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Physiological, psychological and functional changes with Whole Body Vibration Exercise in the Frail Elderly

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

Doctor of Philosophy (PhD)

In Sport & Exercise

at Massey University (Wellington, New Zealand)

Daniel Peter Wadsworth

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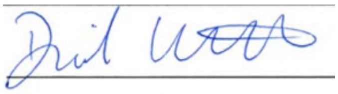
Declaration

I certify that this thesis is the result of my own investigations, except where otherwise stated. All other sources of information have been acknowledged, both in text and in the reference sections. Moreover, this work has not previously been accepted for any degree, and is not being submitted in candidature for any other degree.

Name: Daniel Wadsworth (candidate)

Signed: 

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i. Abstract

Background

The frail elderly endure comprehensive reductions in health, function, independence, wellbeing and Quality of Life. Conventional training attenuates declines but is restricted by requisite intensities and supervisory-requirements. Whole Body Vibration (WBV) exercise presents as a safe and effective training-tool for the mobile elderly, yet a paucity of research exists on its application in the frail elderly, who could benefit most.

Methods

*After pre-screening for contraindications, 117 male and female volunteers (82.5 ± 7.9 years) from residential-care-facilities were randomly allocated to Control (CON), Simulated-exercise (SIM) or WBV-exercise (WBV) groups. Continuing regular-care, WBV- and SIM-participants also underwent thrice-weekly exercise sessions for 16 weeks. Delivered by overload principle, WBV-training began with 5*1-min bouts of rotational-WBV at 6 Hz/2 mm (1:1min exercise:rest), progressing ad libitum to 10*1-min at up-to 26 Hz/4 mm, maintaining knee-flexion. Training for SIM-participants mimicked exercise stance and duration.*

Pre- and post-measures of function (Timed-Up-and-Go (TUG), Parallel Walk (PWT) and 10-m Timed-Walk tests), psychometrics (ABC-UK falls confidence, EURO-QoL-5-D and Barthel Index) and cardiovascular-health (Blood Pressures, resting Heartrate, Augmentation Index (AIx)) were completed up-to 12-months post-intervention. Twenty-participants (84.5 ± 1.7 years) from WBV- and SIM-groups underwent further bone-health assessments (serum Osteocalcin and Vitamin D, urinary Pyridinoline/Deoxypyridinoline, and Bone Mineral Density (BMD)).

Results

High levels of compliance and ease-of-use were reported, with no adverse-effects. Compared to baseline-levels, 8- and 16-weeks of WBV-training elicited clinically-important treatment-effects on participants' functionality, psychometrics and cardiovascular-health. Notably, improvements of 7.3% and 14.9% were seen in TUG- and PWT-performance, respectively, whilst falls-confidence increased by 17.4% and AIx reduced by 23.3%. Many treatment-effects remained in-place up-to 12-months post-intervention. No treatment-effects were observed for BMD-levels, but beneficial treatment-effects were detected on osteocalcin levels.

Findings showed low-level WBV-exercise to be an effective and easily-accessible exercise for the frail elderly. The exercise-intervention delivered sufficient-stimulus to significantly increase functionality, independence, confidence and Quality of Life. Furthermore, the novel vascular-health findings offer insight into the safe use of low-level WBV-exercise in patients with poor cardiovascular-health. Bone-deposition rates increased, albeit not sufficiently to enhance BMD-levels. However, the lack of adverse-effects suggest WBV-exercise is a safe and effective training-tool for this population when other training-goals are the focus.

ii. Acknowledgements

Balancing part-time PhD studies with a full-time tertiary-teaching role has required vast amounts of patience, dedication, organisation and drive on a personal level. Equally important as I reflect on this journey has been the support and assistance I have received from an array of individuals, many of whom were known to me, but many others were met along the way. It is not possible to acknowledge everyone who has helped me complete this path, but there are some whose assistance, support and guidance is particularly deserving of recognition.

First and foremost, I must acknowledge the time and dedication of all participants and staff at each of the residential-care-facilities involved, without whom this project would not have been possible. I cherished my time with so many of the participants in this study; from '10-pound poms' and trips to Fiji on banana boats to surviving earthquakes in Napier and the Wahine disaster, via tales of war-time South Africa, your stories and smiles never ceased to brighten my day and lift my energy. You captivated my interest and attention as much as the strange vibrating-machine captured yours! During this project I was also lucky enough to work with many fantastically-accommodating staff at the care-facilities involved, all of whom made me feel welcome and a part of the team during my 6-month stints at each facility, and for this I am eternally grateful.

I must also acknowledge my colleagues at Massey University and the University of the Sunshine Coast, Australia, who have dedicated patience, time, advice and support to me along the way. Chief amongst these are Rachel Page, Jim Clarke, Judy Thomas, and Ying Jin, whose patience, flexibility and assistance during long-periods of training, data-collection and assessment were invaluable in navigating this time. Likewise, the various students from Massey University's Exercise Practicum program who saw this project as being interesting- and worthwhile-enough to dedicate their valuable time to supervising training sessions. The project gratefully-received financial support from a grant from the New Zealand Accident Compensation Corporation, with additional contributions from Massey University. Without all of this support, time and professionalism from everyone, the study-design and its time-demands would not have been feasible, and I thank you all wholeheartedly.

The contributions of Janet Turnbull, Kate Scott, Paula Monahan and Mike Nowitz have been invaluable at various stages throughout this project. Janet's help and guidance were vital in developing and implementing a working project, whilst the monitoring of feedback by Janet and

Kate not only helped ensure patient safety throughout the study but also put my mind at ease. Paula’s tireless patience with this project was interminable, maintaining a smile when we couldn’t keep an appointment yet always finding the time to help our participants change in/out of gowns and undergo DXA scans. Your outlook, care and professionalism with everyone involved was a real inspiration. Mike’s wisdom and experience have been essential to the bone health component of this study, always accommodating and engaging to work with, you have been a hugely-valuable project member.

Final professional thanks must go to my research-mentor and primary supervisor Dr Sally Lark. I am fortunate enough to have taken this journey with someone whom I consider a friend, and your guidance, advice and eye-for-detail have been invaluable throughout this process, truly helping to make the project what it is. Be it corridor-conversations, video-calls or even our early-morning data collection trips, you have always been ready and willing to assist where possible, making time for and supporting me even when you had very little of both. I’m proud of what we’ve achieved with this project and look forward to a celebratory coffee and cinnamon roll!!

On a personal level, I thank the friends and family members who have consistently been interested enough to follow my research’s progress throughout my recent life. Your curiosity, support and distractions have all been equally important in helping maintain my focus and motivation. My final thanks though, must go to Zoe. Over the time-course of this project we’ve got married, brought houses, sold houses, built houses, moved countries and of course brought our beautiful daughter Poppy into this world. Perhaps I should have got it done a bit quicker don’t you think!?! You’ve been my rock through this process, giving me time to work and focus, encouraging time to relax, but most importantly helping me get through the times when I hit a wall or two along the way, always picking up the pieces and pushing me on. Without your tireless-support by my side, this project would not have got off the ground, let alone reached its conclusion.

To Poppy, with the help of your mum, your dad can do all of this – with both of us behind you, you can do anything…

DW

iii. Preface

This research project originated from initial discussions with Dr Sally Lark around the lack of accessible exercise for older adults that could improve their quality of life. Working as a Tutor in Health Sciences at Massey University at the time, I was also volunteering my time at a Cardiac Rehabilitation Clinic managed at the University by Dr Lark and colleagues with the School of Sport and Exercise. Informal discussions carried on at subsequent clinic sessions, as Dr Lark explained to me the accessibility of Whole Body Vibration exercise, detailing how she felt the accessible nature of this exercise and initial promising results in community-dwelling elderly could apply itself well to the frail elderly. After subsequent research into WBV exercise, I was convinced that it did present as a viable form of accessible exercise for this population, and the research proposal was born.

An extensive Review of Literature helped me to develop the eventual study design followed in this project, guided by discussion and debate with Dr Lark and Dr Janet Turnbull, a Consultant Geriatrician at Capital and Coast District Health Board, Wellington. Co-Supervisors were identified and provided advice for developing the Bone Health arm of the project. With their advice and guidance, I successfully applied for and received Ethical Approval for the proposed project in April 2013. In accordance with a requirement of the Ethical Committee, an additional Consultant Geriatrician, Dr Kate Scott, was also recruited to assist Dr Turnbull in regular monitoring of participant feedback and wellbeing during WBV-training. Receiving some financial-support from Massey University, Dr Lark and I explored various avenues for further support, eventually meeting with and securing funding from the New Zealand ACC which allowed us to purchase a second WBV machine and develop a feasible plan of how to deliver the training intervention to enough participants within the project time-frame.

Over the course of 4 years, I met with numerous Managers of residential-care facilities within the Wellington region, securing the support of 12. I subsequently worked with relevant Clinical Managers and Physiotherapists to identify and approach potential participants. Initial interviews and assessments were conducted by myself in-situ, often preceded by group meetings with a wider-group of potentially-interested participants. Thrice-weekly training sessions were scheduled, managed, and predominantly conducted by myself at 2 residential-care facilities concurrently, with ensuing follow-up periods overlapping the training of future cohorts at different facilities. All assessments were conducted by myself, with the assistance of Dr Lark for phlebotomy, and trained professionals at Pacific Radiology in undertaking DXA scans. During the project, I was also working full-time at Massey University, so recruited-for and managed assistance-by students from Massey University's Undergraduate Exercise-Prescription class to assist with the day-to-day delivery of training sessions.

All data-management, statistical analysis and interpretation were conducted by myself, with guidance and input from Dr Lark. For the Bone Health arm of the project, suitable laboratories were recruited to conduct biochemical analysis of samples, whilst Dr Nowitz assisted in my interpretation and understanding of DXA scan results. All written interpretation and discussion of results is my own work, with guidance from Dr Lark.

This thesis has been presented 'by publication', with a Literature Review and ensuing Methods chapter followed by Experimental chapters in the guise of four manuscripts for publication, and finally an Overall Discussion chapter. The methods chapter includes a modified version of a full methodology paper, published in 2015, which provides in-depth details of the protocols followed. Readers will find some repetition of methods in the experimental chapters, as each outlines the relevant protocols. Due to the 'by publication' structure, separate reference lists can be found at the end of each chapter.

I have found this research project to be extremely rewarding, the highlight of which has undoubtedly been working with and getting to know such an amazing group of people – their stories, chats and words of wisdom will remain with me. That the findings of this project may help to better their lives, and those of others like them, is an extremely gratifying outcome.

Daniel Wadsworth

iv. The Hypervibe

One participant in the research project was so taken by the WBV-exercise training she conducted, she convinced her residential-care facility to later purchase their own machine and was compelled to write an ode to it. She has kindly agreed to let me share it in this thesis, and her poem has been edited to preserve anonymity.

THE HYPERVIBE

At our home in Wellington, there is a stylish gym.
They offer gadgets of all kinds to suit both her and him,
Not greatly used, I must confess, by people who live here,
But recently, to my surprise, a new one did appear.

It stood there proudly, sparkling new.
"Twas labelled "Hypervibe".
I wondered if that shaking
Was something I'd survive.

I read the writing on the wall.
The Hypervibe did boast
That it could do 'most anything-
Except for making toast.

Bone density could be improved
And I may lose some weight!
Circulation would be awesome
And my Balance would be great.

If you thought that that was all you'd gain
You'd be entirely wrong.
Your muscles would be quite relaxed
But also VERY STRONG.

So every time that I take
that trot down to the gym.
I spend ten minutes shaking
Then I look at every limb

To see if promised changes
Leave anything to show.
Not yet – but if I see some change
You'll be the first to know!

[M.B. October 2017]

v. List of Figures and Tables

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vi. List of Common Abbreviations

Term	Abbreviation
10-metre Timed Walk Test	10mTW test
Activities-specific Balance Confidence UK Questionnaire	ABC-UK
American College of Sports Medicine	ACSM
Analysis of Variance	ANOVA
Augmentation Index	AIx
Beats Per Minute	bpm
Bone Mineral Density	BMD
Centimetre	cm
Cerebral Palsy	CP
Coefficients of Variation	CV
Control Group	CON
Diastolic Blood Pressure	DBP
District Health Board	DHB
Dual-energy X-ray Absorptiometry scan	DXA scan
Electromyography	EMG
Frail Elderly Vibration Exercise Responses Study	FEVER Study
Frequency of Vibration	FoV
Heart Rate	HR
Hertz	Hz
Mean Arterial Pressure	MAP
Millimetre	mm
Multiple Sclerosis	MS
National Health Service	NHS
New Zealand Accident Compensation Corporation	ACC
Parallel Walk Test	PWT
Parkinson’s Disease	PD
Peroxisome proliferator-activated receptor-γ coactivator 1α	PGC-1α
Physiotherapy	PT
Pulse Wave Analysis	PWA
Quality of Life	QoL
Resting Heartrate	rHR
Serum Osteocalcin	OC
Simulation Group	SIM
Spinal Cord Injury	SCI
Standard Error of the Mean	SEM
Systolic Blood Pressure	SBP
Timed-Up-and-Go Test	TUG
Urinary Pyridinoline	PYD
Urinary Deoxypyridinoline	DPD
US Centre for Disease Control	CDC
Vascular Endothelial Growth Factor	VEGF
Whole Body Vibration	WBV
World Health Organisation	WHO

vii. Introduction

Age-associated declines in health are markedly prevalent in older adults [1]. In particular, sarcopenia is implicated in declines in mobility and function [2, 3], where associated changes in muscle-mass/strength and gait can jeopardize balance and increase falls-risk [4], in-turn exacerbated by poor vision, diminished proprioception, and weaker muscles [5]. Resultant physical inactivity attenuates mobility and increases the degree of decline. Consequently, older-adults are three-times more likely to suffer a fall and its debilitating consequences [6, 7], whilst individuals within residential-care exhibit the highest prevalence of falls and associated injury [8]. What-is-more, over 70% of older adults display bone density scores indicative of osteoporosis [9], further increasing the incidence of fractures [10]. Hip fractures are particularly problematic in this population, representing over 50% of all fractures [11], requiring an average hospital stay of 7-21 days, and dramatically increasing the risk of residential-level care, further fractures, and even death within the ensuing 12 months [10].

Also exacerbating matters, cognitive function declines with age [12], and in older adults is often coupled with the psychological impact of reduced physical capacity and functional independence [7]. Consequently, this population often suffer from a blend of reduced cognition, self-confidence and independence, culminating in increased levels of frailty and decreased Quality of Life (QoL) and mental wellbeing [13]. What-is-more, the fear of falling itself causes severe restrictions in activity and social interaction [14], and has been identified as a contributing factor to decreased mobility and increased levels of functional-dependence and falls-risk [15]. When combined, these factors can further negatively impact on an individual's QoL and mental wellbeing [16].

Age-related declines in physical function, bone health and cognitive function can however be attenuated or even reversed with targeted exercise interventions. Strength-training successfully reverses age-related muscle- and strength-losses [17], promotes muscle-fibre hypertrophy [18, 19] and enhances bone health [20, 21], whilst targeted balance-training has also displayed success in elderly participants [22, 23]. Regular exercise can similarly have pronounced benefits on the cognitive function and psychological wellbeing of older adults, increasing cranial blood flow [24] and volume of brain matter [25], and concurrently slowing rates of cognitive decline [26]. Additionally, it can improve levels of self-efficacy, confidence and feelings of control in older adults [27]. Such improvements can lead to increasing general health, physical activity and independence, ultimately manifesting as improvements in an individual's physical health, and perhaps most importantly their mental wellbeing and QoL [28].

However, exercise-intensities of 60-85% of maximal effort are often required for such interventions to be successful, restricting the appeal-to and application-in the elderly, resulting in only ~10% of this population engaging in such training [29]. Additionally, combining low-intensity balance- and coordination-exercises with more demanding and complex strength- or aerobic-training may also deter participants [22], whilst the need for a qualified therapist to supervise restricts accessibility and increases costs. As such, successful exercise programs have mainly focussed on community-dwelling/healthy older adults who are better able to cope with the program's demands, ignoring those with greater functional-limitations and falls-risk, the frail elderly within residential-care [30, 31].

Displaying a combination of chronic medical conditions, cognitive- and functional-limitations, no group can feasibly benefit more from exercise than the frail elderly [32], yet paradoxically such factors also significantly limit their ability to exercise conventionally. As little as 2.4% of older adults meet the recommended levels of physical activity [33], therefore appropriately designed and easily-accessible exercise programs are needed for this population to maximise exercise compliance, and its associated benefits, in those willing to attempt physical activity.

Whole Body Vibration (WBV) exercise has gained significant traction as a safe and effective training tool in various populations, including athletes [34], sedentary persons [35, 36] and healthy older adults [37-39]. Used as an athletic training tool, several researchers have documented improvements in strength and power from various WBV-training programs [40-43]. Moreover, WBV exercise also presents as a safe and effective training tool in community-dwelling older adults [37-39], with researchers reporting improvements in balance [37, 44-46], physical function [47-50], muscular strength [36, 51-53], bone health [37-39], and QoL [47, 54, 55], in addition to high-levels of compliance and no adverse effects [35-37].

The minimal demands of WBV exercise make it an easily accessible form of exercise for those with mobility problems or limited cognitive-ability. Taking part is as simple as standing on a platform with knees flexed for 1-minute bouts, interspersed with rest periods. However, few researchers have explored if the use of WBV exercise in frail older adults can produce benefits similar to those reported with conventional exercise.

Some researchers have reported WBV-associated improvements in the physical function [56-61], QoL [56, 59] and bone health [60] of the frail elderly within residential-care. Interventions range in length from 6-weeks [57, 59] to 6-months [58, 60], with short, repeated 30- and 60-second bouts proving sufficient to elicit benefits in frail elderly [56, 61]. Researchers have mainly utilised vertical-WBV at intensities of up-to 35 Hz, combining dynamic-exercises with concurrent WBV-exercise in physically- and cognitively-demanding protocols [56, 59]. In fact, some studies only report functional gains when dynamic-exercise is performed concurrently during WBV [57, 58, 60]. Such demands in an exercise-protocol may not be appropriate for the majority of frail older adults, limiting their effectiveness. Lower-frequencies of WBV are less demanding on participants [62], however to-date few researchers have explored if low-level WBV can elicit benefits in the frail elderly, with only 2 researchers reporting benefits using frequencies of 6-26 Hz from the less-demanding form of rotational-WBV and no concurrent-exercises [59, 61]. Accordingly, the protocols employed by Bruyere et al. [59] and Zhang et al. [61] may be most applicable for successful implementation in this specific population.

The methodological differences between studies outlined above mean that the optimal dose and duration of WBV for use in the frail elderly remains unclear. Moreover, the placebo effects of study participation, for example in the attention received and the incidental-activity conducted [63], have not been fully considered, nor has any possible time-line for detraining after ceasing a WBV-exercise intervention program. Finally, although findings have been reported in the context of the frail elderly, only 18 of 111 participants in the largest studies to-date suffered from a moderate-to-severe degree of frailty [58, 60], whilst another used outpatients [61] who by definition are not as frail or dependant on care.

As the frail elderly frequently suffer from varying degrees of functional-limitations and/or cognitive-impairment, many of the protocols employed may actually be implausible, leading researchers to conclude that the clinical, social, and functional effects of long-term WBV in the frail elderly remain unclear. Therefore, this study aims to establish (i) if this group can attain physiological, functional and psychological benefits from a low-level WBV intervention, (ii) retention of any benefits, and (iii) the time-course of detraining. This study is important as residential care residents are often neglected in initiatives for health yet are the most vulnerable and are least able to engage in more conventional exercise activities.

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1. Literature Review

Part One: Exercise in the Elderly

1.1 Ageing Populations

1.1.1 Prevalence of ageing

In the broadest sense, the term "ageing" can be defined as the "gradual accumulation of a wide variety of molecular and cellular damage" [1], or in other words the process reflecting changes that occur over the lifespan. Using this definition, it is well recognised that the world's population is ageing at a substantial rate, and this brings with it important implications for national economies and societies [2]. At a global level, the number of those over age 60 is projected to have increased from just under 800 million in 2011 (representing 11% of the world population) to in excess of 2 billion in 2050 (representing 22% of the world population) [3]. As an example of this growth on a national level, Australia's population is currently growing at 1.8% per annum, predominantly driven by baby boomers reaching the age of retirement [2]. By the year 2020 it is estimated that, for the first time in history, people aged 65 years and older in the world will outnumber children younger than 5 years old [4]. However, the ageing population continues to grow, and get older still; the period since World War II has seen 12.6 and 12.9 years added to the life expectancy of Australian males and females, respectively [2]. Consequently, the number of "old-old adults" aged 75+ in Australia is projected to increase by 101.1% over the next two decades [2], almost tripling the demand for the aged care workforce in the process [5]. The global rise in people aged 65 years plus can be viewed as one of the greatest success stories of the twentieth century; attributed (at least in part) to commendable advances in medicine and socioeconomic development, coupled with associated reductions in mortality and morbidity rates [4]. However, such demographic and epidemiological changes, in tandem with urbanisation, modernisation and associated lifestyle and risk factor behaviours, have increased the prominence and perpetuation of chronic conditions and the burden that they place on society.

Like most of the developed world, New Zealand has an ageing population [6]. By 2036 it is projected that around one in 4.5 New Zealanders will be aged 65-plus; a 77% increase of 547,300 additional over-65-year-olds from 2016 (Table 1.1). Contrast these projections with those for children under 14 in the same time-frame, where a 7.6% population increase is projected, and New Zealanders over the age of 65 will grow at a rate of 10.5 times faster than those under 14 years old [6]. These projected growth-rates will see the number of New Zealanders aged over

65 years old move from being approximately 220,000 less than those aged under 14 years old in 2016 to over 266,000 more in 2036 (Table 1.1). Based on worldwide trends for increased numbers of "old-old adults" aged 75+ years old, the predicted increase in the number of persons over 80-years old in New Zealand is 132.4%, rising to 150% for those aged over 80 and 95 years old (Table 1.1). When projections are extended to the year 2056, the number of individuals aged over 95 years old climbs to 42,400 - an increase of 631% from 2016 [6].

Table 1.1. New Zealand population statistics and projections (2016-2036).

