., Nadeau, S., & Brouwer, B. (1999). Muscle strengthening and physical conditioning to reduce impairment and disability in chronic stroke survivors. *Archives of Physical Medicine and Rehabilitation*, *80*(10), 1211-1218. doi: [http://dx.doi.org/10.1016/S0003-9993\(99\)90018-7](http://dx.doi.org/10.1016/S0003-9993(99)90018-7)
- Teo, K. K., Ounpuu, S., Hawken, S., Pandey, M., Valentin, V., Hunt, D., Diaz, R., Rashed, W., Freeman, R., & Jiang, L. (2006). Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *The Lancet*, *368*(9536), 647-658.
- Teoh, V., Sims, J., & Milgrom, J. (2009). Psychosocial predictors of quality of life in a sample of community-dwelling stroke survivors: a longitudinal study. *Topics in Stroke Rehabilitation*, *16*(2), 157-166.

- The Stroke Foundation New Zealand. (1998). *Life after stroke: a guide for people with a stroke and their families*. Wellington: The Stroke Foundation New Zealand Inc.
- The Stroke Foundation New Zealand. (2014). Facts about stroke in New Zealand, from <http://www.stroke.org.nz/stroke-facts-and-fallacies>
- Thommessen, B., Thoresen, G. E., Bautz-Holter, E., & Laake, K. (2001). Validity of the aphasia item from the Scandinavian Stroke Scale. *Cerebrovascular Diseases, 13*(3), 184-186.
- Tihanyi, T. K., Horváth, M., Fazekas, G., Hortobágyi, T., & Tihanyi, J. (2007). One session of whole body vibration increases voluntary muscle strength transiently in patients with stroke. *Clinical Rehabilitation, 21*(9), 782-793.
- Tillin, T., Chambers, J., Malik, I., Coady, E., Byrd, S., Mayet, J., Wright, A. R., Kooner, J., Shore, A., & Thom, S. (2007). Measurement of pulse wave velocity: site matters. *Journal of Hypertension, 25*(2), 383-389.
- Tirilazad International Steering Committee. (2000). Tirilazad mesylate in acute ischemic stroke: a systematic review. *Stroke, 31*(9), 2257-2265.
- Tombaugh, T. N., & McIntyre, N. J. (1992). The mini-mental state examination: a comprehensive review. *Journal of the American Geriatrics Society*.
- Tomiyaama, H., Koji, Y., Yambe, M., Shiina, K., Motobe, K., Yamada, J., Shido, N., Tanaka, N., Chikamori, T., & Yamashina, A. (2005). Brachial-ankle pulse wave velocity is a simple and independent predictor of prognosis in patients with acute coronary syndrome. *Circulation Journal: Official Journal of the Japanese Circulation Society, 69*(7), 815-822.
- Torvinen, S., Kannus, P., Sievänen, H., Järvinen, T. A. H., Pasanen, M., Kontulainen, S., Järvinen, T. L. N., Järvinen, M., Oja, P., & Vuori, I. (2002a). Effect of a vibration exposure on muscular performance and body balance. Randomized cross-over study. *Clinical Physiology and Functional Imaging, 22*(2), 145-152.
- Torvinen, S., Kannus, P., Sievänen, H., Järvinen, T., Pasanen, M., Kontulainen, S., Järvinen, T., Järvinen, M., Oja, P., & Vuori, I. (2002b). Effect of four-month vertical whole body vibration on performance and balance. *Medicine & Science in Sports & Exercise, 34*(9), 1523-1528.
- Torvinen, S., Kannus, P., Sievänen, H., Järvinen, T. A., Pasanen, M., Kontulainen, S., Nenonen, A., Järvinen, T. L., Paakkala, T., & Järvinen, M. (2003). Effect of 8-month vertical whole body vibration on bone, muscle performance, and body balance: a randomized controlled study. *Journal of Bone and Mineral Research, 18*(5), 876-884.
- Torvinen, S., Sievänen, H., Järvinen, T. A., Pasanen, M., Kontulainen, S., & Kannus, P. (2002c). Effect of 4-min vertical whole body vibration on muscle performance and body balance: a randomized cross-over study. *International Journal of Sports Medicine, 23*(5), 374-379.
- Toschke, A. M., Tilling, K., Cox, A. M., Rudd, A., Heuschmann, P. U., & Wolfe, C. (2010). Patient-specific recovery patterns over time measured by dependence in activities of daily living after stroke and post-stroke care: the South London Stroke Register (SLSR). *European Journal of Neurology, 17*(2), 219-225.
- Tozzi, C. A., Poiani, G. J., Harangozo, A. M., Boyd, C. D., & Riley, D. J. (1989). Pressure-induced connective tissue synthesis in pulmonary artery segments is dependent on intact endothelium. *Journal of Clinical Investigation, 84*(3), 1005.
- Traub, O., & Berk, B. C. (1998). Laminar shear stress mechanisms by which endothelial cells transduce an atheroprotective force. *Arteriosclerosis, Thrombosis, and Vascular Biology, 18*(5), 677-685.