Age-group	2016 Population	2036 Population (Projected)	% Increase
TOTAL NZ POPULATION	4,693,000	5,400,000	15%
14yrs and under	921,500	991,900	7.6%
65yrs +	711,200	1,258,500	77%
80yrs +	169,000	392,800	132.4%
95yrs +	5,800	14,500	150%

Source: NZ Statistics [6]

1.1.2 Economic burden of ageing

With increased longevity and an ageing population come significant economic consequences, as rapidly ageing societies bring with them a volatile cocktail of diminished workforces coupled with unprecedented levels of dependency, particularly in residential care (Figure 1.1). The UK Department of Work and Pensions forecasts that dependency ratios (calculated as: number of dependant people (children 0-15 + adults > 65yrs) / number of people of working age) will have increased by over 100% in some countries by the year 2050, when compared to 2005 rates (Figure 1.2). Consequently, there will effectively be less people working and paying income tax, yet more people to provide for. If medical science continues to enable people to live longer, but with poor mobility and/or multiple comorbidities to contend with, then the burden of care on society will continue to increase. For example, it is estimated that in the USA the excess annual healthcare expenditures due to sarcopenia alone were US$860 for every sarcopenic man and US$933 for every sarcopenic woman [7]. Consider that many over the age of 65 years old are managing not only sarcopenia but also an array of other chronic diseases, such as coronary artery disease, congestive heart failure, diabetes, asthma/COPD and osteoporosis, and the reasons behind the total US health care spend for elderly in excess of US$414.3 billion become clear [8]. Increased health care demands and levels of dependency mean that a disproportionate level of national health care budgets is spent on those over 65 years old, with more than two-fifths of national health spending in the UK devoted to this group; an 85-year-old man costs the NHS on average GB£7,917 each year, or around 7 times more than a man in his late 30s [9]. In

New Zealand the same trend exists, where older people make up 15% of the population yet use 42% of health services, totalling NZD$983 million in 2014/15, and a population ageing without health improvement will cause this share to further increase [10]. As the world population of those over 65 years old continues to increase, so too will the global expenditure on their health care, leading to a potential overburdening of healthcare systems and available resources.

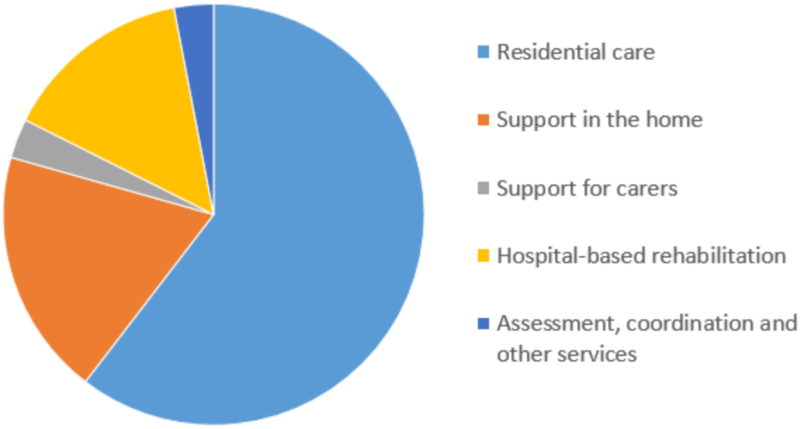

Figure 1.1. Proportional spending on types of support services for older people in New Zealand [10] (reproduced with permission).

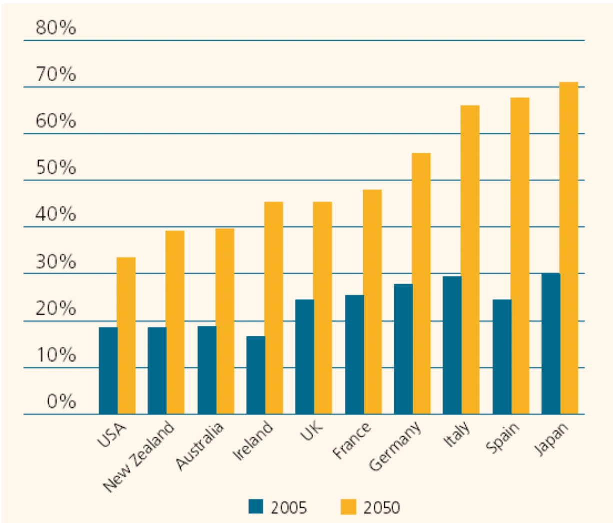

Figure 1.2. Worldwide dependency ratio forecasts [11] (licensed under the Open Government Licence v3.0, http://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/).

So stark are the implications of the ageing world population that recent researchers have stated that it (the ageing of populations) is poised to become the next global public health challenge

[4], with a World Health Organisation (WHO) report concluding that "comprehensive public health action on population ageing is urgently needed" [1]. Moreover, the WHO report recommends a shift in the approach by health systems "away from disease-based curative models" and towards "older-person-centred and integrated [health] care" [1]. Increased numbers of older people, who are in turn living for longer, require a person-centred approach in order to find effective strategies to extend health care and respond to their specific individual needs. The goal of ensuring healthy lives and promoting wellbeing for everyone at all ages cannot be achieved without specific attention to the health of older adults [4]. Ultimately, the message is clear: by targeting effective interventions aimed at improving the functional ability of the world's older people, we can simultaneously enhance their quality of life and freedom/independence, whilst concurrently reducing the burden of care that they present on society.

1.1.3 Age-related decline

Ageing can also be defined as a progressive functional decline or gradual deterioration of physical function with age [12]. Consequently, advancing age is associated with physical declines such as decreased muscular and cardiovascular function, bone loss, impaired cognitive ability and detrimental changes in body composition [13]. Such physiological changes, coupled with chronic low levels of inflammation and accompanying geriatric syndromes such as delirium, falls and incontinence, can dramatically reduce the independence and quality of life of older adults, often resulting in impaired physical function and an ensuing "frailty" [14]. This age-related decline in physical function is associated with an increased risk and incidence of falls in those aged 65 years and over [15]. Moreover, the age-related decline in mobility and physical function in older adults is often exacerbated by co-morbidities, in particular by the presence of sarcopenia [16] and osteoporosis [17].

The presence of one or more of sarcopenia and osteoporosis makes older adults particularly susceptible to falls and fractures (especially of the hip and vertebrae), and is associated with threats to their health and wellbeing, causing trauma, pain, impaired function, a loss of confidence in day-to-day living, a loss of independence, and even death [18]. Moreover, their presence serves to exacerbate mobility problems in this population, potentially leading to an ever-declining spiral of aging (Figure 1.3), in which a loss of mobility contributes to muscle and bone wasting and subsequent increased risk of falling, thus further reducing mobility and exacerbating the cycle, culminating in an increased risk and prevalence of falls. Falls in those over the age of 65 present a specific burden on society, with 55% of all unintentional injury deaths in those aged over 65 years old in the USA in 2012/13 being attributable to falls [19]. Moreover, the prevalence continues to rise, with the age-adjusted fall injury death rate in US adults almost doubling from 29.6 per 100,000 to 56.7 per 100,000 between the years 2000 and 2013 [19]. Fatal falls data in New Zealand follows a similar pattern, with falls in those over 80 years old responsible for approximately two-thirds of all fatal injuries in this age group [15]. Older people's vulnerability and longer recovery periods make falls and associated fractures a particularly serious threat to their health and wellbeing, causing trauma, pain, impaired function, a loss of confidence in day-to-day living, a loss of independence, and even death [18]. The consequences of a fall are far reaching in the elderly, affecting not only their own lives but also having emotional, physical, and financial impacts on relatives and carers.

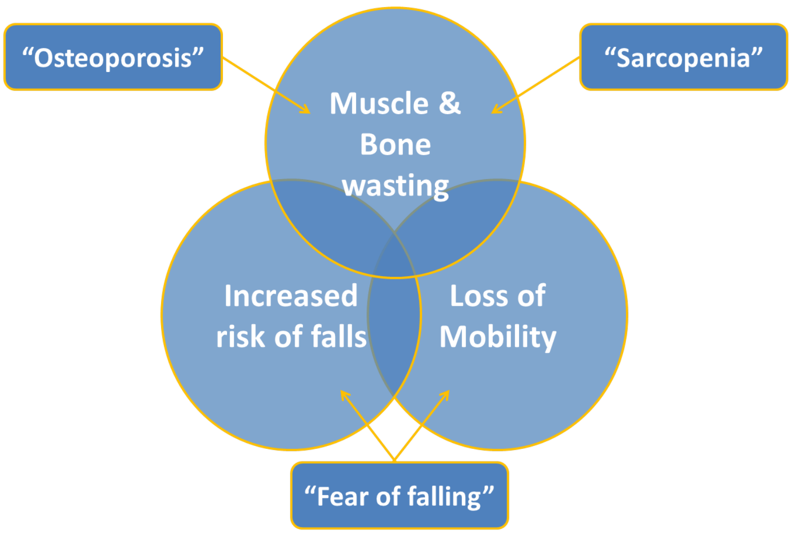

Figure 1.3. The Ageing Spiral.

As the New Zealand population continues to age, the incidence of falls and subsequent burden of care continue to grow. In a recent study of 937 elderly New Zealanders, Kerse et al. [20] showed more than a third (37%) of New Zealanders in advanced age had experienced a fall within the previous 12-months, with 20% of these being hospitalised. The annual cost of injuries from falls is reported to reach between $296m and $418m by 2025 in New Zealand alone [21], with, on average, a hip fracture resulting from a fall in the frail elderly leading to a hospital stay of 21 days, at an in-hospital cost of $800/day, totalling $16,800/stay [22]. Exacerbating the problem, only 7.2% of New Zealanders over 65 years old who were hospitalised for a fracture were independent in their walking on discharge from hospital, and only half of these had regained their pre-morbid level of mobility 12 months on [23]. Although substantial, these costs do not even account for the psychosocial and opportunity costs accompanying a fall [24]. The likelihood of a further fall and fracture is greatly enhanced [25], whilst "post-fall syndrome" and ensuing restrictions in activity, social interaction and independence are extremely debilitating [15]. Such large care costs will only escalate further as the New Zealand population continues to age (Table 1.1). Costs can rise even higher in other countries, with Hartholt et al. reporting a mean cost of a fall rising up to €14,600 for those aged over 85 years old in the Netherlands [26] and the US Centre for Disease Control (CDC) reporting an average hospital cost for a fall injury for people over 65 in the USA of over US$30,000 [27]. Older people's vulnerability and longer recovery periods make falls and associated fractures a particularly serious threat to their health, wellbeing and independence [18], culminating in significant financial-burdens being placed on the public health system.

1.1.4 Sarcopenia

Characterised by "the presence of both low muscle mass and low muscle function" [14], sarcopenia is a major clinical problem for older people with far-reaching clinical and socio-economic consequences. Associated with ageing and more dramatically with sarcopenia, muscular atrophy and weakness are the combined effects of changes in muscle architecture, tendon mechanical properties, neural stimuli and muscle fibre distribution [28]. At a molecular level, this muscular atrophy is a result of a disproportionate decrease in skeletal muscle protein synthesis coupled with an increased protein breakdown [29], in part due to reduced stimuli from anabolic hormones [30, 31] and/or muscular activity/mechanical stimuli [32]. On a muscular level, researchers have shown that specific reduction in high-intensity activities (i.e. exercise at 70-85% of maximal levels [33] leads to the selective atrophy of type II muscle fibres and subsequent reduction in muscle mass and power [34, 35]. The loss of type II fibres has particular implications for the loss of quick corrective movements for balance perturbations, power development and overall strength [34]. Emphasising these declines, denervation has been associated with ageing, reducing the number of functional motor units by up to 25% [36]. Evidence of denervation exists in both the central and peripheral nervous systems [37], compromising an individual's ability to activate muscles and fibres when needed. Further exacerbating atrophy and loss of muscular-function are age-related increases in oxidative stress and pro-inflammatory cytokines, coupled with reductions in anabolic hormones such as testosterone, which result in cellular losses of organelles and proteins from skeletal muscle [38]. In particular, imbalances between muscle protein synthesis and breakdown become apparent, with researchers linking age-related reductions in protein-synthesis to a magnitude of factors including impaired insulin-resistance [39] and chronic inflammation [40]. The progressive loss of muscle mass occurs from approximately 50 years of age, reaching a rate of 15% per decade after the age of 70 years [41], and is coupled with a loss of leg strength of 25-40% per decade from the same age [42].

Older people with muscle weakness will often compensate by altering their gait and shifting the centre of body mass to increase muscle efficiency/reduce pain load [43]. The resultant abnormal gait and displaced centre of gravity can jeopardize balance and increase falls risk, particularly when combined with poor visual cues, decreased proprioception, and/or buckling of lower limbs [44]. Consequently, sarcopenia brings an associated increased risk of falls and concurrent loss of independence [45], negatively impacting an individual's quality of life [46]. Maintenance of muscle function into old age is deemed "critical to sustain normal daily activity and functional independence" [47]. Reduced physical activity levels concurrently reduce neural and mechanical stimuli to maintain/strengthen muscle mass, particularly of the lower-limbs, further exacerbating the loss of mobility and increasing the degree of sarcopenia. Accordingly, sarcopenic individuals are at a greater risk of falling than their non-sarcopenic counterparts, having been shown to be over three times more likely to suffer a fall [48]. A reliable marker of frailty and poor prognosis in older individuals, sarcopenia is regrettably highly prevalent among elderly persons, with rates of up-to 50% reported in males and females over 80 years old [48, 49].

1.1.5 Osteoporosis

Bone's toughness and resistance to fracture, provided by its inorganic matter, declines with age [50]. However, as people age, their bones also gradually lose minerals and become less dense, characterised by reduced bone mineral density (BMD) scores [51]. A BMD of 10-25% below that of a healthy 30-year-old woman, that is a T-score of 1-2.5 standard deviations below the norm, is deemed osteopenic/of low bone density, and represents an important point for preventing further bone loss [52]. Reduced bone mineral density weakens the bones, making them more susceptible to fracture [51]. Consequently, an individual's skeletal fragility, and thus their fracture risk, increases with older age [52]. Further exacerbating the issue is osteoporosis - "a skeletal condition characterized by a low bone density and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture" [53]. A BMD score that is 25% or more below that of a healthy adult female is deemed to be osteoporotic, and is categorised by a T-Score of 2.5 standard deviations below the norm [52]. Although bones naturally lose density and weaken with age, the prevalence of osteoporosis increases with age and is particularly prevalent in post-menopausal women due to reductions in anabolic hormones and their stimulus of bone turnover. Seventy-percent of women aged 80+

years are believed to have low bone density, indicative of osteoporosis [32]. Older males are not immune to bone loss however, reportedly exhibiting approximately half as much bone-loss as post-menopausal females [54]. In particular, fracture of the femoral neck is of major concern in the frail elderly as it represents over 50% of all fractures and accounting for up-to 1.1% of deaths from all causes [55]. Moreover, osteoporosis and associated osteoarthritis and joint pain can result in individuals changing their gait and shifting the centre of body mass to reduce pain load, but concurrently jeopardizing balance and increasing falls risk [43]. Consequently, as the number of older New Zealanders increases, so too does the burden of osteoporosis on the public health system, which was estimated at NZ$1.15 billion per annum in 2007, and continues to rise [56]. In Australia, the total cost of poor bone health in adults aged 50+ for the year 2012 was A$2.75 billion, with 64% being directly associated with treating and managing fractures [57].

An imbalance in bone turnover, with bone resorption significantly in-excess of bone formation, is consistently reported as the causal mechanism behind osteoporosis [58]. Above all, the primary cause of this imbalance, and thus osteoporosis, is a deficiency in anabolic steroid hormones of the gonads, namely oestrogen and to a lesser-extent testosterone. This decline sees enhanced osteoclast activity, and ensuing prolonged bone resorption time, as well as concurrent relative-reductions in osteoblast activity and bone formation [58-60]. Such imbalances in bone formation are amplified by decreases in the frequency and amplitude of growth hormone secretion as the pituitary gland ages [61], and resultant effects on osteoblast activity and differentiation [58]. Reducing the stimulus for bone remodelling, and/or limiting the available-materials for such formation, many secondary factors also determine the rate and extent of bone loss, including medications, vitamin D deficiency, insufficient dietary calcium, physical inactivity and a plethora of endocrine, neurological, and malabsorptive conditions [58, 62]. Resultant decreases in bone health and strength dramatically increase the fracture risk for individuals with osteoporosis, increasing their risk of many long-term health problems and premature death.

Turnover and remodelling also have substantial impact on the material composition and structural properties of bone [63]. The inorganic component of bone, notably calcium and phosphorus in the form of hydroxyapatite crystals, gives bone its characteristic stiffness, whilst the organic component, consisting of structural proteins such as collagen, allows for flexibility within bone [63]. At approximately ~65% mineralized, human bone is a delicate balance of these properties, and subsequent imbalances can compromise the structural integrity of bone. Resultant from an age-associated reduced turnover and remodelling, a proportionately-higher mineral content in bone reduces flexibility when loading, and thus increases the risk of a fracture

[50, 63]. What-is-more, bone mineral crystals increase in size with age, compromising the specific honeycomb-like arrangement of collagen and mineral deposits that increases the structural-integrity of bone in younger people [50]. Further compounding the structural-integrity of bone, as outlined above, an imbalance exists in-favour of bone breakdown when remodelling in older age, meaning less bone is deposited than removed and resulting in bone loss, the thinning of trabeculae, and ensuing porosity [63] often characterising osteoporosis [64]. Formed by osteoblasts during bone formation and trapped in the ensuing new bone matrix, elevated serum levels of osteocalcin are indicative of slower rates of bone deposition, thus making it a common biochemical marker of bone health [65]. Of further note, the age-associated thinning of trabeculae compromises the microarchitectural-structure of bone [63], whilst collagen fibre cross-links mature to become permanent and increase in number [50], increasing the risk of a fracture. Two particular such collagen cross-links are pyridinoline (PYD) and deoxypyridinoline (DPD), and thus the presence of one or both in urine is indicative of bone turnover/breakdown, with urinary PYD and DPD levels deemed a sensitive marker of bone turnover in elderly osteoporotic patients [66]. The depletion and compromise of bone mass, composition, and structure are common consequences of osteoporosis, and directly contribute to the fragile and fracture-prone nature of osteoporotic bone [64].

1.1.6 Osteoporosis and fractures

There are many reasons why older adults are susceptible to falling, including side-effects of medication, impaired vision or balance, and declines in muscle mass and strength. Regardless of why an older person might fall, the incidence of fragility fractures has been shown to increase exponentially with age in both males and females, as a direct result of decreased bone strength, and is further enhanced by the presence of osteoporosis. In the comprehensive UK Million Women Study by Banks et al. [51], over one million middle-aged and older women provided information about their menopausal status and other health and lifestyle factors likely to affect their fracture risk, and were followed up for an average of 3 years [51]. The incidence of hip fractures was shown to increase steeply with age, being seven times higher in older adults (70-74 years old) than in younger post-menopausal women aged 50-54 years old [51]. The onset of the menopause in middle-aged women, and subsequent hormonal changes, means that post-menopausal women lose bone density faster than men as they age, increasing the prevalence of osteoporosis and fracture risk in older females [51]. However, males are not immune to the age-associated decline in bone health, reportedly suffering approximately one-third as many fractures [54]. Moreover, a comprehensive epidemiological study of hip fractures in the USA demonstrated similar age-associated fracture incidence, showing similar trends but lower rates of fracture in males than females [67]. Furthermore, using regression analysis of 1,918 older adults with previous fractures, Johnell et al. [68] demonstrated that the incidence of a previous fracture significantly increased the risk of a further fracture of the spine, hip or shoulder, deemed the “quintessential osteoporotic fractures” [69]. Having experienced one fracture, the chances of another are greatly increased, as are the far-reaching negative connotations of an individual’s quality of life. Indeed, osteoporotic fractures of the hip and spine carry a 12-month excess mortality of up to 20%, because they require hospitalisation and they have subsequently enhanced risk of other complications, such as pneumonia or thromboembolic disease [70].

In extremis, hip fractures can cause long-term health problems and premature death [51]. Although surgical repair of a fractured hip usually only requires a hospital stay of about a week, a quarter of elderly people who were living independently before their fracture have to stay in residential-care for at least a year after their injury and a fifth of elderly people who break a hip die within the year [51].

1.1.7 Function and Mobility

A fall by an elderly person often results in the combination of physical injury and loss of confidence, leading to impaired physical function and mobility, and greatly reducing their independence [18, 71, 72]. Bone, muscle and fat mass all impact on the balance, gait, and overall function and mobility of older adults [73]. In keeping with the ageing spiral (Figure 1.3, Section 1.1.2), older individuals with a combination of low muscle/high fat mass have been shown to exhibit greater functional deficits and poorer bone health, exacerbating the risk of a fall or fracture compared to those with higher muscle mass [73]. This, coupled with a resultant reduction in function, mobility and levels of physical activity, only serves to further reduce muscle mass and bone health due to inactivity, simultaneously increasing the risk of falling and reducing mobility and independence further still. Confirming this trend, the oldest participants in a screening-study of thirty-two independently living 65-92 year-olds exhibited significantly greater falls risk and significantly lower physical functional [71]. Overall, the same study showed total physical function to account for 24% of variance in an individual’s falls risk, compared to 13% for age, leading researchers to conclude that while increasing age is the strongest single predictor of increasing falls risk, poorer physical functionality was strongly, independently related to greater falls risk [71]. Ultimately, regardless of its cause, a fall can have far-reaching consequences on an individual’s function and independence, causing a tremendous amount of morbidity, mortality and use of health care services including premature nursing home admission or death [74].

1.1.8 Psychological wellbeing and Quality of Life

The consequences of a fall reach far beyond associated physical injury/fracture and reduced mobility and independence; once an individual has suffered a fall or fracture, the likelihood of them suffering a further fall (and indeed fracture) is greatly enhanced [25]. Known as "post-fall syndrome", the fear of a further fall is in itself debilitating, causing severe restrictions in activity and social interaction [15] and negatively impacting on an individual's Quality of Life (QoL). To this end, many older adults who have not fallen still frequently report this fear [75]. The prevalence rates of a fear of falling vary, but average prevalence in older adults who do not have a history of falling is reportedly 30% or more, a rate that is then doubled for older adults who have previously fallen [75]. Fear of falling can lead to self-imposed activity restriction, and thus exacerbate mobility problems, muscle and bone wasting, and the risk of falling (the ageing spiral, Figure 3, Section 1.1.2). Indeed, the fear of falling has been associated with poor performance in tests of balance and gait speed, and reduced levels of independence, QoL, general overall health and depressed mood [75]. So pronounced are the effects that a fear of falling has been identified as an independent predictor of falls in older adults [76], and even a contributing factor to decreased mobility and increased levels of functional dependence [77].

An optimal level of mobility is fundamental for maintaining healthy ageing and an individual's QoL [78], while lower levels of mobility can decrease levels of social interaction, having dramatic consequences on an individual's social isolation, loneliness and QoL. In a comprehensive study of 327 elderly Swedish people, Törnvall et al. showed lower levels of QoL to be associated with poorer mobility and a higher falls risk, particularly for females [78]. Lower levels of QoL strongly correlate with feelings of social isolation and loneliness [79], which also lead to lower levels of functional ability and increased mortality. A longitudinal cohort study of 1604 older Americans, with a mean age of 71 years old, not only showed a high prevalence of loneliness (43% reported feeling lonely), but also found strong links between loneliness, functional decline and death [80]. Lonely elderly participants were almost twice as likely to experience decline in activities of daily living (24.8% vs. 12.5%), and significantly more likely to develop mobility difficulties, both for upper and lower extremity tasks [80]. Perhaps most telling of all, loneliness was associated with a significantly increased risk of death (22.8% vs. 14.2%) in this cohort [80]. In a broader context, a meta-analytic review of 148 studies and 308,849 participants of varying age, gender, health-status, and ethnicity, found a consistent 50% increased likelihood of survival for participants with stronger social relationships, comparable with well-established risk factors for mortality such as smoking, obesity or lack of physical activity [81].

1.2 Exercise and Falls Prevention

In tandem with diet and pharmacologic interventions, physical activity levels present as one of the most easily-modifiable lifestyle factors impacting the rate of age-related decline [32]. The benefits of regular physical activity are such that it has been described as the "perfect pill" [82], but as little as 2.4% of older adults meet the recommended levels of physical activity [83]. With increased prevalence of chronic disease processes and co-morbidities, the older population may derive even more benefits from exercise than younger counterparts, even if exercise begins later in life [84]. In fact, regular physical activity in older adults brings a myriad of health benefits, including enhanced physical function, ensuing psychological benefits, and a subsequent increase in general "health", independence and QoL [85].

Despite being defined as "unexpected events in which the participant comes to rest on the ground, floor or lower level", falls are not random events and many can be predicted by the presence of risk factors such as low muscle strength and impaired balance or gait [24]. Such risk factors can be addressed and/or reduced with specific training, thus decreasing the risk of a fall [24]. Reducing the prevalence of falls-related injury and death is beneficial on a multitude of levels, from individual (physical, psychological) through to societal (fiscal). The New Zealand Accident Compensation Corporation (ACC) states that "investing in falls prevention can improve older people's quality of life by reducing pain, fear and isolation, and increasing wellbeing" [15]. Moreover, the current New Zealand "*National Strategy for Preventing Injury from Falls*" identifies adults "over the age of 65 who reside in nursing care homes" as being particularly high-risk for the effects of a fall, recognising them as a priority group for falls-prevention [15]. Despite this, falls-prevention research has mainly focussed on older adults in the community, with the elderly within residential-care being much neglected in both research and the implementation of falls-prevention measures. It is well-established that exercise can be a valid falls-prevention tool [86], with a systematic review of 44 trials encompassing 9,603 participants reporting exercise to reduce the rate of falls in older-adults by 17% [87]. In-fact, researchers suggest that almost 50% of falls can be prevented by well-designed exercise programs [88], and appropriately prescribed exercise interventions, such as those discussed in the following sections, have successfully addressed a number of the specific causes and consequences associated with the physical and financial burden of falls [82].

1.2.1 Sarcopenia and falls prevention

Various studies have shown that physical activity among elderly people leads to a reduction in fat mass between 1 and 4%, and associated improvements in muscle tone and musculoskeletal fitness [89]. Indeed, Reid et al. [47] stated that “maintenance of muscle function into old age is critical to sustain normal daily activity and functional independence”. Traditional resistance/strength training exercises are frequently shown to counter age-related changes in body composition and motor ability/function [13]. Furthermore, the associated increases in muscle strength resulting from resistive exercise make it an important component of interventions to improve balance and prevent falls in the elderly [90-92].

Exercise-based falls-prevention research addressing sarcopenia and muscle weakness has predominantly focussed on older adults within the community, who are generally more mobile and more open to taking part in such exercise programs, but has included some specific interventions for those residing in residential-care. Consequently, delivery methods of such falls-prevention exercise interventions have varied dramatically, from community-based to residential-care, strength to aerobic focused, and individual to group delivery, with varying degrees of success. Aerobic exercise is defined as activity that uses large muscle groups for prolonged periods of time, and includes activities such as brisk walking, swimming and dancing, conducted at a moderate intensity level [93]. Such activities lend themselves well to group-based exercise sessions, often requiring very little equipment or formal training to run. In contrast, resistance-based strength training requires muscles to work against a load, progressively increasing over time and often involving high-intensity protocols to the point of muscle fatigue [93]. Such programs require the support of trained exercise professionals, and are usually based in gymnasiums, making them generally more suited to individual community-based interventions.

Independent older adults (aged 76±4 years) have shown meaningful functional benefits from 6-months of combined endurance and strength training [94]. Furthermore, strength gains of 10-180% have been reported in the frail elderly [95-98], attributable to muscle fibre hypertrophy of up-to 14.5% and associated increases in both type I and II fibres of up-to 30% [99]. However, a caveat to these large benefits, one must consider that considerable gains are more likely with such low starting points. Moreover, when considering the frail elderly, the aim of prescribed physical activity is primarily to improve functional ability without injury [100]. Consequently, converting strength/musculoskeletal gains into quantifiable improvements in functional ability presents as the most effective measure of physical activity’s success. For example, Fiatarone et al. reported significant enhancements in the muscle strength, gait and thigh-circumference of 100 frail residential-care residents (mean age 87.1 years) after a 10-week period of progressive resistance training, most notably citing improvements of 113 and 11.8% for muscle strength and gait velocity, respectively [101]. Moreover, a study of 551 retirement village residents (aged

79.5±6.4 years) showed a 22% reduction in falls, and associated significant enhancements in functionality, for those undertaking a 12-month program of group (weight-bearing) exercise compared to a control group [102]. A recent meta-analysis of 8 trials, consisting of 1068 frail elderly participants aged 75.3 to 86.8 years, showed a variety of exercise programs to successfully enhance function (gait speed and balance) in the frail elderly [103]. A Cochrane review of 159 falls prevention trials involving 79,193 participants [86] concluded that successful falls-reduction exercise programs target two or more components of strength, balance, flexibility or endurance. The above body of work demonstrates that a well-designed physical activity program has the potential to produce associated functional benefits in older adults of varying degrees of physical function.

The most recent wide-reaching government-funded prescribed exercise intervention in New Zealand, the Otago Falls Programme [104], is a strength and balance retraining program designed to prevent falls in community-dwelling older adults. The program targets all aspects highlighted by the Cochrane Review of Gillespie et al. [86], and was shown to effectively reduce the number of falls and fall-related injuries by 35% in community-dwelling older adults, having the greatest impact in those aged 80 and older [105, 106]. However, the program can be considered costly to run, being labour-intensive and requiring highly skilled/trained practitioners working on a 1:1 basis with participants. Various national District Health Boards (DHB) still reportedly use the program successfully, with Canterbury DHB reporting savings equivalent to $17 million over 3 years being attributed to the program's success [107]. However, as acknowledged in a significant meta-review by Thomas et al. [106], the program has only been used/shown to work with community-dwelling older adults, ignoring those with further impaired functional ability, greater falls risk, and a greater potential for quantifiable benefits: the frail elderly within aged care homes in New Zealand.

1.2.2 Osteoporosis and the prevention of falls and fractures

In addition to the prevention of falls, much research has focussed on attempting to reduce the risk of a fall-related fracture, by increasing the bone health of susceptible individuals. Among American women aged 80+, 70% have low bone density, indicating osteoporosis [108]. For these individuals there are three treatment options: dietary, physical therapy or pharmacological therapy. Prevention of fractures with drugs could potentially be as expensive as medical treatment of the fractures themselves (detailed in Section 1.1.2), with the estimated costs of treating 35 million postmenopausal women in the USA with hormone replacement therapy at just $430/person/year totalling almost $15 billion annually [69].

It could be argued that osteoporosis is not in fact a disease of aging, but one of physical inactivity that is magnified in older age. As postulated in Wolff's law, bone structure and shape changes according to loading [109]. Consequently, decreased mechanical usage (physical inactivity) results in a loss of bone, whereas weight-bearing exercise provides substantial loading on bone, particularly when young, and thus stimulus of bone turnover and maintenance [109]. In particular, the mechanical stimulus of weight-bearing exercise promotes osteoblastogenesis [110], the production of new osteoblasts that are responsible for bone formation [50]. Such exercise-stimulated increases in bone health diminish the risk of fractures by mechanically counteracting the thinning of bones and increases in bone porosity [111]. Additionally, the increased muscle mass gained by regular weight-bearing activity further increases the stress on associated bones, and therefore the stimulus on these bones to remodel and maintain or even enhance their structural integrity [109].

Consequently, researchers have explored the potential beneficial effects of exercise on bone health across a variety of settings. In a large prospective-cohort study of 9,704 community-dwelling older American women (65+ years old), Gregg et al. [112] showed higher levels of physical activity (sport activity and/or household chores) and fewer hours of sitting daily to significantly reduce the risk of hip fracture. The most active women had a statistically significant 36% reduction in hip fracture risk compared with the least active women. Moreover, the intensity of activity was also related to fracture risk: moderate to vigorously active women had reductions in risk for hip and vertebral fractures of 42% and 33%, respectively, in comparison to inactive women [112]. Evidencing this reduced fracture risk, several studies with post-menopausal women have shown modest increases in bone mineral density towards a healthy population norm in response to high-intensity exercise [111]. However, not all exercise regimes have the same level of positive effects on bone mass, with the type of exercise deployed being crucial to the success of the program.

Walking remains one of the simplest and most accessible forms of weight-bearing aerobic exercise, yet its direct benefits on bone health remain unclear [113]. Long-term walking programs in post-menopausal women have predominantly shown little to no impact on bone mineral density [114, 115], attenuating loss at best [116]. However, the intensity of such exercise does appear to be important, with Hatori et al. [117] showing higher-intensity walking above the anaerobic threshold to elicit modest improvements in spinal BMD, and programs combining walking with higher intensity activities such as jogging and stair climbing also improving bone health [118, 119].

Strength training is a more successful mode of training for improving bone mass in the elderly. It provides greater mechanical stress on bone, and has been suggested as a causal factor of osteogenesis [120]. As little as 24 weeks of strength training has been shown to maintain BMD levels in postmenopausal women compared to losses exhibited by their untrained counterparts [121]. Furthermore, longer-term training programs of 12 months or more regularly demonstrate significant 1-2% enhancements in the BMD of post-menopausal women, compared to annual-losses of 2.5% per annum in untrained control groups [120, 122, 123]. Studies in elderly men are fewer, but replicate these effects over 16-week [124] and 12-month [125] interventions.

Multi-component exercise training programs combining variations of strength-, aerobic- and flexibility-training have demonstrated mixed results with regards to bone health to-date. Recently, successful interventions combining strength and impact exercises over 12-18 months have elicited increases in BMD comparable to those seen with strength training [126, 127]. Similarly, specific studies working with osteopenic and osteoporotic women showed enhanced BMD over a 20-week aerobic, balance and strength program [128] and an 11-month long multi-component exercise program [128]. However, others have suggested that the benefits of such programs are limited to maintenance of bone health [129-131], or have demonstrated BMD losses equitable to or even exceeding those of the control group [132, 133]. It is important to note that enhancing bone health may not be the primary aim of such multi-component exercise programs, which could instead be targeted at addressing the losses of balance, mobility, function and independence also associated with older age.

1.2.3 Addressing Loss of Function, Mobility and Balance

In addition to addressing the detrimental effects of sarcopenia, resistive exercise is an important component of interventions aiming to improve physical function and balance, and thus prevent falls in the elderly [90-92]. Older adults who have good balance and muscle strength are often better able to correct imbalances due to perturbations when they trip. Undeniably, flexibility, balance & reaction time are considered equally modifiable risk factors for falls [18], and consequently various tailored exercise programs targeting each of these variables have been developed to best prevent falls in the elderly.

Much research investigating the effectiveness of various exercise programs in addressing loss of function, mobility and balance has focused on community-dwelling older adults, with particular-emphasis on postmenopausal women as part of wider research targeting osteoporosis. A randomised-controlled trial of 40 postmenopausal community-dwelling women, aged 50-70 years old, showed regular high-intensity strength training to be of benefit to numerous osteoporosis risk-factors including balance [120]. Specifically, the women who completed twice-weekly strength training exercises for a period of 1 year showed 14% improvements in dynamic balance, and associated improvements in muscle mass and strength, compared to decreases in the untrained control group [120]. However, uptake and compliance in strength training-based programs can be poor in older adult populations [134], but researchers have shown promising balance-training effects with other forms of more accessible exercise [135-137]. In a study of 163 community-dwelling older adults aged 65+ years old, Barnett et al demonstrated a year of weekly community-based exercise classes, supplemented with in-home exercise programs, to significantly enhance balance [135]. Specifically, postural sway and coordinated stability were improved, and accordingly the rate of falls in the intervention group was 40% lower [135]. However, the exercise classes used by Barnett combined low-intensity balance and coordination exercises with more demanding strength and aerobic training delivered by physiotherapists [135]. The more demanding nature of some of the program may have deterred some potential participants, with the authors reporting 90 potential participants declined to take-part, whilst the need for a qualified physiotherapist to run sessions simultaneously restricts the program's accessibility and concurrently increases cost. Low-impact and low-intensity exercises such as Tai Chi or brisk walking present as acceptable exercises for many older adults, can be delivered without the need for a qualified physiotherapist, and show particular-success in low-falls-risk community-dwelling adults. Indeed, Tai Chi has a well-established body of support as a therapeutic exercise for improving physical performance and functional balance in such populations [136, 138, 139]. In particular, the work of Li et al. [136] showed 6-months of Tai Chi training produced significantly better improvements in functional balance, physical performance and falls incidence compared to a stretching-based control group [136]. However, in a study of 90 community-dwelling men and women aged 65-79 years old, Okubo et al. [137] demonstrated a 12-week brisk walking program to be as effective as a balance program (combining Tai Chi, balance and strength training) in improving falls-related physical factors such as gait, strength and dynamic balance [137]. Moreover, only participants in the walking group enhanced falls-related self-efficacy, suggesting additional psychological benefits from this form of exercise [137]. In a comprehensive review of exercise interventions to improve balance, Howe et al. analysed results from 94 studies, totalling almost 10,000 participants, favouring evidence for moderate balance improvements from multi-modal, strength and Tai Chi-based programs [140]. Clearly many successful therapeutic exercise programs exist yet encouraging participation in these programs by higher-risk older adults, such as those in residential-care, can present a significant challenge.

Adults in residential-care are generally physically inactive, spending on average 97% of their day sedentary [141]. Consequently, the benefits of exercise are not limited to the community-dwelling elderly, being strongly-linked to increased functional independence even in those in residential-care [142]. A comprehensive systemic review of 27 studies covering older individuals (aged ≥70 years) in residential care showed firm evidence for training effects on functional performance and balance amongst other parameters [142]. Combining interventions of the reviewed studies with strong or very strong effect sizes, the authors concluded that optimal training for such benefits should combine resistance, balance and functional training, be of moderate to high intensity, and offered three times a week for at least 10 weeks [142].

1.2.4 Falls confidence and Quality of Life

The effectiveness of exercise in preventing falls is long associated with improving physiological parameters such as balance, strength and mobility. However, exercise may influence further associated factors, such as psychosocial parameters including falls-confidence, self-esteem and self-efficacy [143]. Whereas falling can contribute to the worsening of such psychosocial factors, improved mobility can enhance them. Moreover, exercise can be a particularly attractive non-pharmacological falls-prevention tool, replacing psychoactive medications that are known to increase falls risk in older adults [144].

In a cross-over study of 143 community-dwelling older adults, 66 of which had a history of falling, Means et al. [143] found elderly fallers to display poorer psychosocial factors than their non-falling counterparts, further increasing their risk of falls. Moreover, the researchers showed a 6-week strength- and balance-focused exercise program to elicit psychosocial benefits which strongly correlated with mobility and balance improvements resulting from the training. Notably, moderate exercise was enough to improve self-esteem and social activity of previous fallers, whilst concurrently reducing their levels of anxiety and depression [143]. However, it is unclear from these findings if the benefits were directly from the prescribed program, or from the sense of purpose derived from study participation. Focussing on older adults within residential care settings, the systematic review work of Weening-Dijksterhuis et al. [142] also highlighted the positive associations between exercise interventions, activities of daily living and QoL. Enhancing an individual's mobility and independence can have profound concurrent effects on the psychological wellbeing. For example, functional training/strength programs have been shown to successfully improve dynamic balance and coordination while performing daily life tasks [91], whilst self-esteem has been shown to increase as a result of both aerobic- and resistance-exercise programs [145]. Such exercise-associated benefits can empower frail individuals, increasing their confidence, self-esteem, wellbeing and feelings of control, and ultimately enhancing their QoL [146].

1.3 Exercise and Psychological Wellbeing

1.3.1 Physiology – How can exercise help?

Regular exercise can have numerous profoundly positive impacts on psychological wellbeing (summarised in Figure 1.4 at the end of this section). Namely, exercise has been reported to relieve depression, anxiety, Attention-deficit/hyperactivity disorder (ADHD), and stress, and improving memory, sleep, and overall mood. Moreover, exercise can have pronounced acute benefits, causing the release of various neurotransmitters in the brain as postulated by the monoamine and endorphin hypotheses [147]. The monoamine hypothesis proposes that exercise addresses the depleted levels of noradrenaline, serotonin and dopamine associated with depression [148], and reviews have supported it as a tenable explanation of the antidepressant effects of exercise [149]. Purportedly responsible for the short-term feel-good sensations of a “runner’s high”, the endorphin hypothesis links elevated levels of endorphins during exercise [150, 151] with their ability to reduce pain and elicit a euphoric state [152]. Recently however, endogenous neurotransmitters called endocannabinoids have been shown to play a major role in generating these neurobiological rewards [153, 154]. Of further benefit, cerebral blood flow increases as a result of exercise, in order to meet the increased cerebral metabolic demands associated with exercise [155], bringing with it acute improvements in cognitive function. Additionally, other neurotransmitters released as a result of exercise, such as neurotrophins that support brain plasticity and growth, can have far-reaching chronic benefits, literally increasing the size of the brain as result of exercise [156, 157]. Chronic exercise has been termed “brain food” [157], and research in nonhuman animals has demonstrated aerobic exercise to cause growth of new capillaries in the brain, increase dendritic connections between neurons, and even cell production in the hippocampus, leading to increased brain volume [158].

The benefits of regular physical activity extend beyond physiological gains, eliciting significant improvements in an individual’s mental wellbeing and health [159]. Sufficient evidence exists for exercise to have developed an established therapeutic role in the treatment of clinical or subclinical depression and anxiety, with effects of similar size to psychotherapeutic or pharmacological interventions [159]. Moreover, regular physical activity can directly enhance an individual’s mental wellbeing and quality of life through enhanced self-esteem and improved mood states [159]. Bandura's self-efficacy theory supports this, proposing that confidence in one's ability to exercise is strongly related to their capacity to actually perform it [160]. Since exercise poses a challenging task for many sedentary individuals, enhancing one's self-efficacy through a gradual progression of exercise can help encourage further regular physical activity, improving mood and increasing self-confidence and an individual's ability to cope with stressful events [152]. As individuals become more confident and gain mastery of physical challenges, they may take this feeling of control and success into their everyday lives [152]. In addition, regular physical activity can have further indirect psychological benefits, improving one's ability to conduct daily living tasks and enhancing wellbeing and quality of life by keeping disease and premature death at bay [161].

Regular physical activity at any age can facilitate and foster social contact, favourably affecting psychological wellbeing, self-confidence and overall quality of life. The social interaction hypothesis suggests that the social relationships and mutual support which exercisers provide each other may account for a significant portion of the mental benefits associated with exercise [147]. Social interaction is believed to be particularly important at the formative stage of an exercise program, when exercise habits are developed and engrained [162]. A comprehensive review of 132 studies involving 5987 patients aged 60 years and older identified social influences, such as valuing interaction with peers and encouragement from others, as a key determinant of physical activity [163]. The benefit of such relationships can extend beyond the exercise environment, with a population-based cohort study of 2443 older German-adults (75+ years) showing a strong fundamental link between social support and health-related quality of life [164]. Although sometimes individual circumstances and abilities dictate the use of a 1:1 individual exercise program, both group and individual exercise programs have been shown to be effective in mental health treatment [165]. Interestingly, in a study comparing the effects of group, individual and home-based mobility programs on 58 people with Parkinson's Disease, those receiving individual therapy showed the greatest improvements in physical function, whilst group-based exercisers showed larger improvements in psychometric measures including balance-confidence and quality of life [166]. In exploring the benefits of group exercise, researchers highlight that the social interaction, camaraderie and accountability resulting from participating in group exercise can increase variety, keeping people interested because of the social atmosphere and ultimately improving adherence to the program [167, 168].

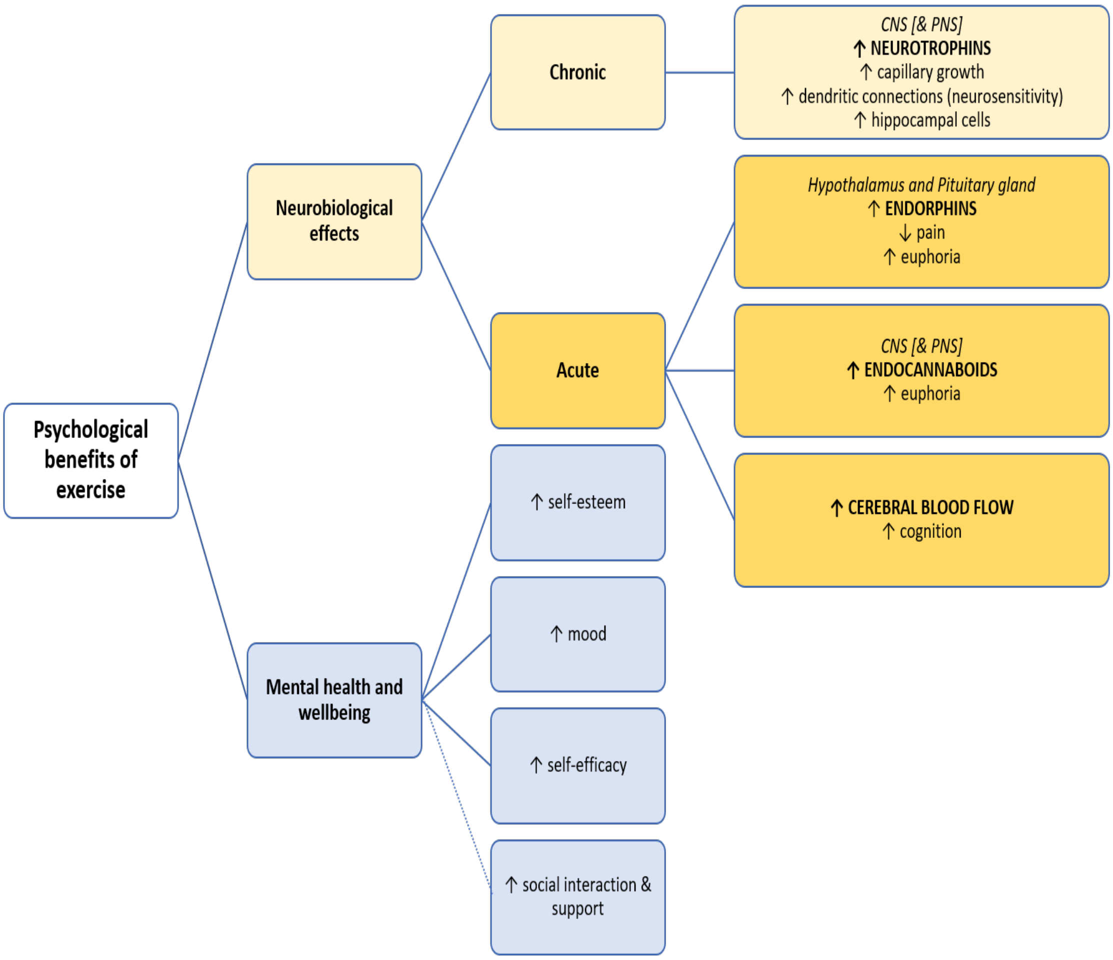

Figure 1.4. Impacts of exercise on psychological wellbeing.