- Tronc, F., Wassef, M., Esposito, B., Henrion, D., Glagov, S., & Tedgui, A. (1996). Role of NO in flow-induced remodeling of the rabbit common carotid artery. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *16*(10), 1256-1262.
- Truelsen, T., Mähönen, M., Tolonen, H., Asplund, K., Bonita, R., & Vanuzzo, D. (2003). Trends in stroke and coronary heart disease in the WHO MONICA Project. *Stroke*, *34*(6), 1346-1352.
- Tsivgoulis, G., Vemmos, K., Papamichael, C., Spengos, K., Daffertshofer, M., Cimboneriu, A., Zis, V., Lekakis, J., Zakopoulos, N., & Mavrikakis, M. (2006). Common carotid arterial stiffness and the risk of ischaemic stroke. *European Journal of Neurology*, *13*(5), 475-481.
- Tuttle, W., & Horvath, S. M. (1957). Comparison of effects of static and dynamic work on blood pressure and heart rate. *Journal of Applied Physiology*, *10*(2), 294-296.
- Tuttolomondo, A., Di Sciacca, R., Di Raimondo, D., Serio, A., D'Aguzzo, G., Pinto, A., & Licata, G. (2010). Arterial stiffness indexes in acute ischemic stroke: relationship with stroke subtype. *Atherosclerosis*, *211*(1), 187-194.
- Tzemos, N., Lim, P., & MacDonald, T. (2002). Is exercise blood pressure a marker of vascular endothelial function? *QJM*, *95*(7), 423-429.
- Tzemos, N., Lim, P. O., Farquharson, C. A. J., Srtuthers, A. D., & MacDonald, T. M. (2000). Dundee Step Test predicts vascular endothelial dysfunction in subjects with mild to moderate essential hypertension. *Circulation*, *102*, 606.
- Tziomalos, K., Athyros, V. G., Karagiannis, A., & Mikhailidis, D. P. (2010). Endothelial dysfunction in metabolic syndrome: prevalence, pathogenesis and management. *Nutrition, Metabolism and Cardiovascular Diseases*, *20*(2), 140-146.
- Ueda, I., Tagawa, T., Watanabe, S., Yamakawa, K., Yasu, T., & Ueda, S. (2008). Comparability and reproducibility of the carotid-femoral pulse wave velocity measurements using a multi-element carotid tonometry sensor. *Journal of Human Hypertension*, *22*(10), 699-703.
- Urbina, E. M., Wadwa, R. P., Davis, C., Snively, B. M., Dolan, L. M., Daniels, S. R., Hamman, R. F., & Dabelea, D. (2010). Prevalence of increased arterial stiffness in children with type 1 diabetes mellitus differs by measurement site and sex: the SEARCH for Diabetes in Youth Study. *The Journal of Pediatrics*, *156*(5), 731-737.
- Uyttenboogaart, M., Luijckx, G., Vroomen, P. C., Stewart, R. E., & De Keyser, J. (2007). Measuring disability in stroke: relationship between the modified Rankin scale and the Barthel index. *Journal of Neurology*, *254*(8), 1113-1117.
- Vaitkevicius, P. V., Fleg, J. L., Engel, J. H., O'Connor, F. C., Wright, J. G., Lakatta, L. E., Yin, F., & Lakatta, E. G. (1993). Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation*, *88*(4), 1456-1462.
- Vallance, P., & Chan, N. (2001). Endothelial function and nitric oxide: clinical relevance. *Heart*, *85*(3), 342-350.
- Van Bortel, L. M., Duprez, D., Starmans-Kool, M. J., Safar, M. E., Giannattasio, C., Cockcroft, J., Kaiser, D. R., & Thuillez, C. (2002). Clinical applications of arterial stiffness, Task Force III: recommendations for user procedures. *American Journal of Hypertension*, *15*(5), 445-452.
- Van Bortel, L. M., Hoeks, A. P., Kool, M. J., & Struijker-Boudier, H. A. (1992). Introduction to large artery properties as a target for risk reduction by antihypertensive therapy. *Journal of Hypertension*, *10*, S123-S126.

- Van Bortel, L. M., Kool, M. J., & Boudier, H. A. S. (1995). Effects of antihypertensive agents on local arterial distensibility and compliance. *Hypertension*, *26*(3), 531-534.
- van de Port, I. G., Wood-Dauphinee, S., Lindeman, E., & Kwakkel, G. (2007). Effects of exercise training programs on walking competency after stroke: a systematic review. *American Journal of Physical Medicine & Rehabilitation*, *86*(11), 935-951.
- van der Heijden-Spek, J. J., Staessen, J. A., Fagard, R. H., Hoeks, A. P., Boudier, H. A. S., & Van Bortel, L. M. (2000). Effect of age on brachial artery wall properties differs from the aorta and is gender dependent a population study. *Hypertension*, *35*(2), 637-642.
- Van Dyke, T. E., & Dave, S. (2005). Risk factors for periodontitis. *Journal of the International Academy of Periodontology*, *7*(1), 3.
- Van Gaal, L. F., Mertens, I. L., & De Block, C. E. (2006). Mechanisms linking obesity with cardiovascular disease. *Nature*, *444*(7121), 875-880. doi: 10.1038/nature05487
- Van Latum, J., Koudstaal, P., Venables, G., Van Gijn, J., Kappelle, L., & Algra, A. (1995). Predictors of major vascular events in patients with a transient ischemic attack or minor ischemic stroke and with nonrheumatic atrial fibrillation. *Stroke*, *26*(5), 801-806.
- van Leeuwen-Segarceanu, E. M., Tromp, W. F., Bos, W. W., Vogels, O. J., Groothoff, J. W., & van der Lee, J. H. (2010). Comparison of two instruments measuring carotid-femoral pulse wave velocity: vicorder versus sphygmocor. *Journal of Hypertension*, *28*(8), 1687-1691.
- van Nes, I. J., Geurts, A. C., Hendricks, H. T., & Duysens, J. (2004). Short-term effects of whole-body vibration on postural control in unilateral chronic stroke patients: preliminary evidence. *American Journal of Physical Medicine & Rehabilitation*, *83*(11), 867-873.
- van Popele, N. M., Grobbee, D. E., Bots, M. L., Asmar, R., Topouchian, J., Reneman, R. S., Hoeks, A. P., van der Kuip, D. A., Hofman, A., & Witteman, J. C. (2001). Association between arterial stiffness and atherosclerosis The Rotterdam Study. *Stroke*, *32*(2), 454-460.
- Van Swieten, J., Koudstaal, P., Visser, M., Schouten, H., & Van Gijn, J. (1988). Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*, *19*(5), 604-607.
- Velayudhan, L., Ryu, S., Raczek, M., Philpot, M., Lindsay, J., Critchfield, M., & Livingston, G. (2014). Review of brief cognitive tests for patients with suspected dementia. *International Psychogeriatrics*, *26*(08), 1247-1262.
- Viscogliosi, C., Desrosiers, J., Belleville, S., Caron, C. D., Ska, B., & Group, B. (2011). Differences in participation according to specific cognitive deficits following a stroke. *Applied Neuropsychology*, *18*(2), 117-126.
- Visser, M., Bouter, L. M., McQuillan, G. M., Wener, M. H., & Harris, T. B. (1999). Elevated C-reactive protein levels in overweight and obese adults. *JAMA*, *282*(22), 2131-2135.
- Vita, J. A., & Keaney, J. F. (2002). Endothelial function a barometer for cardiovascular risk? *Circulation*, *106*(6), 640-642.
- Vlachopoulos, C., Aznaouridis, K., & Stefanadis, C. (2010). Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *Journal of the American College of Cardiology*, *55*(13), 1318-1327.
- Voges, I., Jerosch-Herold, M., Hedderich, J., Pardun, E., Hart, C., Gabbert, D. D., Kramer, H.-H., & Rickers, C. (2012). Normal values of aortic dimensions, distensibility and pulse wave velocity in children and young adults. *Journal of Cardiovascular Magnetic Resonance*, *14*(1), 1-2.

- Vokac, Z., Bell, H., Bautz-Holter, E., & Rodahl, K. (1975). Oxygen uptake/heart rate relationship in leg and arm exercise, sitting and standing. *Journal of Applied Physiology*, *39*(1), 54-59.
- Wada, T., Kodaira, K., Fujishiro, K., Maie, K.-i., Tsukiyama, E., Fukumoto, T., Uchida, T., & Yamazaki, S. (1994). Correlation of ultrasound-measured common carotid artery stiffness with pathological findings. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *14*(3), 479-482.
- Wakeling, J. M., & Nigg, B. M. (2001). Modification of soft tissue vibrations in the leg by muscular activity. *Journal of Applied Physiology*, *90*(2), 412-420.
- Wakeling, J. M., Nigg, B. M., & Rozitis, A. I. (2002). Muscle activity damps the soft tissue resonance that occurs in response to pulsed and continuous vibrations. *Journal of Applied Physiology*, *93*(3), 1093-1103.
- Wald, D. S., Law, M., & Morris, J. K. (2002). Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. *BMJ*, *325*(7374), 1202.
- Waldstein, S. R., Rice, S. C., Thayer, J. F., Najjar, S. S., Scuteri, A., & Zonderman, A. B. (2008). Pulse pressure and pulse wave velocity are related to cognitive decline in the Baltimore Longitudinal Study of Aging. *Hypertension*, *51*(1), 99-104.
- Wang, T. J., Massaro, J. M., Levy, D., Vasan, R. S., Wolf, P. A., D'Agostino, R. B., Larson, M. G., Kannel, W. B., & Benjamin, E. J. (2003). A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community: the Framingham Heart Study. *JAMA*, *290*(8), 1049-1056.
- Wang, X., Keith Jr, J. C., Struthers, A. D., & Feuerstein, G. Z. (2008). Assessment of arterial stiffness, a translational medicine biomarker system for evaluation of vascular risk. *Cardiovascular Therapeutics*, *26*(3), 214-223.
- Ware, J. E. (2004). SF-36 health survey update. *The use of psychological testing for treatment planning and outcomes assessment*, *3*, 693-718.
- Warman, G., Humphries, B., & Purton, J. (2002). The effects of timing and application of vibration on muscular contractions. *Aviation, Space, and Environmental Medicine*, *73*(2), 119-127.
- Weippert, M., Behrens, K., Rieger, A., Stoll, R., & Kreuzfeld, S. (2013). Heart rate variability and blood pressure during dynamic and static exercise at similar heart rate levels. *PLoS ONE*, *8*(12), e83690.
- Weir, C. J., Kaste, M., & Lees, K. R. (2004). Targeting neuroprotection clinical trials to ischemic stroke patients with potential to benefit from therapy. *Stroke*, *35*(9), 2111-2116.
- Wellek, S., & Blettner, M. (2012). On the proper use of the crossover design in clinical trials: part 18 of a series on evaluation of scientific publications. *Deutsches Ärzteblatt International*, *109*(15), 276.
- Wendel-Vos, G., Schuit, A., Feskens, E., Boshuizen, H., Verschuren, W., Saris, W., & Kromhout, D. (2004). Physical activity and stroke. A meta-analysis of observational data. *International Journal of Epidemiology*, *33*(4), 787-798.
- West, R., Hill, K., Hewison, J., Knapp, P., & House, A. (2010). Psychological disorders after stroke are an important influence on functional outcomes a prospective cohort study. *Stroke*, *41*(8), 1723-1727.
- Westerbacka, J., Vehkavaara, S., Bergholm, R., Wilkinson, I., Cockcroft, J., & Yki-Järvinen, H. (1999). Marked resistance of the ability of insulin to decrease arterial stiffness characterizes human obesity. *Diabetes*, *48*(4), 821-827.
- Wevers, L., van de Port, I., Vermue, M., Mead, G., & Kwakkel, G. (2009). Effects of task-oriented circuit class training on walking competency after stroke: a systematic review. *Stroke*, *40*(7), 2450-2459.

- Whisnant, J. P. (1997). Modeling of risk factors for ischemic stroke: the willis lecture. *Stroke*, 28(9), 1840-1844.
- White, C. R., & Frangos, J. A. (2007). The shear stress of it all: the cell membrane and mechanochemical transduction. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 362(1484), 1459-1467.
- White, J. H., Alston, M. K., Marquez, J. L., Sweetapple, A. L., Pollack, M. R., Attia, J., Levi, C. R., Sturm, J., & Whyte, S. (2007). Community-dwelling stroke survivors: function is not the whole story with quality of life. *Archives of Physical Medicine and Rehabilitation*, 88(9), 1140-1146.
- Wilhelmsen, L., Svärdsudd, K., Korsan-Bengtson, K., Larsson, B., Welin, L., & Tibblin, G. (1984). Fibrinogen as a risk factor for stroke and myocardial infarction. *New England Journal of Medicine*, 311(8), 501-505.
- Wilkinson, I. B., Cockcroft, J. R., & Webb, D. J. (1997a). Pulse wave analysis and arterial stiffness. *Journal of Cardiovascular Pharmacology*, 32, S33-S37.
- Wilkinson, I. B., MacCallum, H., Flint, L., Cockcroft, J. R., Newby, D. E., & Webb, D. J. (2000). The influence of heart rate on augmentation index and central arterial pressure in humans. *The Journal of Physiology*, 525(1), 263-270.
- Wilkinson, P. R., Wolfe, C. D., Warburton, F. G., Rudd, A. G., Howard, R. S., Ross-Russell, R. W., & Beech, R. R. (1997b). A long-term follow-up of stroke patients. *Stroke*, 28(3), 507-512.
- Wolf, P. A., Abbott, R. D., & Kannel, W. B. (1991). Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*, 22(8), 983-988.
- Wolf, P. A., D'Agostino, R. B., O'Neal, M. A., Sytkowski, P., Kase, C. S., Belanger, A. J., & Kannel, W. B. (1992). Secular trends in stroke incidence and mortality. The Framingham Study. *Stroke*, 23(11), 1551-1555.
- Wolfe, C. D., Crichton, S. L., Heuschmann, P. U., McKevitt, C. J., Toschke, A. M., Grieve, A. P., & Rudd, A. G. (2011). Estimates of outcomes up to ten years after stroke: analysis from the prospective South London Stroke Register. *PLOS Medicine*, 8(5), e1001033.
- Wolfe, C. D., Taub, N. A., Woodrow, E., & Burney, P. (1991). Assessment of scales of disability and handicap for stroke patients. *Stroke*, 22(10), 1242-1244.
- Wolinsky, H., & Glagov, S. (1964). Structural basis for the static mechanical properties of the aortic media. *Circulation Research*, 14(5), 400-413.
- Wolinsky, H., & Glagov, S. (1969). Comparison of abdominal and thoracic aortic medial structure in mammals. *Circulation Research*, 25(6), 677-686.
- Wong, A., Sanchez-Gonzalez, M. A., Gil, R., Vicil, F., Park, S. Y., & Figueroa, A. (2011). Passive vibration on the legs reduces peripheral and systemic arterial stiffness. *Hypertension Research*, 35(1), 126-127.
- Wood, P. D., Stefanick, M. L., Dreon, D. M., Frey-Hewitt, B., Garay, S. C., Williams, P. T., Superko, H. R., Fortmann, S. P., Albers, J. J., & Vranizan, K. M. (1988). Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *New England Journal of Medicine*, 319(18), 1173-1179.
- Yaggi, H. K., Concato, J., Kernan, W. N., Lichtman, J. H., Brass, L. M., & Mohsenin, V. (2005). Obstructive sleep apnea as a risk factor for stroke and death. *New England Journal of Medicine*, 353(19), 2034-2041.