1.3.2 Specific benefits for the elderly

The age-associated decline in cognitive performance [169], coupled with the psychological impact of reduced physical capacity and functional independence, means older adults stand to benefit greatly from the benefits of regular physical activity [93]. There are promising indications of the protective cognitive effects of exercise, with a recent meta-analytic review of 29 studies totalling 2049 participants demonstrating that moderate aerobic exercise can elicit modest cognitive benefits in older adults and reduce their risk of developing cognitive impairment [170]. Furthermore, the researchers suggest that exercise can have a protective effect for those with mild cognitive impairment [170], findings also supported by a previous meta-analysis of 30 trials totalling 2020 participants with dementia and related cognitive impairment [171].

Indeed, a significant body of evidence supports the role of physical activity as a tool to maintain cognitive performance in older adults, with several randomised trials and longitudinal studies reporting associated benefits in a variety of cognitive outcomes [100]. Prospective cohort studies have found regular physical activity to have preventative effects on the incidence of dementia after up-to 7 years of follow-up [172, 173]. Longitudinal cohort studies such as Elwood et al. [172] have established clear links between physical activity and disease-free survival into old age, including the absence of cognitive impairment and dementia [172]. Spanning over 30 years and monitoring the lifestyle and wellbeing of 2,235 British males aged 45-59 at the start of the research, the work of Elwood et al. [172] demonstrated the physical and cognitive benefits of a long-term healthy lifestyle, suggesting reductions of 60% for the incidence of cognitive impairment and dementia. However, Elwood et al. [172] acknowledged that as few as 1% of the overall population where the study was conducted (Wales, UK) followed the five "healthy lifestyle" markers used in the study. Government-led health-promotion initiatives may feasibly help improve these figures, and thus increase the number of older adults in the future who will benefit from a long-term healthy lifestyle, but what of those individuals already approaching/in old age?

In acknowledging the importance of exercise in maintaining and promoting optimal health, Kilpatrick states that beginning to exercise even later in life can provide "mortality and morbidity benefits similar to life-long exercisers" [82]. Specifically, exercise has been shown to have pronounced effects on the cognitive function and psychological wellbeing of older adults. Colcombe and Kramer [174] conducted a meta-review surveying literature from 1966 through 2001 examining fitness training effects on the cognitive function of non-demented older adults. Across the 18 intervention studies in the analysis, aerobic fitness training was shown to have a positive influence on cognition when compared to a non-exercise control group [174]. Moreover, physical activity programs have been shown to be an effective treatment tool for cognitive impairment in the elderly. In a meta-analysis of 30 trials conducted from 1970 to 2003, Heyn et al. showed significant beneficial effects of exercise on cognitive function and positive behaviour of 2020 participants aged 80±6.1 years with dementia and signs of cognitive impairment [171]. Aside from effects on physical function, the increased cranial blood flow [155], volume of brain matter [158] and overall cognitive function, coupled with lower levels of cognitive decline [175], associated with exercise in older adults suggest that regular physical activity can have significant cognitive benefits. Moreover, the subsequent beneficial effects on cognitive function and psychological wellbeing can have profound impacts on the QoL of older adults.

Regular exercise by older adults can also improve a multitude of physical variables, bringing about a subsequent increase in general health and independence, and ultimately manifesting as improvements in an individual's health, wellbeing and QoL. Regular moderate physical activity has been shown to directly influence health-related QoL in a variety of population groups, including middle-aged [176], old-aged [177] and those with chronic conditions including pain [178] and cancer [179]. The decline in muscle tone and strength frequently associated with ageing makes the performance of daily living tasks harder, increasing feelings of dependence, uselessness and depression. Research suggests that concurrent resistance training and stretching programs can have positive effects on musculoskeletal strength, helping maintain or enhance numerous aspects of independent living [85, 103, 180]. Furthermore, favourable interactions were demonstrated between regular aerobic exercise (3 times a week for 6-months) and scores of depression and anxiety in 60-75-year-old males [177]. Singh et al. [181] showed 10 weeks of resistance training exhibited anti-depressant effects in 18 older adults with varying degrees of depression. Reducing feelings of depression can have an array of subsequent benefits due to its associations with physical and functional decline, cognitive impairment, institutionalisation, frailty, psychological distress and even nonadherence to pharmacotherapy [182]. Blumethal et al. surmise the benefits of a 16-week exercise intervention trial, involving 156 men and women aged 50+ and diagnosed with major depressive disorder, by concluding that exercise training programs can be considered "an alternative to antidepressants for the treatment of depression in older persons" [183].

Regular physical activity at any age can facilitate and foster social contact, favourably affecting QoL, and nowhere are feelings of social isolation and loneliness more prevalent than in older adults [184]. Moreover, strong evidence exists of a relationship between social networks/social support and the health of older people [81, 185], and particularly so in older males [164]. So strong is this relationship that a lack of social support is viewed to be one of the strongest predictors of institutionalisation [186]. However, even short-duration, low-intensity exercise-interventions can have benefits in older adults when delivered in a social environment. Interventions as simple as 6 weeks of walking/social contact have reportedly reduced levels of depression in 30 community-dwelling older adults to an extent equivalent to pharmacological placebos [187]. Netz et al. [188] hypothesised that physical activity interventions provide a mastery experience for older adults whose physical self-efficacy may be deteriorating with their functional abilities [188]. Increased levels of self-efficacy can in-turn improve psychological wellbeing [160], and thus encourage further participation by individuals, supporting a "softly first" approach to exercise interventions in older adults [152]. Undergoing such mastery experiences in the company of others goes beyond the benefits of either social interaction or physical activity alone, effectively multiplying the benefits of the experience. With many exercise interventions within residential-care being delivered via group settings, the benefits of the social aspect of these programs cannot be disregarded.

1.4 Exercise and the Frail Elderly

1.4.1 Specific considerations

The promotion of regular physical activity is considered one of the main non-pharmaceutical measures that should be promoted in older adults, especially regarding a preventive approach for 'successful ageing' [100]. The risks of not exercising far outweigh the risks of a well-balanced and sensible exercise plan [82], with the American College of Sports Medicine (ACSM) describing physical activity as "one of the highest priorities for preventing and treating disease" [189]. The New Zealand ACC's current National Strategy for Preventing Injury from Falls [15] states that "investing in falls prevention can improve older people's quality of life by reducing pain, fear and isolation, and increasing wellbeing" and identifies adults over the age of 65 who reside in care homes as being particularly high-risk for the effects of a fall, recognising them as a priority group for falls-prevention. However, elderly persons face a variety of barriers to exercise, and subsequently show low levels of compliance to many exercise programs.

Many older adults commonly have multiple co-morbidities, low fitness levels and/or functional limitations [189]. However, others exhibit levels of fitness and activity beyond their younger counterparts, meaning clinicians and exercise practitioners working with older adults work with a diverse group displaying a large heterogeneity of fitness levels. Those with chronic medical conditions and functional limitations often display an over-arching "frailty", meaning they exhibit poorer health and a higher burden of care than their more-mobile/less-dependent counterparts. Their increased frailty often means they are unable to exercise conventionally, thus do not gain the associated health and functional benefits of doing so, consequently leading to reduced physical function and independence, and culminating in a decreased QoL.

Prescribed exercise interventions have been successful in addressing many of the age-related declines seen in the elderly, yet many are costly and exclude those who could theoretically benefit most from their application: the frail elderly. A large number of older adults display debilitating degrees of frailty, with 38% of Americans over 65 years old and 74% of those over 80 years old having some degree of disability [93]. Small improvements in the functional capacity of these individuals can have pronounced benefits on their physical and mental wellbeing, even reducing their burden of care at the same time. Yet, their multiple comorbidities, complex needs and inability to exercise conventionally means that numerous specific care considerations need to be in place when developing and implementing an accessible exercise-intervention for this population.

In a practice review for prescribing exercise to frail elders, Heath and Stuart highlight many absolute contraindications to exercise for the frail elderly [190]. Predominantly, these include cardiovascular contraindications such as severe heart disease, congestive heart failure, tachyarrhythmias induced by activity, and critical aortic stenosis. The same authors detail non-cardiac limitations to exercise in this group as the immediate hypoxic period after a pulmonary embolism, retinal detachment, and unstable cervical spinal conditions, whilst recent fractures can further limit exercise ability. Indeed, Heath and Stuart [190] recognise that any condition becoming symptomatic with minimal activity beyond activities of daily living would preclude meaningful exercise.

1.4.2 Current Recommendations

New Zealand recommendations reflect those issued by world-leading groups, the ACSM and the WHO [188; 190]. In order to promote and maintain good health, the ACSM recommend older adults maintain a physically active lifestyle, concluding that "virtually all older adults" should be physically active [189]. Specifically, at the very least they recommend older adults perform moderate intensity aerobic exercise for a minimum of 30 minutes on five days a week (or 20 minutes of vigorous intensity exercise on three days a week), attempting to also include muscle strengthening activities and activities to increase flexibility at least two further times a week each [189]. Guidelines from the WHO follow a similar theme, suggesting that in order to improve cardiorespiratory and muscular fitness, bone and functional health, and to reduce the risk of non-communicable diseases, depression and cognitive decline, older adults should complete a minimum-target of 150 minutes of moderate-intensity aerobic exercise each week [191]. These guidelines also suggest targeted balance and falls-prevention exercises 3 or more times a week for older adults with poor mobility. The WHO acknowledge that not all older adults may be able to meet the recommended amounts of activity due to health conditions, conceding that such individuals should be "as physically active as their abilities and conditions allow" [191].

1.4.3 Exercise Adherence and Avoidance

Approximately one third of adults worldwide are physically inactive (do not meet the recommended levels of physical activity detailed above), with inactivity rising concurrently with age and showing higher prevalence in women than men [192]. Significantly, those most affected by a loss of physical function (the frail elderly), and thus theoretically open to the greatest benefits of physical activity, show the lowest levels of compliance to exercise interventions [193]. A significant review of 53 published reports of physical activity in older adults reported as little as 2.4% of sample populations meeting the recommended levels of physical activity [83].

Such chronic levels of physical inactivity lead to the aforementioned perceived ageing spiral (Figure 1.3), in which participants develop a perception of frailty as a result of reduced physical function, and therefore avoid the very physical activity which could reverse such decline, thus become frailer, and even more likely to avoid such physical activity/suffer a debilitating fall. Demonstrating this issue, Kerse et al. [20] found a fall rate of more than a third (37%) of New Zealanders in advanced age, most of whom exhibited low physiotherapy use.

There is a myriad of factors identified as barriers to exercise participation in older adults, with many facing multiple concurrent barriers and ultimately being unwilling or unable to partake in physical activity (Table 1.2). Ill health, pain and injury are three of the most commonly reported reasons given by older adults for not participating in physical activity [93], and all present clear functional limitations to an individual's ability to exercise. However, many of the barriers older adults face are psychological, and/or even self-fulfilling. A comprehensive review of 132 studies involving 5987 patients aged 60 years and older identified perceived physical limitations as a key determinant of physical inactivity [163]. Furthermore, in a qualitative study interviewing older adults who recently fell yet refused to take part in falls-prevention work, participants frequently citied mobility impairment as a reason for not exercising [194]. In contrast, the more active and mobile participants considered themselves "too healthy" to take part in the same program [194]. Many older adults felt that they received sufficient focus and attention from their GP so as not to need to exercise for health, yet Heath and Stuart cite GPs' lack of knowledge of the benefits of exercise as a key barrier [190]. This lack of knowledge extends to individuals themselves, where individual health concerns over the consequences of exercise have been shown be a specific barrier [190]. Moreover, studies frequently highlight fatigue and a loss of motivation as reasons for low levels of compliance to exercise programs targeting the frail elderly [13, 193]. Access difficulties such as environmental barriers and affordability were also identified as key determinants of physical inactivity in Franco et al.'s review [163], and community-dwelling adults cite transport problems and limited local amenities as important factors limiting physical exercise [93, 194]. Indeed, the provision of free public transport for older adults in the UK was shown to increase not only incidence of travel, but also distance walked/physical activity levels [195]. However, for the frail elderly in residential-care, transport and environmental factors can theoretically be minimised with adequate exercise provision within the home. Undeniably, many of the highlighted barriers can be overcome with appropriately designed and accessible exercise programs to maximise compliance in those willing to attempt physical activity.

Table 1.2. Primary reasons for exercise avoidance in the elderly.

Internal Barriers	External Barriers
Ill Health	GP knowledge and perception of exercise as medicine
Pain	Lack of transport
Injury	Lack of access to equipment / limited local amenities
Fatigue	Lack of access to trained exercise professionals
Perceived physical limitations / low self-efficacy	
Falls history	
Post-falls syndrome	
Impaired mobility	
Loss of motivation	
A perception as being "too healthy" for an exercise intervention	
Feel adequately looked-after by GP	
Lack of knowledge re health benefits/risks of exercise	

1.5 Current Standpoints

1.5.1 International rehabilitation programs

A global report on falls prevention in older age by the WHO [196] highlights the work and recommendations of the Prevention of Falls Network Europe [197], surmising that their recommendations should be "sufficiently general enough to be applicable to populations other than the European population". Amongst others, these recommendations include i) promoting the functional, mobility and general health benefits of falls prevention programs, ii) the importance of social encouragement in such programs, and iii) tailoring interventions for the needs, preferences and capabilities of the individual. In particular, the report acknowledges a growing body of evidence that many older people may prefer exercises delivered at home [196]. The single most-effective intervention strategy for community-dwelling older adults is currently individually tailored muscle strength and balance retraining by trained-health professionals, yet the WHO acknowledge that in practice this may not be the most feasible, affordable and sustainable approach [196]. Specifically, in a meta-analysis of 54 falls-prevention studies to develop best practice recommendations for the New South Wales Health Board, Sherrington et al. [88] recommended exercises for falls prevention should provide moderate to high challenges to balance. Moreover, the authors recommended targeting both the general community and those at high risk for falls via group- or home-based exercises, consisting of strength-, walking- and balance-focused training [88]. For those in residential-care and at a higher risk of falling, brisk walking programs are not recommended [88], yet exercise programs *per se* are highlighted by the WHO as an effective individual strategy and also a component of successful multifactorial interventions, in tandem with staff training and guidance, resident education, environmental assessment and modification, and the use of vitamin D and calcium supplements [196].

1.5.2 New Zealand Specific rehabilitation programs

The New Zealand ACC's current National Strategy for Preventing Injury from Falls [15] identifies adults over the age of 65 who reside in residential-care as being particularly high-risk for the effects of a fall, and recognises them as a priority group for falls-prevention. However, current New Zealand strategy is limited to regional programs by specific DHBs/partnerships such as the "Steady as you go" strength and balance classes run by Age Concern in the Tauranga region [198]. Furthermore, initiatives like the recently-funded Auckland-Waitemata DHB falls prevention program [199] and the Otago Falls Program (the merits of which are discussed in Section 1.2.1) reflect that the majority of New Zealand falls-prevention programs target and work with community-dwelling older adults, neglecting those with further impaired functional ability, greater falls risk, and a greater potential for quantifiable benefits: the frail elderly within aged care homes in New Zealand.

Ultimately, at present in New Zealand there is no prescribed exercise intervention aimed at preventing falls or increasing physical function (or treating diseases such as sarcopenia and osteoporosis) in the frail elderly within residential care settings. Consequently, a requirement exists for an easily accessible, widespread and cost-effective means of exercising these individuals safely, which will produce gains in QoL, physical function and a decreased risk/number of falls, yet still encourage a high level of compliance in this population.

Part Two: Whole-Body Vibration Exercise

1.6 Whole Body Vibration Exercise

1.6.1 History

Environmental exposure to vibrations is common-place for many individuals, for example in the occupational use of vehicles, motor saws or drills. Prolonged overexposure to frequencies between 50 and 300 Hz can result in the occupational hazard known as hand-arm vibration syndrome, or 'vibration white finger', due to the exaggerated vasoconstriction and permanent numbness of fingers [200], leading to the assumption that vibrations were detrimental to health and the development of international industry standards such as those for hand-arm (ISO 5349-1:2001) and later whole-body vibration (ISO 2631-5:2004) exposure [201]. However, in the 1960s Russian scientists explored the potential of vibration therapy on cosmonauts, using it in attempts to enhance muscle and bone strength to counter their loss in low-gravitational outer space. The work with cosmonauts progressed to subsequent work using a combination of vibration- and resistance-training to improve the muscle strength of athletes within the Russian Olympic team [202], concurrent with their success throughout Olympic Games of the 1970s and 1980s. Upon the fall of Communism and the Iron Curtain, Western scientists were able to share in this knowledge and experience, and commercial use of vibration training grew, for example including use by NASA [203], culminating in various scientific studies to assess differing vibration training regimes for health and training.

The term 'vibration training' is broad and can be divided into two distinct categories depending on how vibrations are applied to the body: 'local vibration training' and 'whole body vibration' training. The purported mechanisms of action are discussed in Section 1.7 below, but briefly 'local vibration training' consists of direct contact between a muscle belly/tendon and a vibrating source, whereas in 'whole body vibration' users perform static and dynamic exercises on a platform which generates vibrations that disseminate over the whole body [204].

Whole Body Vibration (WBV) exercise has gained increasing traction as an exercise-training tool, and is the most common and well-studied vibration-training approach [204]. Typically used to strengthen the muscles of the lower limbs, WBV exercise entails individuals performing static or dynamic exercises, mainly of the lower body, on a platform which generates vibrations of varying speed (Frequency of Vibration, FoV) and size (peak-to-peak amplitude). As such, the intensity of WBV-exercise can be dictated either by altering the FoV (Hz) or the degree of displacement/peak-amplitude (mm). Commercially available WBV platforms fall into two basic types: those that produce synchronous vertical vibrations to both legs concurrently (Vertical

WBV), and those that deliver the vibrations asynchronously to one leg and then the other via oscillating or rotational vibrations around a central pivot (Rotational WBV) (Figure 1.5). Vertical WBV delivers vibration at higher frequencies and amplitudes, making it popular with athletes. Conversely, Rotational WBV has much less vertical impact on the body, decreasing energy transfer to the spine and head, reducing stress on the individual due to delivering vibrations at lower frequencies and engaging muscles alternately as in normal walking motion [205], making its use favourable for therapeutic training purposes as the body is more readily able to compensate and absorb the transmission of the rocking vibration.

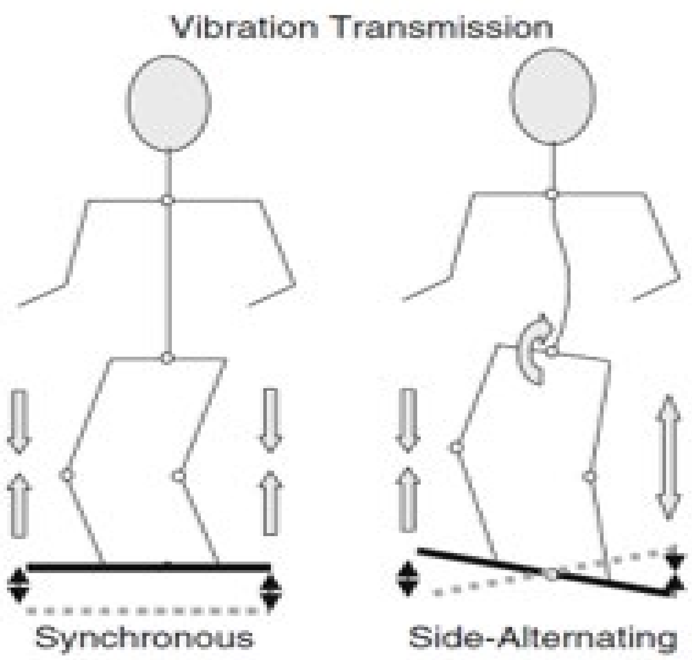

Figure 1.5. Vertical (synchronous) vs. Rotational (asynchronous/side-alternating) WBV platforms [206]. *Image reprinted with permission from Springer Nature: the European Journal of Applied Physiology 'Vibration as an exercise modality: how it may work, and what its potential might be' J. Rittweger [206].*

1.6.2 Use in athletic performance

In recent years, several researchers have documented acute improvements in strength and power as a result of various vibration-exercise training programs [207]. Acute increases in explosive strength have been reported in both elite- and amateur-level athletes, with locally-imposed vibration-stimuli enhancing maximal power/explosive strength and mean power of bicep curls for male athletes from both groups [208]. Notably, the reported immediate increases of maximal power were significantly smaller for amateur athletes than their elite-level counterparts [208]. There is some suggestion that the intensity of WBV could be an influencing factor where explosive strength gains are the training-goal, regardless of training-status, with WBV at 50 Hz increasing peak average power and 1 repetition max performance of 16 trained and untrained subjects whilst frequencies of 20 Hz and 35 Hz did not [209, 210]. In contrast however, acute bouts of WBV at FoV's of 26 Hz [211] and 30 Hz [212] significantly increased the strength and power outputs of trained male athletes. Together, these findings suggest that both WBV-intensity and the training status of individuals may influence the effectiveness of WBV, with highly-trained athletes better-placed to respond positively to higher intensities of WBV. Interestingly, it seems that these WBV-associated acute increases in maximal strength and power can also manifest from chronic training, with 12-weeks of WBV training at 35-40 Hz producing gains in isometric and dynamic knee-extensor strength equitable to those achieved from a conventional resistance-training program [213]. Moreover, the work of Delecluse et al. [213] suggested that untrained females can garner benefits from WBV exercise beyond those from conventional resistance-training, as significant explosive strength gains were only reported with WBV-training, simultaneously dispelling any notion of gender- or training-status-influence and concurrently discounting any placebo effect contributing to reported gains [213]. Of further note is that although Vertical WBV has been favoured for athletic training protocols, both Rotational WBV [211] and Vertical WBV [209, 210, 212, 213] have reported demonstrable strength- and power-benefits, suggesting that both forms of WBV-delivery can be effective training tools in athletes able to tolerate high frequencies.