- Yamaguchi, T., Sano, K., Takakura, K., Saito, I., Shinohara, Y., Asano, T., & Yasuhara, H. (1998). Ebselen in acute ischemic stroke a placebo-controlled, double-blind clinical trial. *Stroke*, *29*(1), 12-17.
- Yang, Y., Wang, R., Lin, K., Chu, M., & Chan, R. (2006). Task-oriented progressive resistance strength training improves muscle strength and functional performance in individuals with stroke. *Clinical Rehabilitation*, *20*(10), 860-870.
- Young, F. B., Lees, K. R., & Weir, C. J. (2003). Strengthening acute stroke trials through optimal use of disability end points. *Stroke*, *34*(11), 2676-2680.
- Young, F. B., Lees, K. R., & Weir, C. J. (2005). Improving trial power through use of prognosis-adjusted end points. *Stroke*, *36*(3), 597-601.
- Young, J. M. (2011). *Metabolic regulation of endothelial dysfunction and cardiovascular risk*. Doctoral dissertation, University of Otago, Christchurch, New Zealand.
- Yusuf, S., Hawken, S., Ounpuu, S., Bautista, L., Franzosi, M. G., Commerford, P., Lang, C. C., Rumboldt, Z., Onen, C. L., & Lisheng, L. (2005). Obesity and the risk of myocardial infarction in 27 000 participants from 52 countries: a case-control study. *The Lancet*, *366*(9497), 1640-1649.
- Yusuf, S., Hawken, S., Ôunpuu, S., Dans, T., Avezum, A., Lanas, F., McQueen, M., Budaj, A., Pais, P., & Varigos, J. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *The Lancet*, *364*(9438), 937-952.
- Zarins, C. K., Zatina, M. A., Giddens, D. P., Ku, D. N., & Glagov, S. (1987). Shear stress regulation of artery lumen diameter in experimental atherogenesis. *Journal of Vascular Surgery*, *5*(3), 413-420.
- Zhang, M., Bai, Y., Ye, P., Luo, L., Xiao, W., Wu, H., & Liu, D. (2011). Type 2 diabetes is associated with increased pulse wave velocity measured at different sites of the arterial system but not augmentation index in a Chinese population. *Clinical Cardiology*, *34*(10), 622-627.
- Zhang, R., Chopp, M., Zhang, Z., Jiang, N., & Powers, C. (1998). The expression of P- and E-selectins in three models of middle cerebral artery occlusion. *Brain Research*, *785*(2), 207-214.
- Zhu, H., & Friedman, M. H. (2003). Relationship between the dynamic geometry and wall thickness of a human coronary artery. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *23*(12), 2260-2265.
- Zieman, S. J., Melenovsky, V., & Kass, D. A. (2005). Mechanisms, pathophysiology, and therapy of arterial stiffness. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *25*(5), 932-943.
- Zorowitz, R., Baerga, E., & Cuccurullo, S. (2004). *Types of stroke*. New York, NY: Demos Medical Publishing.
- Zou, M., Cohen, R. A., & Ullrich, V. (2004). Peroxynitrite and vascular endothelial dysfunction in diabetes mellitus. *Endothelium*, *11*(2), 89-97.

List of Appendices

Appendix A.....	168
Appendix B.....	171
Appendix C.....	175
Appendix D.....	176
Appendix E.....	177
Appendix F.....	183

Appendix A



School of Sport & Exercise
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 356 9099

PRE-EXERCISE HEALTH SCREENING FORM

Please read the following questions carefully. If you have any difficulty, please advise the researchers who are conducting the performance tests.

Please answer all of the following questions by ticking only one box for each question:

This questionnaire has been designed to identify the small number of persons (15-69 years of age) for whom physical activity might be inappropriate. The questions are based upon the Physical Activity Readiness Questionnaire (PAR-Q), originally devised by the British Columbia Dept of Health (Canada), as revised by Thomas *et al.* (1992) and Cardinal *et al.* (1996), and with added requirements of the Massey University Human Ethics Committee. The information provided by you on this form will be treated with the strictest confidentiality.

PERSONAL INFORMATION

Name: _____

Age: _____ Birth Date: ____ / ____ / ____

Address: _____

Telephone: _____ (hm) _____ (wk)

Emergency: Contact Name: _____ Telephone _____

1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?

Yes No

2. Do you feel a pain in your chest when you do physical activity?

Yes No

3. In the past month have you had chest pain when you were not doing physical activity?

Yes No

4. Do you lose your balance because of dizziness or do you ever lose consciousness?

Yes No

5. Have you suffered from recent thromboembolic or infectious disease?

Yes No

6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition? If yes, what?

Yes No _____

7. Do you have a bone or joint problem that could be made worse by vigorous exercise?

Yes No

8. Do you have any implants (e.g. pacemaker) or prosthesis (e.g. ossicular, stibocycosis)?

Yes No

9. Do you have acute inflammation of the upper limb?

10. Do you have a recent fracture?

11. Do you suffer any inner ear problems or vestibular dysfunction?

12. Do you suffer from cardiac valvular stress?

13. Have any immediate family had heart problems prior to the age of 60?

Yes No

14. Have you been hospitalised recently?

Yes No

15. Do you have gallbladder or kidney stones?

Yes No

16. Are you pregnant?

Yes No

17. Do you know of any other reason why you should not do physical activity?

Yes No

ONE MONTH POST-VIBRATION FOLLOW UP QUESTIONS

This will be conducted by a phone call one month post-vibration to find out if you have suffered from symptoms which might be related to the vibration

18. Have you suffered any ill-effects or discomfort that was directly related from the vibration exposure?

Yes No

If you answered yes to Q. 18 answer the following questions

19. What type of ill effect or discomfort was it?

20. How long after the vibration did the ill-effect or discomfort occur?

21. How long did the ill-effect or discomfort last for?

22. Did you seek medical treatment for the ill-effect of discomfort?

23. Are you still undertaking medical treatment for the ill-effect of discomfort?

You should be aware that even amongst healthy persons who undertake regular physical activity there is a risk of sudden death during exercise. Though extremely rare, such cases can occur in people with an undiagnosed heart condition. If you have any reasons to suspect that you may have a heart condition that will put you at risk during exercise, you should seek advice from a medical practitioner before undertaking the following tests.

I have read, understood and completed this questionnaire.

Signature: _____ Date: _____

References

1. Thomas S, Reading J and Shephard RJ. Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Can J Sport Sci* 17(4): 338-345.
2. Cardinal BJ, Esters J and Cardinal MK. Evaluation of the revised physical activity readiness questionnaire in older adults. *Med Sci Sports Exerc* 28(4): 468-472

Appendix B



Participant Information Sheet

Does Whole Body Vibration Exercise Affect Indicators of Cardiac Risk in Stroke?

Researchers:

Christie Yule
Ph: 027 3443884
Email: C.E.Yule@massey.ac.nz

Dr. Darryl Cochrane
Ph: (06) 356 9099 ext 84532
Email: D.Cochrane@massey.ac.nz

Dr. Lee Stoner
Ph: (04) 801 5799 ext 62403
Email: L.Stoner@massey.ac.nz

You are invited to participate in a study on the effect of whole body vibrations on indicators of cardiac risk in stroke survivors, with particular interest on carotid arterial stiffness. Participation is entirely voluntary and you will have the right to withdraw without explanation at any time. The study would commence on the 31st of March 2014 and should conclude by the 20th of June 2014. This is a supervised student research study through the School of Sport and Exercise at Massey University Palmerston North.

We are recruiting eighteen sedentary male and female stroke survivors who suffered a stroke between 6 months to 5 years prior, and are aged between 40-65 years. The first 18 eligible people will be required for 12 weeks and be randomly allocated into two equal groups (Group A and Group B). Both groups will complete 4 weeks of whole body vibration training, 4 weeks of their normal daily activity, and be required for 4 separate testing's. Group A will start with the 4 weeks whole body vibration training whilst the Group B will continue their normal daily living activities. Once this is completed these groups will then swap over, so Group B now participates in whole body vibration training whilst Group A continues their normal daily living. The whole body vibration will be completed at the Stewart Centre in Palmerston North for up to 20 minutes of exercise, three times a week. It should be noted that sedentary means you do not participate in at least 30 minutes of moderate intensity physical activity on at least 3 days of the week, for at least 3 months.

We hope to find that whole body vibration has a positive effect on carotid arterial stiffness, quality of life and cognition in stroke survivors. However, it is possible that your participation will reveal no beneficial effects from this type of training. Nevertheless, the knowledge we obtain from undertaking this study will be of benefit to patients undertaking exercise programs following a stroke.

You are ineligible to participate if you have:

- *Already been treated with Whole Body Vibration.*
- *Gallbladder or kidney stones.*
- *You suffer from inner ear problems.*
- *Any recent bone fractures.*
- *Any misalignments.*
- *A cardiac pacemaker.*
- *Recent thromboembolic or infectious disease.*
- *Unstable angina pectoris.*
- *Congestive heart failure.*
- *Peripheral arterial disease.*
- *You are pregnant.*
- *Impaired ability to follow simple verbal instructions.*
- *Any other reason to consider you will not be suitable for this investigation.*

Why Whole Body Vibration?

Whole Body Vibration (WBV) is a novel exercise intervention performed on specialised vibration machines. It was originally developed in the former Eastern Block countries to improve power and strength development in athletes. Repeated exposure to WBV training improves measures of strength and power in the elderly, and significant benefits to balance and gait have been seen within as little as six weeks in elderly physically inactive individuals. It has been shown to be an effective intervention for improving gait and coordination with patients suffering from Parkinson's disease. However, no studies have looked at vibration training and its effects on carotid arterial stiffness in stroke survivors. Arterial stiffness is a well-established cardiovascular risk factor and is consequently associated with stroke patients. Therefore vibration training and its effects on arterial stiffness in stroke could provide benefits that aid in the improvement of risk factors for stroke survivors.

Test procedure

All 18 participants will be asked to attend a familiarisation session at the Stewart Centre around a week prior to beginning the training to become familiar with the whole body vibration machine, and the measurements that will be taken throughout the study. Unfortunately not everyone will be exposed to the vibration exercise programme immediately after the familiarisation as there is a need for a comparison group. However, you will all be exposed to the vibration exercise programme at some point during the 12 week study. Group A will be completing the vibration exercise programme during week 2 through to week 5. Group B will commence their vibration exercise programme during week 7 through to week 10. In terms of testing, everyone will be asked to come into the Stewart Centre on a minimum of 3 separate occasions but if you are randomly allocated to the first group, you will be required on 4 separate occasions.

The vibration sessions consist of 5 minutes of vibration interspersed with 5 minutes of rest; this will then progress throughout the study. You will need to attend these sessions three times a week for 4 weeks. At the end of the four weeks we will ask all 18 participants to repeat the tests that you did at the beginning back at the Stewart Centre. If you are allocated into the first group you will then come in the following week and complete these same tests again. All 18 participants will be asked to repeat these tests a final time at the end of the 12 weeks.

The total time required for those allocated to Group A will be 7.5 hours; this consists of 4 testing sessions and 4 weeks of whole body vibration training. Group B participants will be required to commit to 6.75 hours; this will consist of 3 testing sessions and 4 weeks of vibration training. See attached flow chart for more information.

Measurements

All 18 participants will have measurements taken from both the SphygmoCor and Ultrasound machines. These machines are non-invasive, quick, and painless. The SphygmoCor is used as an assessment of the cardiovascular system and will be placed on the skin of the neck, wrist, and upper leg of the participant. It will gather information in regards to carotid arterial stiffness and blood pressure. The Ultrasound similarly looks at the carotid arterial stiffness and will be placed on the skin of the neck also.

As this is a supervised student research study the measurements and WBV sessions will be administered by the student researcher. She will not have her supervisor present at all times; however, she does hold a current first aid certificate and will have a telephone and emergency contacts on hand in case of an unlikely emergency.

Compensation

Compensation will be given to all participants for your time and travel costs to the Stewart Centre, depending on which group you are allocated to will depend how much you are compensated.

Possible risks and discomforts

The procedures involved in this study are of low risk. Nevertheless, as with any physical activity, there are small risks and some discomfort may be experienced. We advise participants to consult their GP prior to volunteering.

Whole Body Vibration

The vibration involves exercising on a specially designed machine that vibrates the whole body and causes muscle contractions. There is a hand rail attached for your support. The vibrations are not harmful, however in some instances you may experience redness and muscle itchiness in your legs, up to 2-3 minutes after the vibration exercise, this is a normal side effect that is harmless and is due to the temporary changes in leg blood flow.

Participants Rights

- You can ask questions on any aspect of the project at any time, and we will do our best to answer them to your satisfaction.
- As a participant in the study you will provide information on the understanding that your name will not be used unless you give permission to the researcher.
- You have the right to view your own data at any stage and have it explained to you.
- You will also be given access to a summary of the project findings when it is concluded.
- You can withdraw from the project at any time, without giving any reason and this will not affect your current or future health care.

At the end of the research you will be given a report detailing the outcome of the study, this will be personally named and sent out to your mailing address.