1.7 Proposed Mechanisms

1.7.1 Tonic Vibration Reflex

First proposed by De Gail et al. [214], the Tonic Vibration Reflex suggests that mechanical vibration of a single skeletal muscle induces a tonic reflex contraction in that muscle and concurrent relaxation of its antagonists. The vibration-induced contraction and relaxation produces subsequent cyclic contractions, continuing the reflexive cycle and temporarily increasing muscle activity [214]. The stimulus provided by WBV exercise has been demonstrated to activate neural pathways sufficiently to generate this tonic vibration reflex in participants, with muscles stimulated to continuously contract and relax cyclically until the stimulus stops [215]. That is to say, WBV exercise increases muscle activity by inducing a cyclical stretch-shortening of muscles, otherwise known as cyclical eccentric:concentric muscle contractions [216]. Subsequently, muscles have been shown to respond to these reflexive contractions with increased activity, size, and strength, all indicative of a successful training approach.

Specifically, WBV exercise has been consistently shown to increase muscle activity [216-220]. There is some suggestion that the tonic vibration reflex and associated increase in muscle activity is elicited by WBV at frequencies of 1–30 Hz [221], yet conversely others suggest a dose-response where greater FoV induces higher muscle activity [222]. Ultimately, frequencies ranging from 2 Hz [220] up-to 46 Hz [219] have all been shown to increase muscle activation to varying degrees, whilst the magnitude of mechanical stimulation has been shown to be similar with both rotational and vertical WBV [217, 220]. Resulting from the training effect of the tonic vibration reflex and associated increased muscle activation, WBV exercise across a range of different participant groups (from trained males through to individuals confined to bed-rest) has been shown to induce increases in muscle growth [223, 224], strength [223] and power [225] to such extents that WBV exercise has been deemed to produce "*similar or greater strength improvements compared with conventional resistance training*" [226].

1.7.2 Enhanced Blood Flow and Fluid Dynamics

Whole Body Vibration exercise is also associated with shifts in fluid dynamics, vasodilation of capillaries [227] and resultant increased peripheral circulation [219]. Sufficient research has not been conducted to identify if this response is intensity- or dose-dependent, but this effect is particularly prominent in the lower extremities [228], which receive the greatest level of stimulation from WBV exercise when performed on either vertical or rotational vibration platforms, delivering plantar-based vibration stimuli. These shifts in fluid dynamics are associated with increased localised blood flow, with acute bouts of WBV exercise shown to significantly enhance muscular blood circulation in the calf and thigh, doubling mean blood flow velocity in the popliteal artery from 6.5 to 13.0 $cm \cdot s^{-1}$ [218]. Furthermore, the addition of WBV exercise to concurrent squatting significantly increased localised blood flow and reduced muscle oxygenation levels in the vastus lateralis muscles of young trained males [216, 229], indicative of enhanced muscle activity. Supporting this notion, localised vibration stimuli have elicited increases in peripheral blood flow of 14 [230], 20 [231], and even 46% [232]. It is hypothesised that observed increases in blood flow may be due to increased muscle activity, decreased blood viscosity, decreased vascular resistance, or a combination of these factors [233]. Whilst researchers acknowledge the need for further research in this area [233], such localised increases in peripheral blood flow of the lower limbs are often reported anecdotally by participants taking part in WBV exercise as a "tingling" or "warmth" in the lower limbs, and ultimately result in enhanced nutrient delivery, waste removal [234], lymphatic flow and venous drainage [232].

Furthermore, mechanical stresses to the skeletal system caused by WBV exercise are thought to enhance bone loading, with WBV exercise-induced shifts in fluid dynamics associated with resultant mechanostransduction and increased osteogenesis [215, 235, 236]. Specifically, WBV-induced increases in venous drainage, and subsequent fluid flow through the extracellular spaces of the bone's canaliculi and lacunae, are thought to increase sheer stresses and stimulate bone cells' osteogenesis [215, 232]. Consistent with this, mechanical stimuli such as enhanced fluid flow and hydrostatic pressure have been shown to stimulate osteocytic release of factors such as transforming growth factor-B and prostaglandins, influencing osteoblastic and osteoclastic activity and having resultant anabolic effects on the skeleton [237], whilst short periods of increased fluid flow have been shown to promote the proliferation and survival of osteoclasts [238]. Consistent with this, animal-based *in-vitro* studies have shown WBV to specifically up-regulate osteoblast differentiation, matrix synthesis and mineralization [239]. In support, *in-vitro* work by Uzer et al. [240] showed osteocytes to be responsive to low-intensity vibrations, such as those elicited with WBV, although the authors were unable to determine specific anabolic or catabolic responses [240]. What-is-more, bone may also concurrently respond to the applied muscular-forces as a result of morphological adaptation, in accordance with the muscle-bone theory encompassed in Wolff's Law, promoting further osteogenesis as strength and muscle-tone increase with training [215]. These mechanisms could be of particular significance for individuals with age-related bone loss and/or osteoporosis, where decreased levels of weight-bearing activity result in reduced loading of bone tissue and associated reductions in fluid dynamics and osteogenesis. Consequently, shifts in fluid dynamics present as a plausible mechanism for the WBV-effects on bone health discussed in 1.8.3 below.

1.7.3 Hormonal Changes

Research also suggests links between WBV exercise and increased circulating levels of anabolic hormones [50, 215, 241, 242]. In particular, studies have reported enhanced circulating levels of Growth Hormone [225, 242] and Testosterone [225, 242], both known anabolic hormones strongly-associated with musculoskeletal growth. In addition, Goto et al. reported increased circulating levels of adrenaline and noradrenaline with WBV training [243]. Such changes have predominantly been reported in young adult males [225, 242, 243], but the work of Cardinale et al. suggests that this may also be true of older adults aged 66-85 years, where insulin-like growth factor 1 was elevated by acute WBV exercise, but Growth Hormone and Testosterone levels were unchanged [244]. Similarly, animal studies have shown mechanical vibration to activate growth factors and cell matrix synthesis [245], whilst evidence exists to suggest that WBV exercise can upregulate factors promoting angiogenesis [246, 247]. In tandem with the fluid dynamic shifts discussed above, this provides further plausible mechanistic explanation for the purported anabolic effects of WBV on muscle and bone (as discussed in 1.7.1 and 1.7.2).

1.7.4 Proprioception

It has been proposed that the challenge of maintaining equilibrium during WBV can have balance-training effects [193]. Indeed, a review by Cardinale and Rittweger expands on this theory, suggesting that WBV exercise can not only train proprioceptive responses to challenges in balance, but also neuronal sensitivity to them [241]. That is to say, WBV exercise can help train individuals to i) identify challenges to balance earlier through enhanced neuronal sensitivity, and then ii) better react to these challenges with improved reaction time [225, 241]. Additionally, in building on the Tonic Vibration Reflex and Hormonal changes discussed above, WBV exercise has been shown to increase muscle mass and strength of the lower-limbs, and particularly at the mid-calf, an area important for balance [223]. Specifically, rotational WBV has been shown to elicit the highest levels of muscle activation in the tibialis anterior muscles of the calf as opposed to any other muscle/group in comparison to vertical WBV and no WBV exercise [248]. The explicit muscle activation evidenced by Abercromby et al. [248] carries great significance for the proprioceptive mechanistic action of WBV exercise, as Di Guilio et al. [249] advise that the tibialis anterior muscle is best-linked to an individual's centre of gravity. Training and strengthening the tibialis anterior muscle is thus enhancing an individual's ability to maintain their centre of gravity, enhancing their proprioceptive function and ability to react to somatosensory signals, and hence maintain their dynamic balance. What-is-more, significant increases have been reported in neuromuscular activation of the gastrocnemius [248] and other triceps surae muscles [250], suggesting that WBV can tone and strengthen other muscles of the mid-calf important for balance control. Furthermore, in a broader-sense, WBV-associated increases in muscle mass have been shown to correlate with better movement and stability [251]. Combining these findings, WBV exercise results in individuals being better placed to recognise and react to challenges in balance, with their muscles able to do so with greater force. That is to say, in real-life/therapeutic application terms, rotational WBV exercise in particular presents as a viable method for proprioceptive training, and thus dynamic balance enhancement, bringing with it associated increases in functional ability and falls-related confidence.

1.8 WBV and Community-Dwelling Elderly

1.8.1 Overview

Effects of WBV-exercise in the mobile/community-dwelling elderly (60-75 years old) appear to depend on the type of vibration, amplitude and length of training. Successful studies have used a variety of settings (15-50 Hz; 2-14 mm), frequency of training sessions (1-7 sessions/week), and durations (4-10 minutes/session over 6-8 months). Compliance levels for WBV in the mobile elderly are high, with no reported side-effects [32, 252]. Short duration sessions (up to 2x10 minutes per day at 30Hz) of treatment are well tolerated and have not produced adverse effects [13, 32, 253]. Reported benefits include improved function and balance [217, 220, 235, 251, 254-257], as well as musculoskeletal improvements in muscle-strength [253, 258, 259], -power [260], -mass [217] and -activation [226], and bone health [252, 257, 260-263]. Psychological benefits such as enhanced QoL have also been reported [254, 255, 257, 264], making it a safe and effective training tool for this population.

1.8.2 Function

Whole Body Vibration (WBV) exercise has gained significant traction as a safe and effective training tool for improving physical function in older adults [235, 245, 253]. The healthy elderly appear to respond well to WBV exercise, with the mobility-related effects of WBV-based interventions being relatively well-established in post-menopausal women and healthy/mobile community-dwelling elderly. Multiple researchers have reported WBV-associated improvements in balance [217, 235, 251, 256], physical function [220, 254, 255, 257], and muscular strength [253, 259, 265, 266] in this population from a variety of protocols. Methodological differences are apparent with respect to duration and frequency of training sessions, with most employing physically-challenging programs consisting of vertical WBV at FOVs of 30-40 Hz and directing participants to conduct some element of dynamic exercises whilst receiving WBV. Compliance levels in this able-bodied population are high, with short duration sessions (up to 2x10 minutes per day) of treatment were shown to be well tolerated and not producing any adverse chronic effects [235, 259, 267].

Outcome measures of functional improvement have been varied. As a well-validated assessment tool for use in older adults [268], multiple researchers have favoured the Timed-Up-and-Go (TUG) test as a primary outcome measure of the functional changes elicited by WBV training. Improvements in TUG performance of 9-12% [220, 258, 269] have been reported as a result of WBV-interventions from 6- to 10-weeks long. Moreover, related improvements of up-to 14.9% in walking speed and step-length have been reported following 2-months [256] and 6-

months [257] of low-level WBV exercise at 10-20 Hz. Furthermore, improvements in balance and stability of up-to 29% have been reported [235], in addition to enhanced stability and movement control [251], with 3-8 months of WBV at 12.6-20 Hz. Interestingly, a recent meta-analysis suggests that rotational WBV may be more effective than vertical WBV in enhancing both static and functional balance [270].

Mobility and performance in functional tests are not the only benefits that have been reported from WBV use in healthy/mobile older adults. Significant strength gains have been reported in this population with WBV-exercise, with dynamic strength gains of 16% have been reported as a result of 6 months of dynamic exercises combined with WBV [259]. The same study reported isometric strength gains of 15% [259], comparable to the 9.8% increase reported by Bogaerts et al. [217] following 12-months of WBV training, but substantially below a 38% increase reported from just 10 weeks of high-intensity WBV training [258], suggesting that the magnitude of response is intensity-dependent. Participants in all three studies conducted dynamic exercises in addition to WBV-exercise (i.e. whilst on the machine), but the findings suggest that WBV exercise can form part of an efficient fitness program to increase strength in sarcopenic individuals. Indeed, in addition to the aforementioned strength-gains, WBV-exercise has been shown to increase levels of muscle activation [226] and induced increases in muscle mass [217] and mid-calf cross-sectional area [223]. Together, these results provide credible support for the Tonic Vibration Reflex, and associated muscle hypertrophy, as a mechanistic action of WBV exercise.

1.8.3 Bone Health

Supporting the mechanisms discussed in Section 1.7.2 & 1.7.3 above, significant evidence exists for the beneficial effects of WBV-exercise on the bone health of older adults, particularly the more healthy/mobile individuals residing in the community [245, 252, 257, 259, 261, 263, 267]. However, unlike the clear-cut effects on physical function discussed above, numerous studies have reported no change in BMD as a result of WBV exercise [260, 262, 271-273], with one group reporting a WBV-associated decline in bone health [274]. The preferred measure for changes in BMD, DXA scans are used to measure bone health in the majority of these studies, yet the magnitude of effects has varied from study-to-study dependant on design.

One of the first studies to assess WBV use in the elderly, Rubin [267] reported one year of regular WBV exercise at 30 Hz to induce a 2.7% relative benefit of treatment in the Whole-Body BMD of postmenopausal women. However, subsequent researchers have predominantly measured and reported BMD changes at specific anatomical sites, with the most prevalent being the femoral neck/hip and lumbar regions. These particular sites are of great relevance to this population as the incidence of hip fractures is seven times higher in older adults (70-74 years old) than in younger post-menopausal women aged 50-54 years old [51], dramatically increasing their risk of residential-level care, further fractures, and even death within the ensuing 12 months [51], increasing mortality risk 3-fold [275]. Furthermore, much mechanical stress/strain from WBV training is absorbed at these joints, making them particularly prudent measures for assessing the effects of WBV-exercise on bone health.

Reported WBV-associated increases in the femoral neck/hip BMD of this population range from 0.3 [262] to 3.2% [245], whereas increases of the lumbar spine range from 0.5 [262] to 4.3% [245]. Interestingly, the smallest benefits, reported by von Stengel [262], were associated with 12 months of rotational WBV at lower frequencies (12.5 Hz), whereas the larger benefits elicited from 6 months of vertical WBV at 30 Hz [245], appearing to suggest that the type and/or FoV of WBV may be more important than the duration of the intervention. Indeed, WBV-based interventions just 12-weeks in length have reported BMD improvements [261], suggesting that shorter-duration training-programs can still be beneficial.

The 12-month WBV-intervention of von Stengel [262] included participants receiving either rotational WBV at 12.5 Hz or vertical WBV at 35 Hz, and whilst the increase in BMD at the femoral neck was larger with vertical WBV (1.1 vs 0.3% for the rotational WBV), it was still substantially less than the values reported by Ruan [245]. Additionally, 8 weeks of low-level rotational WBV at 12.5Hz has been shown to reduce markers of bone resorption by 34.6% in postmenopausal females [252], suggesting that both forms of delivery are of potential benefit to the bone health of older adults. Rat-based models have suggested higher-frequencies can elicit larger bone formation rates, with a 28-day protocol eliciting 159% greater rates at 90 Hz than either 45Hz or a control group, both of which were unchanged [276]. Considering that prolonged overexposure to frequencies between 50 and 300 Hz is associated with ‘vibration white finger’ [200], the efficacy of delivering frequent bouts of therapeutic WBV at 90 Hz to humans would need to be questioned, however a subsequent trial involving 202 post-menopausal females with a mean age of 60 years old, have dispelled this notion, deploying WBV at similar frequencies (90 Hz and 30 Hz) for 12 months and showing no significant effect on BMD at the lumbar spine, total hip, or femoral neck for either FoV [273].

Considering an average annual decline of 5 and 8% in BMD at the femoral neck/hip and lumbar spine, respectively, in individuals with osteoporosis [277], even studies such as Slatskova et al. [273] that reported no change in BMD levels following WBV exercise can be considered successful in addressing this decline. That is to say, WBV has been shown to help maintain current levels of bone health [260, 262, 272, 273, 278], with very few studies suggesting any significant negative influence on the bone health of "healthy" older adults [274]. Again dispelling the notion that the length of WBV-intervention is a deciding variable in the intervention's success, WBV training programs from 11 wks to 12 and even 18 months in length have all reported such maintenance of (i.e. no change in) BMD [260, 262, 271-273]. The same is true for FoV and type of WBV, with maintenance of BMD levels reported from low-level protocols deploying 12 Hz of rotational-WBV [260] through to higher frequencies of 30 and even 90 Hz of vertical-vibration [273]. Furthermore, programs delivering WBV-exercise alone (with no added training) have reported maintenance of the initial BMD levels in healthy postmenopausal women [260, 271, 273]. Likewise, the addition of WBV to conventional strength- and multifunctional-training programs did not enhance the effectiveness of either training element, resulting in maintenance of BMD at best [262] and even significant losses in whole body Bone Mineral Content (BMC) levels in other studies [274]. Rubin et al recognised that the largest improvements in BMD were seen in those individuals with lowest body mass (i.e. the most frail) [267]. This echoes Rees' [279] sentiments regarding greater WBV-associated functional enhancement in the elderly, suggesting that WBV exercise may be of particular benefit to this population.

1.8.4 Psychological Wellbeing

To-date, only four studies have investigated the effects of WBV exercise on the QoL of community-dwelling older adults. Mori et al. [257] showed thrice-weekly sessions of WBV-exercise at 10-15 Hz to significantly improve QoL in 40 females aged 60-80 years old, as assessed using the Japanese Osteoporosis Quality of Life questionnaire. The largest benefits were reported in the areas of pain and social activity; however, a lack of control group means that there is no way of specifically attributing these benefits to the WBV-exercise alone. Two further studies have demonstrated successful improvements in community-dwelling older adults' QoL with WBV-interventions compared to matched-controls, employing 6-week and 3-month WBV interventions [254, 264]. Both studies deployed the full SF-36 questionnaire as the QoL assessment tool, the length of which has been shown to have potential problems with compliance and consistency in older adults [280]. Furthermore, the sample size for Pessoa et al.'s research was only 30 participants spread across three treatment groups [264], meaning that whilst these findings suggest promise, the psychological benefits of WBV-exercise on the elderly remains unclear.

1.9 WBV and "Special Populations"

Whilst the healthy elderly appear to respond well to WBV exercise, it may be most beneficial for those persons who have extremely limited movement capabilities and therefore cannot exercise conventionally, as the exercise only requires the participant to stand on the platform with slight knee flexion, supported with handrails in one-minute bouts. Indeed, researchers have shown that those with the poorest initial assessment scores for measures of leg strength, function and/or balance demonstrated bigger WBV-related beneficial effects [45, 253]. Participants in both studies were community-dwelling/mobile elderly, suggesting that those with more significant levels of frailty and dependence may reap greater levels of benefit. Moreover, the rest periods given between each repeated bout of WBV only serve to enhance its applicability as a therapeutic tool. Consequently, there is a small, but growing, body of research investigating the use of WBV exercise with various special population groups with increased levels of frailty and/or dependency, as outlined in the following subsections.

1.9.1 WBV and Parkinson's Disease

Individuals with Parkinson's Disease (PD) suffer numerous physical impairments, predominantly comprising of postural instability and ensuing disruptions to gait, mobility, falls-risk and independence [281]. Promising improvements in such parameters resulting from WBV training in healthy individuals of all ages (discussed in Sections 1.6.2 and 1.8) have led researchers to explore its efficacy as a potential training tool for use by patients with PD, with mixed results to-date [282]. Acute bouts of WBV exercise, delivered at 6 Hz for 5*1-minute bouts, were reported to increase postural control in 52 patients with PD when compared to a moderate walk of the same duration [281]. Comparable findings were reported by Haas et al. [283] using similar parameters, albeit employing a cross-over design, with the authors highlighting particular improvement of up-to 25% in rigidity and tremor scores of postural stability assessment in those receiving WBV. However, in comparing the effectiveness of different frequencies of acute WBV exercise, Chouza et al. reported no effect of WBV training at 3, 6 or 9 Hz on balance or gait of patients with PD when compared to a placebo exercise, raising the possibility of a placebo effect [284]. Similarly, longer-term training interventions have also reported mixed-results with the deployment of WBV exercise in patients with PD. Interventions of 3- and 5- weeks in length, delivering WBV at 25 and 6 Hz respectively, both reported no evidence of superior effects of WBV training on measures of mobility, balance or gait in comparison with placebo exercise and conventional physiotherapy/balance training [285, 286]. However, those findings are not to discount the effectiveness of WBV training in patients with PD, as both WBV protocols did elicit improvements in motor function compared to baseline levels [285, 286], suggesting chronic, lasting effects of WBV training on patients with PD are possible. Supporting this, short-term interventions of 4- and 12-sessions of WBV exercise have reported benefits. Four sessions of WBV at 7 Hz reportedly increased postural stability by 17.5%, in comparison to no-change in a sham-WBV control group [287], whereas 12-sessions of dynamic exercises conducted with concurrent WBV at 35 Hz brought no changes to balance but improved the gait and QoL of patients with PD [288]. Evidently, both acute- and chronic-benefits of WBV are possible in patients with PD, and WBV exercise appears favourable for mobility & balance in comparison to no activity for these patients. However, when compared to another active interventions or placebo there remains insufficient evidence to prove or refute the effectiveness of WBV on PD [282, 289].

1.9.2 WBV and Multiple Sclerosis

Multiple Sclerosis (MS) results in a number of impairments, the most incapacitating of which are ataxia and impaired balance [290]. As such, the positive proprioceptive and functional effects of WBV exercise, discussed above in sections 1.7.4 and 1.8.2, may help address the reduced postural control and impaired ambulation experienced by many MS patients. Researchers have explored the effectiveness of WBV training in patients with MS, reporting positive effects. One-off bouts of WBV, delivered across 1-30 Hz, have been shown to increase the muscle activation in the lower-limb muscles of 5 MS patients [291]. The highest activation rates were reported with rotational WBV at 29 Hz for vastus medialis and erector truncae muscles, 25 Hz for the gastrocnemius medialis and 19 Hz for the tibialis anterior muscle [291], suggesting that this form of WBV can be effective across a variety of frequencies. Translating these findings of enhanced muscle-activation into clinically-important functional benefits, a small intervention pilot-study involving 12 MS patients, showed low frequencies of WBV at 2-4.4 Hz delivered in 5*1-minute bouts significantly improved performance in the Sensory Organisation and TUG tests for up-to 2 weeks [290]. A similar-sized study involving 16 MS patients receiving 4 weeks of WBV training at 40-50 Hz suggested some improvement in function, with enhanced 10-m walk and TUG test performance, albeit not to statistical significance [292]. Additionally, a more comprehensive 8-week WBV intervention at 20 Hz and 2.6 mm amplitude also improved levels of function, with 25 MS patients improving Patient Determined Disability Steps and MS Functional Composite scores [293]. Clearly the small sample-sizes is a limiting factor in the studies of Schuhfried [290] and Schyns et al. [292], but the results of these studies and that of Yang et al. [293], coupled with the increased lower-limb muscle activation reported by Madou et al. [291] indicate that WBV training can positively influence postural control and mobility in patients with MS.