The information gained from this study will be reported at conferences and published in research journals. All data collected including the consent and exercise safety forms will be stored in a locked filing cabinet in the researchers Massey University office. Data will also be stored in electronic form onto the researcher's desktop computer (password sensitive) that is only accessible by the researcher. The participant's personal identification number will be used to ensure that your identity is not disclosed. The results will be confidential to the researcher and research assistant and any publications resulting from it.

After the completion of the study electronic files will be kept on the computer and all raw data will be kept in a lockable filing cabinet and all video tapes will be deleted. After five years has elapsed all data will be destroyed. After this time paper data will be shredded and electronic files will be deleted.

Compensation for injury

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC in accordance with the Accident Compensation Act 2001. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum

compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

Approval of study

This project has been reviewed and approved by the Massey University Human Ethics Committee: Southern A, Application 13/82. If you have any concerns about the conduct of this research, please contact:

Dr Brian Finch, Chair, Massey University Human Ethics Committee: Southern A

Telephone: 06 350 5799 ext 84459

Email: humanethicsoutha@massey.ac.

Appendix C



School of Sport & Exercise
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 356 9099

PARTICIPANT CONSENT FORM

This consent form will be held for a period of five (5) years

I have read the Information Sheet and have had the details of the study explained to me. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time.

In the case of an emergency, I agree that the researcher can contact my emergency person stated on my PAR-Q form.

I agree to participate in this study under the conditions set out in the Information Sheet.

Signature of Participant _____

Participants Full Name – printed _____

Date ____/____/____

Appendix D



MASSEY UNIVERSITY
TE KUNENGA KI PŪREHUROA

20 March 2014

Christie Yule
c/- School of Sport & Exercise
PN621

Dear Christie

Re: HEC: Southern A Application – 13/82
Does vibration exercise effect cardiac indices in stroke?

Thank you for your letter dated 19 March 2014.

On behalf of the Massey University Human Ethics Committee: Southern A I am pleased to advise you that the ethics of your application are now approved. Approval is for three years. If this project has not been completed within three years from the date of this letter, reapproval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

Yours sincerely

A handwritten signature in cursive script, appearing to read "B Finch".

Dr Brian Finch, Chair
Massey University Human Ethics Committee: Southern A

cc Dr Darryl Cochrane
School of Sport & Exercise
PN621

Prof Stephen Stannard, HoS
School of Sport & Exercise
PN621

Appendix E

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Thank you for completing this survey!

For each of the following questions, please mark an in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent

Very Good

Good

Fair

Poor

2. Compared to one year ago, how would you rate your health in general now?

Much better
now than one
year ago

Somewhat better
now than one
year ago

About the
same as one
year ago

Somewhat worse
now than one
year ago

Much worse
now than one
year ago

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a <u>Vigorous activities</u> , such as running, lifting heavy objects, participating in strenuous sports.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
b <u>Moderate activities</u> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
c Lifting or carrying groceries.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
d Climbing <u>several</u> flights of stairs.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
e Climbing <u>one</u> flight of stairs.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
f Bending, kneeling, or stooping.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
g Walking <u>more than a mile</u>	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
h Walking <u>several blocks</u>	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
i Walking <u>one block</u>	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
j Bathing or dressing yourself.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3

SF-36® Health Survey © 1988, 2002 by Medical Outcomes Trust and QualityMetric Incorporated. All Rights Reserved.
 SF-36® is a registered trademark of Medical Outcomes Trust.
 (SF-36 Standard, US Version 1.0)

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	Yes	No
Cut down on the <u>amount of time</u> you spent		
<input type="checkbox"/> on work or other activities	<input type="checkbox"/> 1	<input type="checkbox"/> 2
<u>Accomplished less</u> than you would like.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2
Were limited in the <u>kind</u> of work or other activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2
Had <u>difficulty</u> performing the work or other <input type="checkbox"/> activities		
(for example, it took extra effort).....	<input type="checkbox"/> 1	<input type="checkbox"/> 2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	Yes	No
Cut down on the <u>amount of time</u> you spent <input type="checkbox"/> on work		
or other activities	<input type="checkbox"/> 1	<input type="checkbox"/> 2
<u>Accomplished less</u> than you would like.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2
Did work or other activities <u>less carefully</u> <input type="checkbox"/> than usual.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2

SF-36® Health Survey © 1988, 2002 by Medical Outcomes Trust and QualityMetric Incorporated. All Rights Reserved.
 SF-36® is a registered trademark of Medical Outcomes Trust.
 (SF-36 Standard, US Version 1.0)

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
<input type="checkbox"/>				

7. How much bodily pain have you had during the past 4 weeks?

None	Verymild	Mild	Moderate	Severe	Very Severe
<input type="checkbox"/>					

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
<input type="checkbox"/>				

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

All of the time	Most of the time	A great bit of the time	Some of the time	A little of the time	None of the time
-----------------------	------------------------	-------------------------------	------------------------	----------------------------	------------------------

a Did you feel full of

pep?..... 1..... 2..... 3..... 4..... 5..... 6

b Have you been a very nervous person?..... 1..... 2..... 3..... 4..... 5..... 6

c Have you felt so down in the dumps that

nothing could cheer you up?..... 1..... 2..... 3..... 4..... 5..... 6

d Have you felt calm and peaceful?..... 1..... 2..... 3..... 4..... 5..... 6

e Did you have a lot of energy?..... 1..... 2..... 3..... 4..... 5..... 6

f Have you felt downhearted and blue?..... 1..... 2..... 3..... 4..... 5..... 6

g Did you feel worn out?..... 1..... 2..... 3..... 4..... 5..... 6

h Have you been a happy person?..... 1..... 2..... 3..... 4..... 5..... 6

i Did you feel tired?..... 1..... 2..... 3..... 4..... 5..... 6

SF-36® Health Survey © 1988, 2002 by Medical Outcomes Trust and QualityMetric Incorporated. All Rights Reserved.
SF-36® is a registered trademark of Medical Outcomes Trust.
(SF-36 Standard, US Version 1.0)

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
<input type="checkbox"/>				

11. How TRUE or FALSE is each of the following statements for you?

Definitely true	Mostly true	Don't know	Mostly false	Definitely false
--------------------	----------------	---------------	-----------------	---------------------

a I seem to get sick a little easier

than other people..... 1..... 2..... 3..... 4..... 5

b I am as healthy as anybody I know..... 1..... 2..... 3..... 4..... 5

c I expect my health to get worse..... 1..... 2..... 3..... 4..... 5

d My health is excellent..... 1..... 2..... 3..... 4..... 5

Thank you for completing these questions!

SF-36® Health Survey © 1988, 2002 by Medical Outcomes Trust and QualityMetric Incorporated. All Rights Reserved.
SF-36® is a registered trademark of Medical Outcomes Trust.
(SF-36 Standard, US Version 1.0)

Appendix F

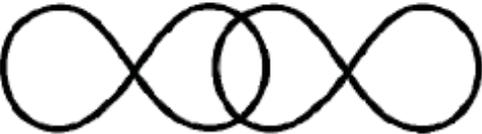
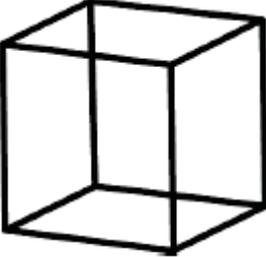
ADDENBROOKE'S COGNITIVE EXAMINATION – ACE-III New Zealand Version A (2012)																										
Name: _____ Date of Birth: _____ Hospital No. or Address: _____			Date of testing: ___/___/___ Tester's name: _____ Age at leaving full-time education: _____ Occupation: _____ Handedness: _____																							
ATTENTION																										
➤ Ask: What is the	Day _____	Date _____	Month _____	Year _____	Season _____	Attention [Score 0-5] <input style="width: 30px;" type="text"/>																				
➤ Ask: Which	No./Floor _____	Street/Hospital _____	Suburb/Town _____	City/District _____	Country _____	Attention [Score 0-5] <input style="width: 30px;" type="text"/>																				
ATTENTION																										
➤ Tell: "I'm going to give you three words and I'd like you to repeat them after me: lemon, key and ball." After subject repeats, say "Try to remember them because I'm going to ask you later." ➤ Score <i>only</i> the first trial (repeat 3 times if necessary). ➤ Register number of trials: _____						Attention [Score 0-3] <input style="width: 30px;" type="text"/>																				
ATTENTION																										
➤ Ask the subject: "Could you take 7 away from 100? I'd like you to keep taking 7 away from each new number until I tell you to stop." ➤ If subject makes a mistake, do not stop them. Let the subject carry on and check subsequent answers (e.g., 93, 84, 77, 70, 63 – score 4). ➤ Stop after five subtractions (93, 86, 79, 72, 65): _____						Attention [Score 0-5] <input style="width: 30px;" type="text"/>																				
MEMORY																										
➤ Ask: "Which 3 words did I ask you to repeat and remember?" _____						Memory [Score 0-3] <input style="width: 30px;" type="text"/>																				
FLUENCY																										
➤ Letters Say: "I'm going to give you a letter of the alphabet and I'd like you to generate as many words as you can beginning with that letter, but not names of people or places. For example, if I give you the letter "C", you could give me words like "cat, cry, clock" and so on. But, you can't give me words like Catherine or Canada. Do you understand? Are you ready? You have one minute. The letter I want you to use is the letter "P"."						Fluency [Score 0 – 7] <input style="width: 30px;" type="text"/>																				
						<table style="width: 100%; border-collapse: collapse;"> <tr><td style="border: none;">≥ 18</td><td style="border: none; text-align: right;">7</td></tr> <tr><td style="border: none;">14-17</td><td style="border: none; text-align: right;">6</td></tr> <tr><td style="border: none;">11-13</td><td style="border: none; text-align: right;">5</td></tr> <tr><td style="border: none;">8-10</td><td style="border: none; text-align: right;">4</td></tr> <tr><td style="border: none;">6-7</td><td style="border: none; text-align: right;">3</td></tr> <tr><td style="border: none;">4-5</td><td style="border: none; text-align: right;">2</td></tr> <tr><td style="border: none;">2-3</td><td style="border: none; text-align: right;">1</td></tr> <tr><td style="border: none;">0-1</td><td style="border: none; text-align: right;">0</td></tr> <tr><td style="border: none;">total</td><td style="border: none; text-align: right;">correct</td></tr> <tr><td style="border: none;"> </td><td style="border: none;"> </td></tr> </table>	≥ 18	7	14-17	6	11-13	5	8-10	4	6-7	3	4-5	2	2-3	1	0-1	0	total	correct		
≥ 18	7																									
14-17	6																									
11-13	5																									
8-10	4																									
6-7	3																									
4-5	2																									
2-3	1																									
0-1	0																									
total	correct																									
➤ Animals Say: "Now can you name as many animals as possible. It can begin with any letter."						Fluency [Score 0 – 7] <input style="width: 30px;" type="text"/>																				
						<table style="width: 100%; border-collapse: collapse;"> <tr><td style="border: none;">≥ 22</td><td style="border: none; text-align: right;">7</td></tr> <tr><td style="border: none;">17-21</td><td style="border: none; text-align: right;">6</td></tr> <tr><td style="border: none;">14-16</td><td style="border: none; text-align: right;">5</td></tr> <tr><td style="border: none;">11-13</td><td style="border: none; text-align: right;">4</td></tr> <tr><td style="border: none;">9-10</td><td style="border: none; text-align: right;">3</td></tr> <tr><td style="border: none;">7-8</td><td style="border: none; text-align: right;">2</td></tr> <tr><td style="border: none;">5-6</td><td style="border: none; text-align: right;">1</td></tr> <tr><td style="border: none;"><5</td><td style="border: none; text-align: right;">0</td></tr> <tr><td style="border: none;">total</td><td style="border: none; text-align: right;">correct</td></tr> <tr><td style="border: none;"> </td><td style="border: none;"> </td></tr> </table>	≥ 22	7	17-21	6	14-16	5	11-13	4	9-10	3	7-8	2	5-6	1	<5	0	total	correct		
≥ 22	7																									
17-21	6																									
14-16	5																									
11-13	4																									
9-10	3																									
7-8	2																									
5-6	1																									
<5	0																									
total	correct																									

MEMORY			
<p>➤ Tell: "I'm going to give you a name and address and I'd like you to repeat the name and address after me. So you have a chance to learn, we'll be doing that 3 times. I'll ask you the name and address later."</p> <p>Score only the third trial.</p>			<p>Memory [Score 0 – 7]</p> <input type="text"/>
	<i>1st Trial</i>	<i>2nd Trial</i>	<i>3rd Trial</i>
Harry Barnes 73 Church Street Woodville Hawkes Bay	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____
MEMORY			
<p>➤ Name of the current Prime Minister.....</p> <p>➤ Name a woman Prime Minister of New Zealand</p> <p>➤ Name of the USA president.....</p> <p>➤ Name of the USA president who was assassinated in the 1960s.....</p>			<p>Memory [Score 0 – 4]</p> <input type="text"/>
LANGUAGE			
<p>➤ Place a pencil and a piece of paper in front of the subject. As a practice trial, ask the subject to "Pick up the pencil and then the paper." If incorrect, score 0 and do not continue further.</p> <p>➤ If the subject is correct on the practice trial, continue with the following three commands below.</p> <ul style="list-style-type: none"> • Ask the subject to "Place the paper on top of the pencil" • Ask the subject to "Pick up the pencil but not the paper" • Ask the subject to "Pass me the pencil after touching the paper" <p>Note: Place the pencil and paper in front of the subject before each command.</p>			<p>Language [Score 0-3]</p> <input type="text"/>
LANGUAGE			
<p>➤ Ask the subject to write two (or more) complete sentences about his/her last holiday/weekend/Christmas. Write in complete sentences and do not use abbreviations. Give 1 point if there are two (or more) complete sentences about the one topic; and give another 1 point if grammar and spelling are correct.</p>			<p>Language [Score 0-2]</p> <input type="text"/>
LANGUAGE			
<p>➤ Ask the subject to repeat: 'caterpillar'; 'eccentricity'; 'unintelligible'; 'statistician' Score 2 if all are correct; score 1 if 3 are correct; and score 0 if 2 or less are correct.</p>			<p>Language [Score 0-2]</p> <input type="text"/>