1.9.3 WBV and Cerebral Palsy

In a similar vein to those with MS, individuals with Cerebral Palsy (CP) most commonly exhibit impairment in muscle function, reduced muscle mass, and ensuing impaired mobility [294]. Accordingly, researchers have started to explore the application of WBV exercise as a training tool for patients with CP, again reporting promising benefits [294, 295]. Eight-weeks of thrice-weekly 6-minute bouts of WBV training at 25-40 Hz proved sufficient to reduce spasticity and increase the leg muscle strength of 7 CP patients at levels equitable to a conventional resistance-trained CP control group [295]. Measures of Gross Motor Function were also reportedly enhanced in the WBV group, though performance in the more-often used 6-minute walk test did not change as a result of the WBV training regime [295]. However, a longer 20-week clinical trial, delivering 9-minute bouts of WBV four-times-a-week at 12-20 Hz to 40 adolescents and young adults with CP, not only reported positive anthropometric changes in lean mass and BMD but also improved the distanced walked in the 6-minute walk test by up-to 35% [294]. Notably, those with more significant functional impairment demonstrated greater improvements of mobility [294], in accordance with similar findings reported for the use of WBV by the elderly [267, 279]. Evidently, work in this specific field is somewhat limited, but as with MS patients, it shows great promise.

1.9.4 WBV and Spinal Cord Injuries

The rapid stretch-contraction cycles, autonomous muscle activation, and challenges of postural displacement occurring during WBV exercise have led to researchers considering its effectiveness as a training tool for individuals with Spinal Cord Injuries (SCI). Delivered in various guises, WBV training has produced beneficial effects on measures of neuromuscular function and tone, ensuing ambulatory function (including gait, velocity and balance), Bone Mineral Density (BMD) and Cardiovascular function for individuals with varying degrees of SCI, as discussed below.

Individuals with an SCI experience a number of complications, chiefly their restricted ambulatory function and concurrent atrophy and degradation of their musculoskeletal system [296]. There is a small-body of research to suggest that WBV exercise can provide a successful intervention tool to help address these issues, reflexively-increasing muscle-activity of lower limbs [296, 297] and numerous measures of a patient's walking function [298]. In a study comparing the acute WBV-responses of 6 able-bodied individuals and 4 with SCI in C2-T10 of moderate-to-complete impairment, higher frequencies of 45 Hz and 1.2 mm amplitude were most-reliable in eliciting muscle activation of the lower limbs for those with an SCI [296]. Furthermore, 6 repeated 3-

minute bouts of WBV at 10, 20 and 30 Hz all significantly increased Electromyography (EMG) activity of the Vastus Lateralis and Medialis muscles in 8 patients with complete SCI (C5-L1) [297]. Moreover, acute bouts of WBV at 30 Hz have reportedly elicited significant improvements in both static balance and postural sway of 6 motor-incomplete SCI patients, in comparison with a sham-exercise control group [299]. Translating these benefits into chronic-training and ensuing functional changes, 4 weeks of WBV training (3 days/week) significantly increased the walking speed, cadence, step length and intralimb coordination of 17 patients with motor-incomplete SCI (C3-T8), with the magnitude of changes comparable to that observed with traditional locomotor training [298]. Such clinically meaningful changes suggest that WBV is an effective method to activate muscle mass in patients with differing degrees of SCI, with potential to be incorporated into their rehabilitation programs and elicit lasting improvements in walking function [296-298].

Evidence suggests that BMD rapidly declines in the years following an SCI [300], yet very little investigation has occurred exploring the potential for WBV exercise to address this, despite its ease-of-use and the promising findings discussed in Section 1.8.3 above. Of most promise is a 6-month WBV based exercise programme, consisting of 20-minutes at 34 Hz five times a week, which has been shown to mitigate BMD decline in 9 patients aged 20-50 years old with complex paraplegic SCI (T3-12) [301]. The lack of a control group makes it impossible to quantify these findings and attribute effects specifically to WBV exercise, but they echo those described in postmenopausal women and other healthy older adults [260, 262, 271-273], suggesting that maintenance of BMD levels is possible with WBV in frail individuals exhibiting poor bone health, including those with SCIs.

Cardiovascular function of SCI patients has also been shown to improve with WBV exercise, enhancing blood flow and muscle oxygenation levels. Acute WBV sessions 3-6 min in length at 30, 40 & 50 Hz have all been shown to elicit small but significant increases in muscle oxygenation levels, with larger increases seen in patients with motor-complete SCI (C4-T6) than able-bodied control participants [302]. Furthermore, 6 repeated 3-minute bouts of WBV at 20 and 30 Hz significantly increased the peak blood velocity of the femoral artery in 8 patients with SCI, indicative of increased lower-limb blood flow [297]. Such findings have led researchers to conclude that WBV is an effective method to increase leg blood flow and sustain tissue-integrity in SCI patients, increasing oxygen saturation of muscles in the lower limbs and potentially helping void the difficulties of orthostatic hypotension encountered during rehabilitation programs [297, 302]. In a review, Felter [300] acknowledges the need for larger sample sizes and the implementation of longitudinal studies exploring the use of WBV exercise in SCI patients, but recognises positive outcomes and the safe ease-of-use in this population.

Overall, from Section 1.9 it is evident that individuals with diverse levels of frailty and/or dependency, arising from different neuro-musculoskeletal health conditions, are able to tolerate WBV training well and receive numerous positive benefits to their Neuromuscular, Cardiovascular and Bone health as a result, making it a feasible and effective training tool for use with frail populations.

1.9.5 WBV and Cardiovascular Health

A common mechanistic-theory for the effects of WBV exercise involves WBV-induced shifts in fluid dynamics [218, 232], vasodilation of capillaries [227] and resultant increased peripheral circulation [219] (explored in Section 1.7.2). Increases in peripheral blood flow in-excess of 50% are reported from acute bouts of WBV exercise [218, 232], and as such the WBV-induced vasodilation of lower-limb vessels, and ensuing erythema may be seen as positive vascular changes. However they could potentially lead to pooling of blood and subsequent orthostatic intolerance [303]. This effect may be exacerbated in individuals with poor vascular health, for example where increased arterial stiffness (AIx) can reduce wave reflection back to the heart [304]. Moreover, orthostatic intolerance may subsequently result in episodes such as dizziness, postural vasovagal syncope, or postural tachycardia syndrome, simultaneously increasing the risk of injury from a sudden-fall and reducing an individual's independence and quality of life [303].

WBV exercise is considered an effective strength-training alternative to resistance training [217, 223], which is pertinent as it has been reported that resistance exercise may increase AIx [305-307], thus increasing the likelihood of atherosclerosis [308], left ventricular failure [309, 310] and myocardial ischemia [306, 311]. It could therefore be prudent to speculate that WBV-exercise may likewise increase AIx/decrease vascular health in compromised individuals. However, further to the work exploring the impact of acute and chronic WBV exercise on the vascular function of SCI patients explored in Section 1.9.4, investigations into the effects of WBV exercise on the vascular health of other population groups are conversely reporting some promising effects.

To-date, researchers have considered the acute-effects of WBV-exercise on a limited amount of younger- and older-participants, delivering WBV at a FoV of between 6-40 Hz. Resultant acute reductions in systemic AIx have been reported in young healthy adults, with significant decreases observed up-to 40 minutes following 10*1-minute sets of static squats concurrent with vertical WBV at between 26-40 Hz and 1-4 mm amplitude [312, 313]. The acute-effects of WBV exercise on older adults have also been explored to a small extent, by 2 research groups. Interestingly, in a study of 9 frail older adults completing a one-off session of 10*60-seconds of rotational-WBV at 6 Hz and 2 mm amplitude interspersed with rest periods, Abdolhosseini et al. reported WBV-associated decreases in central SBP and DBP vs. a control group mimicking the exercise without WBV-stimulation, and importantly found no overall indication of orthostatic intolerance with WBV exercise [314]. Though also reporting a small increase in AIx with WBV, Abdolhosseini et al. found that this was not different between conditions when AIx was normalized to a heart rate of 75 beats per minute to account for fluctuations in heart rate, and thus concluded that the low-level of WBV deployed in the study was safe for frail older adults to use [314]. What-is-more, passive vibration at 25 Hz and 2 mm amplitude, delivered directly to the legs when sat on a WBV platform, was shown to improve the AIx of 11 older post-stroke patients in comparison to a non-exercising control group [315]. The findings of Abdolhosseini et al. [314] and Koutnik et al. [315] indicate the safe and potential beneficial use of vibration exercise for those with compromised vascular health.

The chronic-effects of WBV exercise on vascular health/AIx have also been explored to an extent by researchers. Thrice-weekly sessions of vertical-WBV training, conducted at 30-35 Hz and varying amplitude for 6 weeks, reduced systemic AIx in 38 young, healthy but overweight/obese females (aged 18-25 years) in comparison to a non-exercising control [316]. However, participants completed various dynamic exercises concurrently to the WBV-exercise whilst the control group did no exercise [316], meaning the effects cannot be attributed directly to the WBV-stimulus alone. Many of the same research group also report beneficial effects of WBV on the AIx of young- and postmenopausal-obese females after 6, 8 and 12 weeks of dynamic-exercise sets performed whilst receiving vertical-WBV at 25-35 Hz/ 1 mm amplitude [317-319]. Interestingly, researchers reported strong correlations between decreased arterial stiffness and increased leg muscle strength, yet, with only comparison to non-exercising control groups there again is no way to attribute these benefits directly to either the WBV exercise or the simultaneous dynamic-exercise sets performed [317, 319]. A further study delivering 3-months of vertical-WBV at 30 Hz and 3.2 g, with no concurrent exercises, reported beneficial decreases in the arterial stiffness of 38 mobile middle-aged and elderly women and men (61.9 years-old) in comparison to a non-exercising control, although this did not reach statistical significance between groups [320]. Despite the early promise of these findings, the effects of long-term WBV-interventions on vascular health, and in particular the AIx of less-mobile/frail older adults, are unknown. Of note, to-date no research has considered the chronic-effects of low-level rotational-WBV on vascular health. Considering the characteristically poor vascular health displayed by frail older adults [321], caution must be shown with this population when prescribing any WBV exercise until concerns around localised-erythema and orthostatic intolerance can be fully allied.

1.10 WBV and the Frail Elderly

1.10.1 Overview

With multiple co-morbidities and subsequent higher levels of dependency and burden of care, the frail elderly in residential-care exhibit the highest rate of falls-related hospitalisation and mortality. Like those populations discussed in Section 1.9 above, the majority have extremely limited movement capabilities and therefore cannot exercise conventionally. Consequently, they could stand to benefit most from an easily-accessible therapeutic-exercise intervention such as WBV exercise. Ultimately this may help them enhance their function, mobility and confidence to such levels that they can begin to take part in conventional group training sessions and/or conduct more of their own daily living and care tasks, improving their QoL and concurrently reducing their burden on physiotherapists and care staff, respectively. However, a paucity of research exists focussing specifically on the use of WBV exercise with this population (Table 1.3). The limited research to-date has followed inconsistent study designs, employing varying WBV training and delivery methods on differing sample sizes of patients, yet the biggest variable to-date is inconsistent levels of frailty amongst participants. This is acknowledged by Bogaerts et al. [322] as limiting the research's representation of the frail elderly, the very targets of the research, with the frailest not being included. Despite these limitations, researchers have reported high levels of compliance, suggesting that the frail elderly may indeed obtain benefits from WBV exercise on several parameters, as discussed in the following sections.

Table 1.3. Clinical applications of WBV in the frail elderly within residential-care.

Lead Author	Patients (mean age)	Vibration Type	Vibration Duration	Study Design	Outcome
Bautmans [193]	n = 24 (77.5 yrs)	35-40 Hz 2-5 mm vWBV	1/3* 30-60 sec	3*wk 6 wks (vs. Ex Con)	WBV ↑ function and balance.
Bruyere [323]	n = 42 (81.9 yrs)	10-26 Hz 3-7 mm rWBV	4*60 sec	3*wk 6 wks (vs. Ex Con)	WBV ↑ function and QoL
Bogaerts [322]	n = 113 (79.6 yrs)	30-40 Hz < 2.2 g vWBV	15-60 sec, for 1-12 min	3*wk 6 mo (vs. Control)	WBV ↑ function and ↓ falls risk
Verschueren [324]	n = 113 (79.6 yrs)	30-40 Hz < 2.2 g vWBV	15-60 sec, for 1-12 min	3*wk 6 mo (vs. Control)	WBV ↑ strength (bone health?)
Pollock [325]	n = 77 (81 yrs)	15-30 Hz 2-8 mm rWBV	5*60 sec	3*wk 8 wks (vs. Ex Con) 6 mo F/up	WBV ↑ function (Lost within 6 mo); n/c in balance or fear of falling;
Beaudart [326]	n = 62 (83.2 yrs)	30 Hz 2 mm vWBV	5*15 sec	3*wk 3 mo (vs. Control)	n/c in parameters
Zhang# [327]	n = 44 (85.3 yrs)	6-26 Hz 1-3 mm rWBV	4/5*60 sec	3-5*wk 8 wks (vs. Control)	WBV ↑ function, balance, strength, health status
Alvarez-Barbosa [328]	n = 29 (84.9 yrs)	30-35 Hz 4 mm vWBV	3*30 sec	3*wk 8 wks (vs. Control)	WBV ↑ function and QoL
Buckinex [329]	n = 62 (83.2 yrs)	30 Hz 2 mm vWBV	5*15 sec	3*wk 3 mo (vs. Control)	n/c between groups

#frail hospital outpatients; Ex Con = Exercise control group; Control = non-exercising control group; F/up = Follow-up; rWBV = Rotational WBV; vWBV = Vertical WBV.

1.10.2 Function

Much like the work with community-dwelling elderly, promising beneficial effects on a variety of parameters of function and mobility have resulted from WBV exercise interventions in the frail elderly [193, 322, 323, 325, 327, 328]. Researchers appear to have predominantly favoured Vertical WBV at higher frequencies (30-40 Hz), with the majority reporting functional benefits [193, 322, 328], yet others found no increase at similar frequencies with this mode [326, 329].

Moreover, Bruyere et al. [323] and Zhang et al. [327] demonstrated functional benefits from Rotational WBV at lower frequencies (6-26 Hz); as this form of WBV has much less vertical impact on the body, and thus reduces stress on the individual, its use may be more applicable in the frail elderly/therapeutic setting than Vertical WBV. Functional benefits were demonstrated in TUG test performance and gait tests after relatively short 6-week [193, 323] and 8-week [325, 328] intervention programs. These benefits were comparable to those reported by Bogaerts et al. [322] following a 6-month intervention, suggesting that shorter-duration interventions are equally applicable. However, the duration of WBV applied per session does appear to influence its effectiveness at improving mobility, as the Beaudart/Buckinex group demonstrate [326, 329], where repeated short 15-second bouts of WBV were not sufficient to elicit functional improvements. All other researchers delivered WBV via repeated 30- to 60-second bouts, a method that was sufficient to improve measures of functionality of the frail elderly participants involved.

In addition to variations of WBV type and durations of both training-intervention and individual WBV-sessions/bouts, significant methodological differences are apparent with respect to the specific exercises conducted on the WBV platform, sample size, and the control group with whom research comparisons were made. Most researchers directed participants to conduct a variety of dynamic exercises whilst receiving WBV, with for example Pollock et al. [325] added WBV-exercise to the OTAGO falls program. The notable exceptions to this approach are Bruyere et al. [323] and Zhang et al. [327] who merely instructed participants to stand/adopt a “partial squat” on the WBV machine. The inclusion of exercises on the WBV machine can be prohibitive to the frail elderly, who often lack the confidence and/or ability to complete such exercises. The more challenging elements of these exercise programs deters potential participants [135], and consequently the frail elderly show the lowest levels of compliance to such programs [193]. Accordingly, the protocols employed by Bruyere et al. [323] and Zhang et al. [327] may be most applicable for successful implementation in this specific population. Sample sizes varied dramatically for the studies involved (Table 1.3), with only the work of Bogaerts [322] having what can be deemed a large sample size of 113 participants. However, the authors reported that only 18 of the participants in this study suffered from a moderate to severe degree of frailty, and as such the findings of these participants in the Verschueren et al. and Bogaerts et al. studies [322, 324] may not be representative of the overall frail elderly population. The only research to-date to revisit participants after the end of their WBV intervention, Pollock et al. report that the significant functional gains elicited by 8-weeks of WBV training were all lost within 6-months and all participants had returned to baseline levels [325]. However, without a non-exercising control group for comparison, it is not possible to ascertain if this reflects a positive impact (reduced rate of functional loss) in comparison to age-related deterioration. Evidently, the functional improvements reported, particularly with larger sample sizes, suggest that WBV exercise may be successful in a wider application, yet the time-line for detraining/loss of WBV-related benefits remains unclear.

Possible mechanisms for the reported functional improvements are highlighted in the findings of previous researchers [193, 322, 324, 327]. The strength improvements reported [324, 327] are clinically significant in size, ranging from 8 [324] to 52% [327] improvements in isometric and dynamic strength respectively, albeit assessed by varying methods. These correlate with reported improvements in dynamic performance such as the TUG test [193, 323, 325, 327, 328], providing a plausible mechanism for such improvements. This in turn lends weight to the Tonic Vibration Reflex theory, discussed in Section 1.7.1, whereby WBV exercise is purported to activate more motor units and thus enhance neuromuscular response [241]. Furthermore, the reported balance improvements [193, 327] and reduced falls risk [322] may also be attributed, in part at least, to enhanced neuromuscular function in this population. The converse may also be true; reported improvements in balance may have contributed towards improvements in functional performance [322]. Finally, as fear of falling is a significant contributing factor to decreased mobility and increased levels of functional dependence in this population [77], WBV-associated improvements in falls-related confidence (discussed in 1.10.4) may in turn manifest as enhanced levels of physical activity and functionality in a self-fulfilling cycle for this population, who are known to display low levels of falls-related confidence and self-efficacy.

1.10.3 Bone Health

The incidence of fractures is seven times higher in women aged 80+ years [51], with 70% of this population displaying bone density scores indicative of osteoporosis [32]. Hip fractures are particularly problematic in this population, with fracture of the femoral neck representing over 50% of fractures [55]. Despite this, and the relative success of WBV exercise on the bone health of community-dwelling/mobile elderly participants (Section 1.8.3), only one research group has investigated the effects of WBV exercise on the bone health of the frail elderly [324]. In fact, the results from the 6-month WBV intervention by Verschueren et al. [324] demonstrate the somewhat mixed-messages reported for this parameter with community-dwelling/mobile elderly, as researchers reported only a small 0.75% increase in total-hip BMD with the WBV group, but no significant difference between WBV and non-exercise groups, leading to the conclusion that the WBV program used provided no additional musculoskeletal benefit over vitamin D supplementation. Although with community-dwelling elderly, the work of Zha et al. [330] is pertinent to consider here, as the reported WBV-derived improvements in the BMD of elderly participants were particularly notable in osteoporotic participants in the study, i.e., the more frail of the study participants. Given this consideration, it is notable that Verschueren et al. [324] acknowledge a lack of frailty in their participants as a limitation in their study. However, some positive associations have been demonstrated between WBV and the bone health and remodelling of mobile elderly participants (Section 1.8.3). When coupled with the fact that age-related bone loss is associated with reduced mechanical loading [32], this means that the role of WBV in the bone health of frail elderly patients is an area that still warrants further exploration.

1.10.4 Psychological Wellbeing

Often displaying low levels of confidence, self-esteem and self-efficacy, the frail elderly can make pronounced gains in confidence and independence from well-designed, easily-accessible exercise interventions. Indeed, their combination of low levels of confidence, frailty and physical function is well-matched with the ease-of-use of WBV exercise and its potential psychological benefits. However, to-date limited studies have built upon the work with mobile/healthy elderly (Section 1.8.4), with only four studies assessing the psychological benefits of WBV exercise for the frail elderly residing in aged-care facilities [323, 325, 327, 328].

Methodology in the four studies is mixed, with participant numbers varying from n=29 to 77, WBV delivered via a mix of vertical and rotational WBV at frequencies of 6-35 Hz, and various tools used to assess psychological benefits relating to QoL and falls confidence. However, intervention-duration was similar across all four studies, at 6-8 weeks, whilst three of the four interventions combined WBV exercise with additional physical therapy/strength and balance training [323, 325, 327].

Findings from these four studies are generally positive, with all reporting some benefits to participants' QoL as a result of WBV-based training. As with research into the psychological effects of WBV exercise on the community-dwelling elderly, researchers have favoured the SF-36 [323] or shortened SF-12 [325, 327] measure of QoL, with only Alvarez-Barbosa [328] utilising the EuroQOL health assessment tool. Rotational WBV training alone at 6-26 Hz was reported to increase falls-confidence and general health, as measured by the SF-12 scale, in comparison to 8 weeks of "usual care and exercise" [327]. Likewise, the addition of WBV at 30-35 Hz to an 8-week exercise program enhanced mobility and overall health scores in the EuroQOL assessment, versus a non-exercising control group [328], suggesting that WBV training can successfully elicit psychological benefits. However, the addition of WBV to existing physiotherapy (PT) programs has been of more questionable psychological benefit for the frail elderly. Six-weeks of WBV+PT reportedly increased SF-36 scores in comparison with a stand-alone PT program [323], and although a similar 8-week program caused WBV-associated increases in balance, falls-confidence and physical components of the SF-12, these were at a similar rate to the PT program alone [331]. The latter researchers did follow-up assessments 6-months after completion of the exercise intervention, but all benefits had been lost by this time, giving some indication of possible time-line for detraining of such benefits [331]. Adherence levels in this study were low for the WBV group, with the mean total time using WBV being just 37% of the maximal time-offered; as such it remains unclear if better attendance levels could have elicited further benefit for participants undergoing WBV training [331]. Nevertheless, the limited mobility and confidence of many frail elderly means most cannot exercise conventionally, so one must question if comparison with a PT/exercise control group is most valid for a group where exercise-non-adherence and high levels of physical inactivity are core reasons behind their ensuing frailty (Section 1.4.3). Consequently, in comparing WBV-therapy to "usual care and exercise" it is the research of Zhang et al. [327] that offers the best insight into the true value of WBV in eliciting psychological benefits in the frail elderly, building levels of self-efficacy and ensuing physical activity in a self-fulfilling cycle.