Updated 17/1/2013

LANGUAGE	
<p>➤ Ask the subject to repeat: 'All that glitters is not gold'</p>	<p>Language [Score 0-1] <input type="text"/></p>
<p>➤ Ask the subject to repeat: 'A stitch in time saves nine'</p>	<p>Language [Score 0-1] <input type="text"/></p>
LANGUAGE	
<p>➤ Ask the subject to name the following pictures:</p> <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p> <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p> <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>  <p>_____ <input type="text"/></p>	<p>Language [Score 0-12] <input type="text"/></p>
LANGUAGE	
<p>➤ Using the pictures above, ask the subject to:</p> <ul style="list-style-type: none"> • Point to the one which is associated with the monarchy • Point to the one which is a marsupial • Point to the one which is found in the Antarctic • Point to the one which has a nautical connection 	<p>Language [Score 0-4] <input type="text"/></p>

Updated 17/1/2013

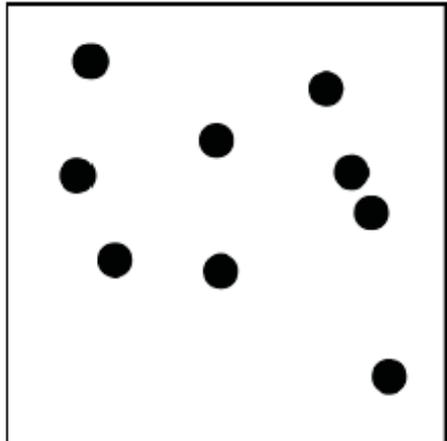
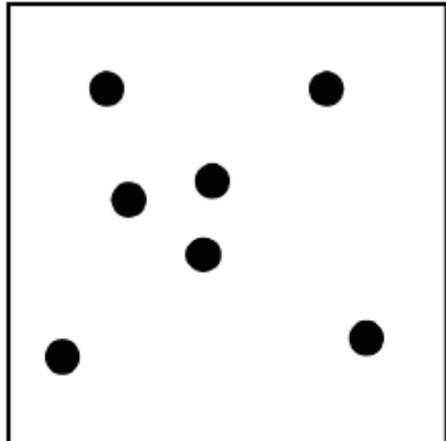
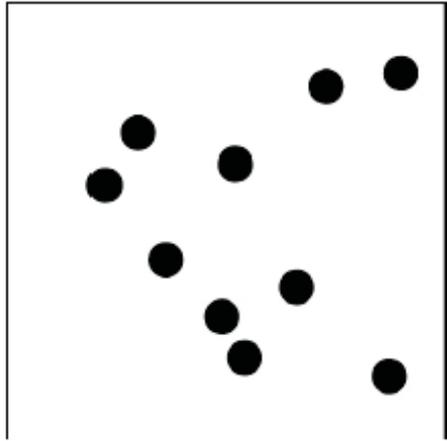
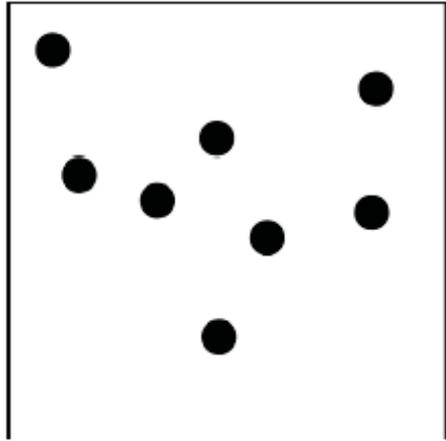
LANGUAGE	
<p>> Ask the subject to read the following words: (Score 1 only if all correct)</p> <p style="text-align: center;"> sew pint soot dough height </p>	<p>Language [Score 0-1]</p> <input type="text"/>
VISUOSPATIAL ABILITIES	
<p>> Infinity Diagram: Ask the subject to copy this diagram</p>	<p>Visuospatial [Score 0-1]</p> <input type="text"/>
	
<p>> Wire cube: Ask the subject to copy this drawing (for scoring, see instructions guide).</p>	<p>Visuospatial [Score 0-2]</p> <input type="text"/>
	
<p>> Clock: Ask the subject to draw a clock face with numbers and the hands at ten past five. (For scoring see instruction guide: circle = 1, numbers = 2, hands = 2 if all correct).</p>	<p>Visuospatial [Score 0-5]</p> <input type="text"/>

Updated 17/1/2013

VISUOSPATIAL ABILITIES

➤ Ask the subject to count the dots without pointing to them

Visuospatial
[Score 0-4]



VISUOSPATIAL ABILITIES			
➤ Ask the subject to identify the letters			Visuospatial [Score 0-4] <input style="width: 30px; height: 15px;" type="text"/>
		<input style="width: 30px; height: 15px;" type="text"/>	<input style="width: 30px; height: 15px;" type="text"/>
		<input style="width: 30px; height: 15px;" type="text"/>	<input style="width: 30px; height: 15px;" type="text"/>
MEMORY			
➤ Ask "Now tell me what you remember about that name and address we were repeating at the beginning"			
Harry Barnes 73 Church Street Woodville Hawkes Bay	Memory [Score 0-7] <input style="width: 30px; height: 15px;" type="text"/>	
MEMORY			
➤ This test should be done if the subject failed to recall one or more items above. If all items were recalled, skip the test and score 5. If only part was recalled start by ticking items recalled in the shadowed column on the right hand side; and then test not recalled items by telling the subject "ok, I'll give you some hints: was the name X, Y or Z?" and so on. Each recognised item scores one point, which is added to the point gained by recalling.			Memory [Score 0-5] <input style="width: 30px; height: 15px;" type="text"/>
Jerry Barnes	Harry Barnes	Harry Bradford	recalled
37	73	76	recalled
Church Road	Cathedral Street	Church Street	recalled
Norsewood	Woodville	Dargaville	recalled
Hawkes Bay	Hicks Bay	Bay of Plenty	recalled
SCORES			
TOTAL ACE-III SCORE			/100
Attention			/18
Memory			/26
Fluency			/14
Language			/26
Visuospatial			/16

Updated 17/1/2013