Ultimately, the vast differences in participants' levels of frailty and study protocols, coupled with the above limitations in study design, have led researchers to conclude that the clinical, social, and functional effects of long-term WBV in the frail elderly remain unclear and more research is needed in order to develop an easily-accessible WBV program in the frail elderly.

1.11 References

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2. Research Aims and Hypotheses

This research project aims to assess the suitability of low-level WBV-exercise as an accessible exercise-training tool and treatment-prescription program for use by the frail elderly. Contributing to this, the primary outcomes that this research aims to assess are the effects of low-level WBV on functional and psychological parameters in this population. Secondary outcome measures include the effects on cardiovascular and bone-health parameters. Furthermore, the research also aims to identify how-long any potential benefits remain after ceasing WBV-training, identifying for the first-time a time-line for detraining with this exercise.

Specifically, the research project has the following hypotheses:

Primary Outcomes

- The mobility and function of the frail elderly can be improved by chronic low-level Whole-Body Vibration exercise.

- The psychological wellbeing, falls-confidence, independence and Quality of Life of the frail elderly can be improved by chronic low-level Whole-Body Vibration exercise.

Secondary Outcomes

- The frail elderly can receive sufficient mechanical stimulus from chronic low-level Whole-Body Vibration exercise to improve their bone health.

- The cardiovascular health of the frail elderly will not be adversely-affected by chronic low-level Whole-Body Vibration exercise.

- Benefits elicited by the chronic Whole-Body Vibration exercise-intervention will last beyond the training period.

3. Methodology

3.1 Chapter Overview

The following chapter outlines how the current research project was conducted, and how the efficacy and effects of low-level WBV were assessed.

Full methodology is detailed in Section 3.2, in the guise of a modified version of the published FEVER Methodology and Protocol Paper ([1], Appendix A), with changes to reflect the approaches taken. Published at the beginning of the project, the protocol paper aimed to garner further expert and international feedback on the methods by peer review. Briefly, the research project consisted of an open, randomised feasibility study, consisting of multiple parallel arms and a longitudinal element. Thrice-weekly sessions of low-level WBV-exercise were delivered over 16-weeks, with effects compared to those of a Simulated-WBV exercise and a non-exercising Control. Including both exercising (SIM) and non-exercising control (CON) groups was essential for being able to account for any possible placebo effect arising from study participation.

Assessments were conducted at 6 time-points throughout the study: at baseline (0 week), after 8 and 16 weeks of the training intervention period, and 3-, 6- and 12-months after completion of the last training session (to identify a time-line for detraining). Assessments in the Bone Health arm of the project were conducted at baseline (0 week), upon completion of the training intervention (16 weeks) and 12-months post-intervention only.

All assessment tools employed were valid and reliable assessment tools, used in previous published-research and reflective of day-to-day living tasks. A small-subsection of participants in the WBV and SIM groups also underwent assessment of Bone Health (Part B). Methods for Part B differ slightly to the FEVER Methodology and Protocol Paper, where because of participant drop-out no CON group participants were included in the Bone Health arm of the project.

Additionally, a small in-lab assessment was conducted of the WBV machines used in the study, to ensure that the delivery of WBV-stimuli was indeed reliable. The results of this accelerometery examination are detailed after the FEVER Methodology and Protocol Paper in Section 3.3.

3.2 Methodology

3.2.1 Rationale

The frail elderly (predominantly nursing home residents, aged 70+ years) often exhibit poorer health and a higher burden of care than more-mobile/less-dependent healthy elderly. Their increased frailty means they are unable to exercise conventionally and gain the associated health and functional benefits, leading to reduced physical function and independence and culminating in a decreased QoL. Consequently, falls and associated fractures are a particularly serious threat to the health and well-being of frail elderly, causing trauma, pain, impaired function, a loss of confidence in day-to-day living, a loss of independence, and even death [2]. The consequences of a fall are far reaching in the elderly, affecting not only their own lives but also those of relatives and carers; as the number of older New Zealanders increases, so too does the incidence of falls and ultimately the financial-burden placed on the public health system. Prescribed exercise interventions have been found to be successful in addressing these issues [3], but are often costly to run, labour-intensive, require highly skilled/trained practitioners and do not always encourage compliance.

At present in New Zealand there is no prescribed exercise intervention aimed at preventing falls or increasing physical function (or treating diseases such as sarcopenia and osteoporosis) in the frail elderly. This is because the frail elderly cannot undertake conventional exercise at an intensity to provide health benefits, and show the lowest compliance rates for such exercise [4]. A common treatment prescribed for elderly New Zealanders, with respect to bone health and falls-prevention, is increased dietary calcium coupled with supplementation of vitamin D at 1.25 mg/month to decrease fractures from a fall [5]. Consequently, a requirement exists for an easily accessible, widespread and cost-effective means of exercising the frail elderly safely, which will produce gains in QoL, physical function and a decreased risk/number of falls, yet still encourage a high level of compliance in this population.

Easy to use and relatively cheap to purchase, the demands of WBV exercise are minimal for both participant and practitioner - taking part in WBV exercise can be as simple as standing on a platform with knees flexed at approximately 20° for 1-minute bouts interspersed with 1-minute rest periods - making it an easily accessible activity for those with mobility problems or limited cognitive ability. Whole Body Vibration (WBV) has been deemed a safe and effective means of enhancing muscular strength and bone health in various populations, including sedentary persons [6] and the healthy/mobile elderly aged 60-75 years old [7, 8]. Mechanical stresses to the bone caused by WBV are thought to enhance bone loading (stimulating osteogenesis), thus increasing bone mineral density and bone health [7, 8]. With some studies showing no improved bone health as a result of WBV interventions [9-11], there remains a lack of clarity on the effects of WBV on this parameter. However, the Tonic Vibration Reflex proposes that WBV-stimulated muscle contractions and elevated localised blood flow can enhance anabolic hormone levels, further strengthening the musculoskeletal system [12], thus not just effecting bone health but also muscle strength and physical function. Moreover, WBV interventions in post-menopausal women and the healthy/mobile elderly (aged 60-75 years old) have brought about improvements in lower-limb muscular strength and associated functional performance and quality of life [7, 8]. However, there is a paucity of research focusing specifically on the institutionalised, frail elderly who, with the highest levels of dependence and the highest rate of falls-related hospitalisation and mortality, would stand to benefit most from a well-developed, accessible treatment prescription utilising WBV exercise.

To-date research utilising WBV to enhance health and independence in the frail elderly remains sparse, with no clear treatment prescription identified. Studies [4, 13-15] have shown WBV to improve functionality, quality of life, lower-limb muscle strength and bone health of frail elderly participants, coupled with a reduced falls-risk. Ultimately, differences in participants' levels of frailty, study protocol and limitations in study design have led researchers to conclude that the clinical, social, and functional effects of long-term WBV in the frail elderly remain unknown and more research is needed in order to develop a WBV program in the frail elderly. Furthermore, there has been no investigation of any lasting effects after WBV-based exercise interventions have ceased, nor any attempt to identify a time-line of detraining.

Therefore, the aims of the FEVER (Frail Elderly Vibration Exercise Response) study are to establish i) an effective WBV-based treatment prescription program to maximise improvements in physical function and quality of life in the frail elderly, ii) if the frail elderly undergo any maintenance of, or improvement in, bone health and/or muscle strength as a result of WBV training, iii) which beneficial effects (if any) are retained post-intervention, or iv) the time-course of de-training.

3.2.2 Study Design

FEVER followed an open, randomised feasibility study. The study design consisted of three parallel arms, was placebo-controlled, and included a longitudinal response element. Figure 3.1 presents a schematic time-line of the study design following initial participant recruitment. The study protocol had ethical approval from the Health and Disability Ethics Committee of New Zealand (12/NTB/78), and Universal Trial Registration (UTN: U1111-11367146).

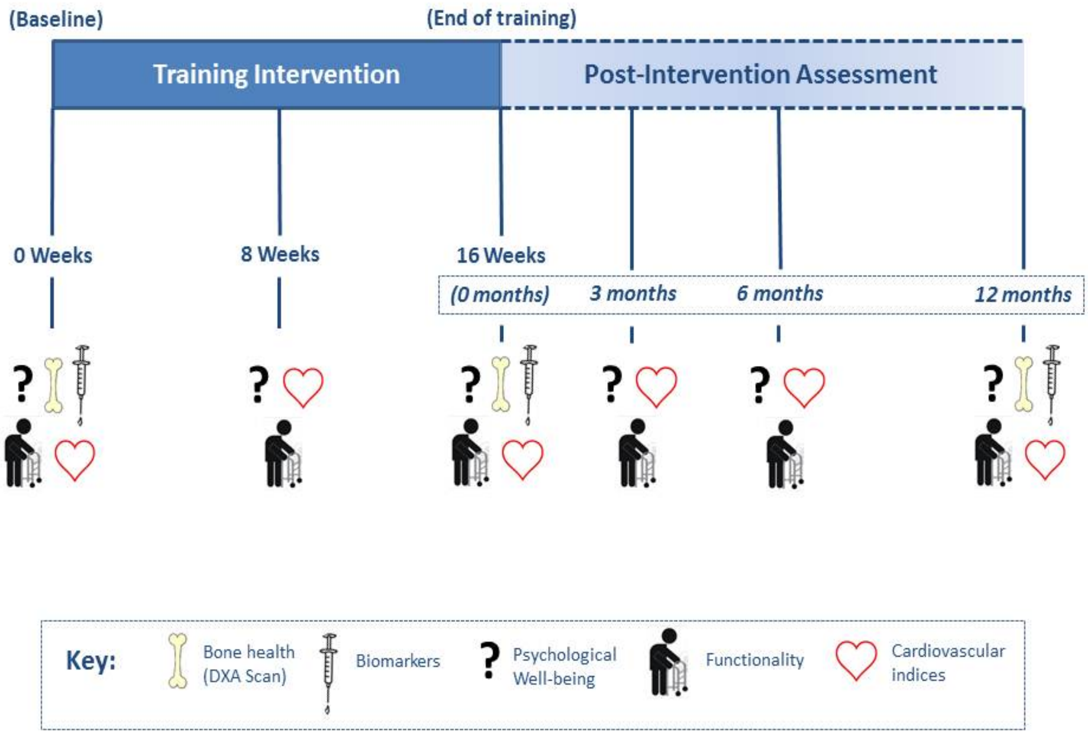

Figure 3.1. Schematic time-line of study design.

Participants

The study targeted a total of 180 frail elderly volunteers (60 per group including 20% drop out) from care home facilities based in the Greater Wellington Region/Urban Centre. Eligible volunteers aged 70 years and older underwent pre-screening for inclusion and exclusion criteria (Table 3.1) by consultant gerontologists and Clinical Managers/GPs associated with their place of residence. Briefly, eligible participants were assessed as having a degree of 'frailty', meaning that they are unable to undertake everyday activities unaided, as defined by the Functional Ambulation Categories outlined by Holden et al [16]. Transportation is a particular impediment to exercise in this population group [17]; in order to minimise disruption to participants, and thus encourage compliance, all exercise and assessment sessions were completed *in-situ* within care homes where possible, with participants transported to external assessments when required (e.g. DXA). The WBV machine remained *in-situ* at the participating care home for the duration of the exercise intervention.

Table 3.1. Inclusion and exclusion criteria.

INCLUSION CRITERIA	Aged 70 years and older
	Institutionalized in a care home
	Categorised as frail individuals by a Functional Ambulation Categorisation of 2-5
	Asymptomatic for pain
EXCLUSION CRITERIA	***Part A & B of study***
	Knee or hip prosthesis
	A recent history (<12 months) of venous thrombosis, fracture or surgery
	Individuals with spinal tumours or metastases, disc herniation or aortic aneurisms
	A cognitive ability score below 22 in the RUDAS assessment [18]
	Individuals with a pacemaker, Epilepsy, or Diabetes with neuropathy
	Biochemical indicators of pathologies such as Paget's disease, renal disease, or diabetes
	Part B only
	Individuals suffering from hypoparathyroidism or diseases/conditions resulting in hypercalcaemia and/or hypercalciuria
	Fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency

Exercise Interventions (Part A)

All participants continued to receive access to standard care home care and activities during the intervention, which may have included chair-based exercise sessions and a variety of social activities (e.g. bingo, bowls, golf putting, and arts and crafts). Using a random number generator tool (random.org), eligible participants were randomly assigned to one of three different groups: (1) a Control group (CON) who received standard care only, (2) a Simulated-WBV (SIM) group who received 16 weeks of simulated-WBV exercise training (mimic the stance and duration of WBV), and (3) a WBV group (WBV) who received 16 weeks of WBV exercise (Galileo Fitness Control 0544, Novotec, Germany). Participants in the SIM and WBV groups completed three sessions a week, all of which were supervised by research staff and trained exercise-practicum students, with compliance and adherence noted. Participants in the WBV and SIM-exercise groups exercised together, in order to account for any psychosocial effects of study involvement/social interaction on wellbeing [19] and in order to maximise enjoyment and social interaction, thus encouraging compliance.

Participants in the WBV and SIM groups undertook three exercise sessions a week, training based on the overload principle. Starting with 2 weeks of 5*1-minute bouts of WBV/SIM-exercise, each interspersed with 1-minute rest periods, sessions increased by 1 minute/week until 10*1-minute bouts were reached. The starting level of WBV intensity for all participants was 6 Hz/2.0 mm amplitude (foot position #1; the lowest settings of the machine); upon reaching 10*1-minute bouts of exercise, progression of FoV and amplitude were self-determined (by increasing Hz and widening stance on the machine, respectively) in order to maximise compliance, dependent upon an individual's ability to tolerate the low-level vibration (up to a maximum 26 Hz.). The WBV (and SIM-exercise) exercise were performed standing with isometric knee flexion ~20° (± 5°), which provides a damping effect to prevent spine or head vibration [10].

In order to monitor the impact of WBV sessions and any adverse events, participants were regularly asked to rate their perceived level of exertion and discomfort using the 11-point OMNI-Vibration exercise scale [20], the results of which were made available to a team of geriatric consultants from the Capital and Coast District Health Board in Wellington.

Bone Health (Part B)

A sub-set of up-to forty participants (i.e. 20 SIM and WBV groups) were approached and volunteered to undergo additional assessments to investigate whether WBV exercise further enhances the current bone-health-treatment regime of dietary calcium and vitamin D supplementation. Participants in this subset underwent various markers of bone health assessment (detailed below) at baseline, at the end of the exercise intervention period, and 12-months post-intervention.

Follow-up Assessments

To address a specific gap in the literature, the study investigated whether any beneficial effects of WBV are retained post-intervention, aiming to establish a time-course of de-training. To do so, outcome measures were also assessed at 3, 6 and 12 months after completion of the exercise intervention program (with the measures taken upon concluding the exercise intervention acting as a 0-month post-intervention time-point, Figure 3.1).

Measurement Procedures

The primary outcome measures for this study are Functionality and participants' Quality of Life (QoL). Secondary outcome measures are Bone Health, Lower Limb Strength, and Cardiovascular indices. All parameters were measured prior to commencing the exercise intervention (pre-exercise/baseline), during the intervention, upon completion of the intervention, and at periods during the 12-month period following the intervention. The specific data collection time-points for each parameter are indicated in Figure 3.1.

Primary Outcome Measures

- **Functionality**. Functionality was assessed using the Timed Up-and-Go [21] and Parallel Walk [22] tests, complemented by the Barthel Index Questionnaire [23]. The Barthel Index Questionnaire measures the independence of a patient in mobility and personal care (daily functionality) [23]. The Timed Up-and-Go Test assesses functional mobility, and has been shown to be a reliable tool for predicting falls in the elderly [21]. The Parallel Walk Test is a quick and simple and validated method of measuring dynamic balance during gait in the elderly [22].

Secondary Outcome Measures

- **Quality of Life**. Participants' QoL was assessed using the EuroQol EQ-5D-3L health questionnaire [24] and the Activities-specific Balance Confidence (ABC-UK) scale [25]. Widely used in older populations, the EuroQol EQ-5D-3L is particularly sensitive for use in rating the health state of frail populations [26]. Participants falls- and confidence-related QoL will assessed using the Activities-specific Balance Confidence (ABC-UK) scale [25].
- **Bone health**. Bone health was assessed using Dual-energy X-ray Absorptiometry (DXA) scans to assess total bone mineral density (BMD), in addition to specific BMD measures at the left-hip and lumbar region. Furthermore, changes in biochemical markers of osteoblast/osteoclast activity and vitamin D status were measured from first/second pass urine collections and fasted-blood samples. Dual-energy X-ray absorptiometry (DXA) scans were conducted, using the Hologic Horizon A densitometer (Hologic, Inc., Bedford, MA, USA), to quantify BMD – although not a mechanical property, BMD is easily measured by DXA, and has strong relationships with the probability of fracture [27]. Established

biomarkers serum osteocalcin and urinary pyridinoline/deoxypyridinoline were measured by accredited laboratories to quantify bone turnover and bone resorption (osteoclast activity), respectively. Furthermore, serum 25-OH-vitamin D levels were also assessed as a measure of vitamin D levels, levels of which are shown to be inversely linked to rates of fracture and osteoporotic bone loss [28].

- **Lower-Limb Strength**. Participants' Lower-Limb Strength was inferred using their performance in a 10-metre timed walk. An inverse relationship has been shown between leg-muscle strength and walking time over comparable differences in this age-group [29].
- **Cardiovascular indices**. To monitor previous anecdotal reports of localised erythema, changes in cardiovascular parameters (resting heart rate and systolic/diastolic BP, arterial wave reflection, central BP, and pulse pressure) were monitored throughout the study (both during the exercise intervention and in the follow-up assessment period) using the PulseCor R7 Cardioscope (PulseCor, Auckland, New Zealand) to measure brachial artery pressure waves and conduct Pulse Wave Analysis (PWA). This is a simple, non-invasive, valid and reliable technique that has been widely used to investigate central blood pressures and arterial stiffness [30].

Sample Size

Sample size was calculated based on a study of WBV effects on functionality in frail elderly women where the measure of functionality is Timed Up-and-Go performance [14]. Effect size curves of Thomas & Nelson [31] were used, effect size based on mean changes of 2.999, with 0.8 power and alpha at 5% ($p<0.05$) giving a total of 180 participants (60 per group; up-to 216 total including 20% drop out).

Sample size for the bone health subgroup is based on previous reported WBV-induced changes in lumbar BMD [32], with an effect size of 1.56 and a power of 0.8, giving a total of 20 participants. Considering the participants in this previous study were all diagnosed with osteoporosis (and we are unsure if this will be the case in the current study), the study aimed to double the calculated sample size to 20/group for this measure.

3.2.3 Statistical Analysis

Results are presented as group mean ± standard error of the mean (SEM), either as absolute-values or percentage-change from baseline. All statistical analyses were undertaken using SPSS Version 24 (SPSS, Inc., Chicago, IL, USA). Missing data points were accounted for using 5-step Multiple Imputation (on average 16% of data imputed), in accordance with Sterne et al. [33].

Data was then tested for skewness and kurtosis for normal distribution. All treatment effect-sizes were calculated in accordance with the methods outlined by Cohen's d [34], with clinical-importance inferred at Moderate (0.5-0.8) and Large (0.8+) effect-sizes in accordance with Page [35]. Main Functional, Psychological and Cardiovascular effects of the training intervention were analysed by repeated-measures ANOVA, with specific treatment*time differences identified using subsequent one-way ANOVA and Bonferroni post-hoc tests. As the Augmentation Index (AIx) is influenced by heart rate and the equation involves blood pressure, univariate analysis with Mean Arterial Pressure and resting-HR as covariates [36] were carried out to determine the level of influence on AIx for frail elderly, whilst paired-samples t-tests were used to identify within-group changes for AIx and SBP. In addition to repeated-measures ANOVA, effects of the training intervention on indices of Bone Health at specific timepoints were analysed by independent samples t-tests. Significance for all statistical tests was set at p=0.05.

3.2.4 Discussion

As compliance in the frail elderly group is an issue in other intervention studies [7] it is important to ensure ease of use and appropriateness of exercise interventions. One needs to visualise how any successful intervention will be continued beyond the study. Taking part in WBV exercise can be as simple as standing on a platform with knees flexed at approximately 20° for bouts of up to 1 minute interspersed with 1-minute rest periods, making it an easily accessible activity for those with mobility problems or limited cognitive ability who cannot undertake conventional strength exercises, such as the frail elderly. Accordingly, high levels of compliance to WBV exercise have been shown in the mobile elderly [6, 7, 10, 14, 15]. However, the lack of a simulated-exercise group in these studies means that compliance could have been due to the social interaction of participating in the study. Of the four previous WBV studies with frail elderly the compliance was relatively high, ranging from 72.7% of participants completing a 6-week intervention [14] to >90% session-attendance in both 6-week- and 6-month-long interventions [4, 13, 15]. With the sole cost being the initial outlay for a machine, and no requirement for highly-trained personnel such as physiotherapists, WBV-exercise presents as a feasible, cost-effective treatment prescription for specifically targeting falls-prevention in the frail elderly. However, at present there is a paucity of research focussing on WBV exercise in this group who, with the highest levels of dependence and the highest rate of falls-related hospitalisation and mortality, would stand to benefit most from a well-developed, accessible treatment prescription utilising WBV exercise.

A potential limitation of the FEVER study methodology was the diverse nature in participants and the diet and standard care which they receive from their care home. Complete dietary control (i.e. prescribed diet) is not feasible in a study of this nature and scope, but researchers note that all residents receive prescribed-diets within residential-care that should be equitable in their nutritional value (in accordance with Government care guidelines). Likewise, researchers were confident that residential-care homes all offer similar activities of social engagement and exercise to their residents (again in accordance with Government care guidelines) and acknowledge the importance of such routine in this population. In order to best counter these concerns, all changes were assessed as change from baseline (that is, change within an individual).

The FEVER study aimed to provide some clarity on the use and effectiveness of WBV-exercise by the frail elderly, and ultimately determine its potential for use as a prescription exercise for this specific population. The study design incorporated a significantly larger sample size than previous research and included a simulated-WBV group in order to specifically identify any placebo effect. Additionally, the FEVER study design included a long follow-up assessment period, allowing us to investigate if any longitudinal benefits are retained post-intervention, and/or the time-period for detraining. It is considered that this design best allowed the monitoring of the acute and chronic effects of WBV exercise on primary outcome measures (functionality and QoL), with the aim of secondary measures being to provide background and explanation to such effects.

With particular-emphasis on addressing health and wellbeing inequalities of the frail elderly, this research targeted one of the most-neglected groups with respect to health-care research. Expanding the knowledge-base of WBV use in this population, by developing a successful WBV-based treatment prescription programme this research has the potential to deliver pronounced individual health benefits within this group, increasing their confidence, function and quality-of-life and concurrently reducing their dependency on others for care/assistance with daily-living tasks. The project received support from the New Zealand ACC, with which the successful wide-spread implementation of said treatment prescription feasibly has the potential to significantly reduce primary and secondary health-care costs in New Zealand by decreasing the incidence of falls/after-care and fatal injury in the frail elderly.

3.3 WBV Machine Reliability

A lab assessment of the reliability of the WBV machines used in this research project (Galileo Fitness Control 0544, Novotec, Germany) was completed. In particular, the accuracy and consistency of the FoV delivered and experienced by participants regardless of differing body mass needed to be established. Additionally, the consistency of the peak amplitude of 2 or 4mm, as per the technical note for the machine, was assessed.

A commercially-available accelerometer (Vibsensor, Now Instruments and Software, Inc., CA USA) was used to measure the FoV, displacements and power generated by the WBV-machine. Peak-peak amplitudes were later calculated from peak-to-peak displacement in MATLAB (Mathworks, Massachusetts, USA).

Figure 3.2. Foot position markers of the Galileo Fitness Control 0544 WBV machine (https://www.galileo-training.com/de-english/products/p40/galileo-fitness---product-obsolete.html).

After being attached to the WBV platform, accelerometer readings were collected over 30-second periods of vibration, with each trial conducted twice. The peak-to-peak displacement MATLAB programme disregarded the first two and last two seconds of recordings, due to the lag time for the vibration plate to reach consistent maximal peak and degradation of peaks at the end of 30-seconds. Readings were taken with the machine unloaded, and likewise with 3 different participants of differing body mass for loading the machine, at a variety of combinations of amplitudes of 2-4 mm and FoV of 6-12 Hz. As per manufacturer guidelines, amplitudes were determined by foot-placement on the WBV-platform, being 2 mm for foot position 1 and 4 mm for foot position 3 (demonstrated in Figure 3.2). These specific parameters were used as they were deemed to best reflect the most commonly-used parameters in the current research project.

In-order to calculate amplitudes, the raw acceleration data x, y, z (m/s^2) over time (now 26-seconds) was band-pass filtered with an FoV of 0.5*Hz as the low cut-off and 2*Hz as the high cut-off and gravity accounted for using MATLAB. The resultant acceleration data was then bi-directionally band-pass filtered and then integrated to attain velocity, with the process then repeated on velocity to attain displacement. Finally, the filtered bi-directional displacement (y-direction) was calculated, and the power spectrum x, y, z (m^2/s^3), over a FoV (0.3 – 49.4 Hz) was produced (Figure 3. 3) to visually ascertain a normal repetitive signal as a final check of data.

Participant characteristics are detailed in Table 3.2, with results in Table 3.3 and Figures 3.4 and 3.5. Vibration frequency regulation of the WBV machine was shown to be highly-reliable, being unaffected by either load or foot placement (Table 3.3, Figure 3.4), whilst Amplitude was also highly-reliable being unaffected by load (Table 3.3, Figure 3.5). Peak-to-peak amplitude traces did reveal a regular modulation of maximal peak which may be due to a very small amount of horizontal displacement (Figure 3.4).

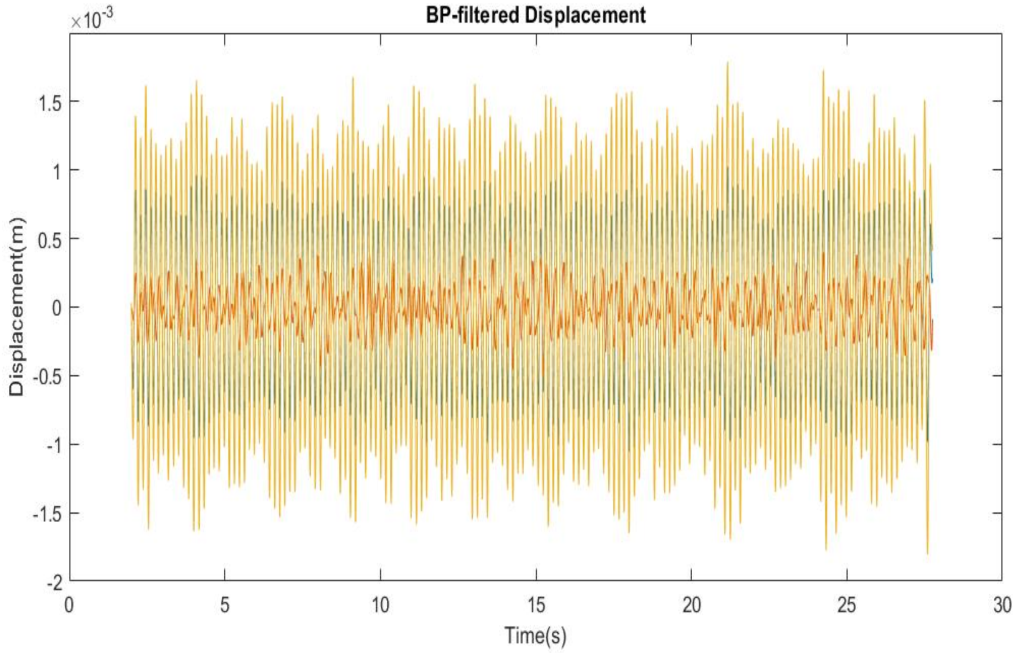

Figure 3.3. Example displacement-time figure, detailing displacement at 6Hz / 2mm.

Table 3.2. Participant characteristics.

Participant	Weight (kg)	BMI (kg/m^2)	Gender
1	47.5	19.8	F
2	86.5	26.8	M
3	86.0	27.8	M

Table 3.3. Measured frequencies and amplitudes of the Galileo WBV machine.

Condition	Measured Parameters (mean ± SEM)	
	Frequency of Vibration (Hz)	Amplitude (mm)
6 Hz / 2 mm Unloaded	6.21 ± 0.01	2.51 ± 0.04
6 Hz / 2 mm Loaded	6.20 ± 0.03	2.54 ± 0.01
6 Hz / 4 mm Unloaded	6.22 ± 0.01	4.35 ± 0.03
6 Hz / 4 mm Loaded	6.22 ± 0.00	4.34 ± 0.01
12 Hz / 2 mm Unloaded	12.05 ± 0.00	2.29 ± 0.01
12 Hz / 2 mm Loaded	11.89 ± 0.01	2.25 ± 0.01
12 Hz / 4 mm Unloaded	12.02 ± 0.00	3.91 ± 0.01
12 Hz / 4 mm Loaded	11.87 ± 0.01	3.93 ± 0.01

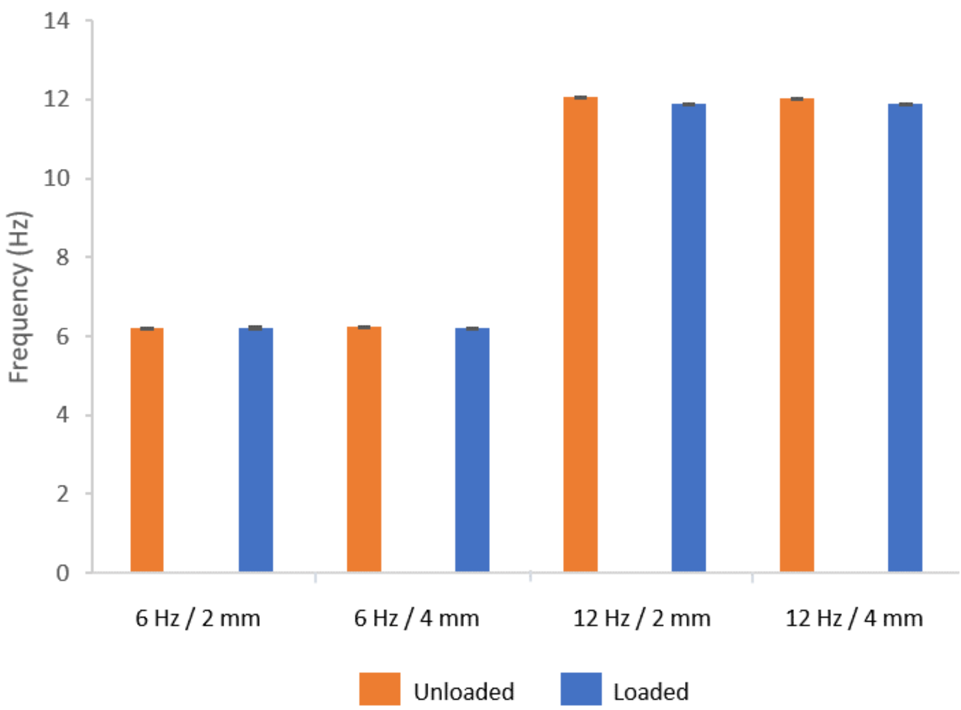

Figure 3.4. Vibration frequency regulation of the Galileo WBV machine (mean ± SEM).

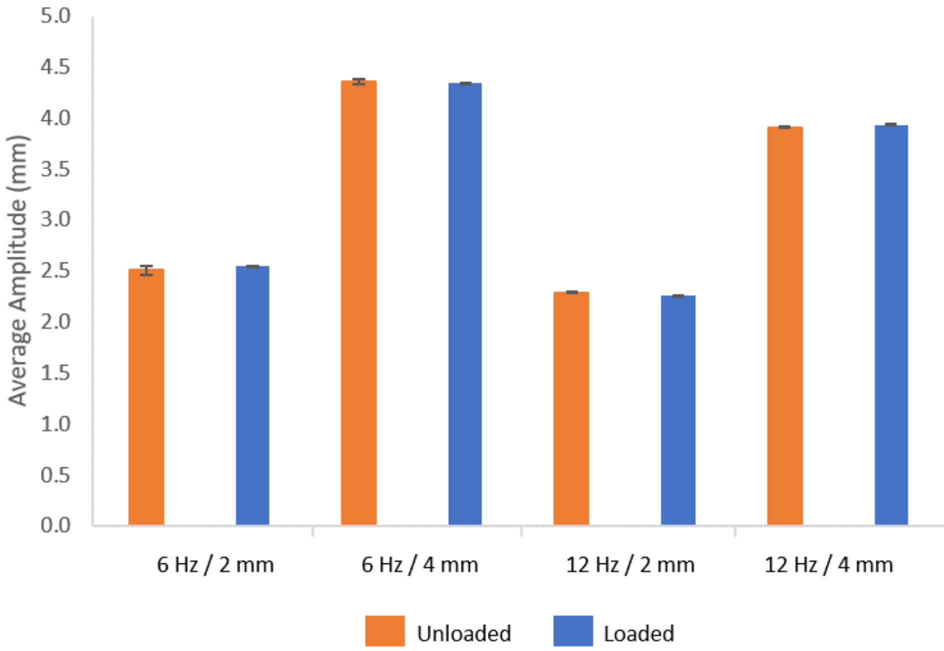

Figure 3.5. Amplitude regulation of the Galileo WBV machine (mean ± SEM).

In conclusion, the findings from this in-lab assessment demonstrate that the WBV machines utilised in the study did indeed deliver WBV at the intended FoV. Amplitude values were minimally-different from expected values, most-likely due to inexact placement/centring of the accelerometer on the WBV-platform foot-position, however remained the same irrespective of loading and were within manufacturer technical parameters (Appendix H). Finally, there was a degree of horizontal vibration, but at the low frequencies of 6 and 12 Hz this was minimal.

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4. Physical Function Results

4.1 Chapter Overview

The following chapter focuses on the physical function results from the current research project. Presented as a paper for journal submission (currently at revised submission stage with the *Archives of Physical Medicine and Rehabilitation* Journal), the general methodology and protocol are as previous chapters, but the focus on the functional assessments. The findings and discussion address 2 primary outcomes of the research project, namely the effects of chronic WBV-training on i) the mobility and ii) the independence of the frail elderly. The secondary-outcome regarding the time-line of detraining for these measures is also explored in this chapter.

4.2 EFFECTS OF WHOLE BODY VIBRATION TRAINING ON THE PHYSICAL FUNCTION OF THE FRAIL ELDERLY

4.2.1 ABSTRACT

Individual dependency and falls-risk are increased by sarcopenia and age-related declines in mobility and function. Conventional training counters such declines but is restricted in the elderly due to requisite intensities and supervisory-requirements. Whole Body Vibration (WBV) exercise presents as a safe and effective training-tool for the mobile elderly, yet a paucity of research exists on its application in the frail elderly, who could benefit most.

*After pre-screening for contraindications, 117 male and female volunteers (82.5 ± 7.9 years) from residential care-facilities were randomly allocated to a Control (CON), Simulated-exercise (SIM) or WBV-exercise (WBV) group. All participants received regular care, whilst WBV- and SIM-participants also underwent thrice-weekly exercise sessions for 16 weeks. Delivered by overload principle, WBV-training began with 5*1-min bouts of rotational-WBV at 6 Hz/2 mm (1:1min exercise:rest), progressing to 10*1-min at up-to 26 Hz/4 mm, maintaining knee-flexion. Training for SIM participants mimicked exercise stance and duration. Pre- and post-measures for Timed-Up-and-Go, Parallel Walk and 10-m Timed-Walk tests were completed, in addition to the Barthel Index Questionnaire.*

High levels of compliance and ease-of-use were reported, with no adverse effects. In comparison to baseline-levels, WBV-training elicited clinically-important treatment-effects in all parameters compared to SIM and CON groups. Treatment-effects remained apparent up-to 12-months post-intervention for Parallel Walk and 10-m Timed-Walk tests. Functional-test performance declined during- and post-intervention in non-WBV groups.

Findings suggest that 16-weeks of low-level WBV-exercise provides easily-accessible, adequate stimulus for the frail elderly to attain muscular and proprioceptive benefits sufficient to transfer into improved levels of functionality and independence.

4.2.2 INTRODUCTION

Sarcopenia is a highly-prevalent cause of the age-related declines in mobility and function seen in older adults [1, 2]. Compensations include altering gait and shifting the centre-of-mass to increase muscle efficiency and/or reduce pain [3]. However, resultant shifts can jeopardize balance and increase falls-risk, which is further exacerbated by poor visual cues, diminished proprioception, and weaker muscles [4]. Physical inactivity further accelerates the loss of mobility and increases the degree of sarcopenia. Consequently, such individuals are three-times more likely to suffer a fall and its debilitating consequences [5, 6].

Strength-training programs have successfully reversed age-related muscle- and strength-losses [7], promoting muscle-fibre hypertrophy in the healthy elderly [8, 9]. However, exercise-intensities of 60-85% maximum-effort are required, restricting their appeal-to and application-in the elderly, consequently under 10% of this population engage in such training [10]. Targeted balance-training has also elicited success in elderly participants [11, 12], yet often combines low-intensity balance- and coordination-exercises with more demanding strength/aerobic-training. The more challenging elements of these programs may deter potential participants [11], whilst the need for a qualified therapist to run sessions restricts accessibility and increases costs. Such programs have mainly focussed on community-dwelling older adults, ignoring those with greater functional-impairment and falls-risk, and yet a greater potential for quantifiable benefits: the frail elderly within residential-care. Less-able to exercise conventionally, an accessible and cost-effective musculoskeletal exercise that reduces falls-risk in this population is required.

Whole Body Vibration (WBV) exercise has gained prominence as a safe and effective strength-training tool in various populations including older adults [13-15]. In particular, researchers have reported improvements in the balance [13, 16-18], physical function [19-22], and muscle-strength [15, 23-25] of community-dwelling older adults. Methodological differences are apparent with respect to duration and frequency of WBV training-sessions, with most employing physically-challenging programs of vertical WBV at 30-40 Hz and concurrent dynamic-exercises. Compliance levels in this population are high, with sessions (up-to 2x10 minutes/day) being well-tolerated with no adverse effects [13, 25, 26]. However, there is a paucity of research focussing on the functional benefits of WBV exercise for the frail elderly.

Previous studies working with frail elderly participants have compared WBV-plus-exercise protocols to physical therapy [27] or low-level exercise [28] alone. In both cases, WBV exercise improved Timed-Up-and-Go (TUG) test performance and gait. However, both studies used only 6 weeks of WBV-training and included no follow-up to investigate how long benefits lasted post-training. Furthermore, any placebo effect that may have enhanced function was not fully considered. Taking part in such research can change an individual's behaviour, both in the attention they receive and the incidental-activity associated with participation [29]. Further studies have reported WBV-related improvements in function, balance and strength of the frail elderly [30-32]. However, on closer inspection sample populations were not wholly representative of the frail elderly. Only 18 of 111 participants in the largest studies suffered from a moderate-to-severe degree of frailty [30, 31], whilst another used outpatients [32] who by definition are not as frail or dependant on care.

The optimal duration of individual-bouts of WBV-exercise for attaining physical benefits remains unclear. Eight-week long training-interventions of repeated 30- and 60-second bouts of WBV are sufficient to elicit functional benefits in frail elderly [32, 33]. However, other studies have found no functional benefits when delivering shorter bouts (15 seconds) of WBV over significantly longer 3-month training-interventions [34, 35]. Furthermore, many studies only report functional gains when exercise is performed simultaneously whilst receiving WBV [28, 30, 31]. As the frail elderly frequently suffer from varying degrees of functional- and/or cognitive-impairment, such protocols may be implausible for this population. Therefore, the current study aims to establish (i) if this group can attain physical and functional benefits from an easily-accessible low-level WBV intervention, (ii) whether any beneficial effects are retained post-intervention, and (iii) the time-course of detraining.

4.2.3 METHODS

Study Design and Participants

The study received ethical approval from the Health and Disability Ethics Committee of New Zealand (12/NTB/78; Universal Trial Registration number: U1111-11367-146). A methodology paper details study design and specific recruitment procedures [36]. Following written informed-consent, eligible volunteers from rest home facilities in the Greater Wellington area underwent pre-screening for inclusion-criteria, that is frailty as determined by functional ambulation using a scale of 0-6, where less-than-6 indicates a degree of functional limitation and frailty [37]. Exclusion criteria were: a RUDAS assessment of cognitive function with minimum-score of 20 [38]; a lower-limb/spinal fracture within 12-months; hip- or knee-prosthesis; conditions including peripheral-neuropathy, cancer tumours, diabetic neuropathy; and participation in over 3 hours/week of exercise (fully-detailed in [36]).

Continuing to receive access to standard residential-care and activities throughout the study, participants were randomly assigned (using a random number computer-generator tool; random.org) to a: i) Control group (CON), ii) Simulated-exercise group (SIM), or iii) WBV-exercise group (WBV). Participants in the SIM and WBV groups exercised together 3-times/week for 16 weeks. The SIM group was included to account for any possible placebo-effect elicited by the musculoskeletal- and balance-demands of participation, both in the static-exercise performed in training and in the incidental activity in attending sessions (walking to/from sessions) and frequently rising/sitting during training, as well as the social-interaction/attention associated with participation.

Training Protocol

Participants in the WBV group exercised by standing with isometric knee flexion ≈20˚ (±5˚) whilst receiving 1-minute bouts of rotational-WBV, interspersed with 1-minute rest periods. Training load increased over the 16-week intervention according to self-determined progression. Participants began with 5*1-minute bouts of WBV exercise and rest (1:1) at 6 Hz/2.0 mm amplitude (Galileo Fitness Control 0544, Novotec, Germany), increasing until 10*1-minute bouts of WBV-exercise and rest were reached. Progression of Hz and/or amplitude were then self-determined by participants, up to a maximum of 26 Hz/4.0 mm. Frequency of vibration (FoV) and amplitude of the WBV-machines used were independently-assessed using an accelerometer (Vibsensor, Now Instruments and Software, Inc., CA USA). Participants in the SIM group mimicked exercise-stance and duration. All participants in training groups rated their perceived levels of exertion using the OMNI-Vibration Exercise Scale [39] and provided feedback weekly, independently-monitored by geriatricians.

Functional Assessment Procedures

Functionality was assessed using the Parallel Walk, 10-m Timed Walk and Timed Up-and-Go tests, complemented by the Barthel Index Questionnaire. Assessments were conducted at baseline (0 week), after 8- and 16-weeks of the training-intervention, and 3-, 6- and 12-months post-intervention. To minimise variation, tests were conducted within 1 hr of the original assessment time, participants completed all assessments shod, and external factors (test order, location, floor-surface, chair-type used) were kept consistent throughout. After familiarisation at baseline, duplicate trials of physical tests were conducted for each assessment, and an average time calculated. Participants were instructed to use their assistive ambulatory devices during assessments.

The Parallel Walk Test (PWT) is a quick, simple and validated method of assessing physical function and dynamic-balance during gait in the elderly [40, 41]. Participants were timed as they walked 6 m between 2 parallel lines marked on the floor at a width of 30 cm. They scored 1 point for foot placement on a line, or 2 points for placement outside of the line. As many completed the test using assistive ambulatory devices such as a walker, points were also awarded in a similar fashion for this device touching or crossing a line. The 10-m Timed Walk (10mTW) Test provides a simple assessment of function and inference of lower-limb strength, with an inverse-relationship shown between leg-muscle-strength and walking-time [42], and a correlation existing between gait-speed and survival rates [43]. The Timed Up-and-Go (TUG) test is a sensitive, validated and reliable tool frequently used for assessing physical function, balance, and lower-limb strength, and falls-risk in the elderly [44].

Participants completed the Barthel Index Questionnaire [45, 46] as an interview for a measure of their activities of daily living. The questionnaire has previously demonstrated high reliability [47].

Statistical Analysis

Statistical analyses were conducted using SPSS Version 24 (SPSS, Inc., Chicago, IL, USA). Missing data points were accounted for using 5-step Multiple Imputation (on average 11% of data imputed), in accordance with Sterne et al. [48]. Data was then tested for skewness and kurtosis for normal distribution. Treatment effect-sizes were calculated in accordance with the methods outlined by Cohen's d [49], with clinical-importance inferred at Moderate (0.5-0.8) and Large (0.8+) effect-sizes in accordance with Page [50]. Main effects of the training intervention were analysed using repeated-measures ANOVA, with specific treatment*time differences identified using subsequent one-way ANOVA and Bonferroni post-hoc tests. All data is presented as group mean ± standard error of the mean (SEM) with significance at $p \leq 0.05$.

4.2.4 RESULTS

Participants

From a potential 140 eligible individuals, 117 participants consented to participate (Figure 4.1). Participant characteristics for each group are outlined in Table 4.1, with no significant differences found between groups at the onset, aside from the mean age of WBV and CON groups ($p = 0.014$). Overall, participants displayed a moderate degree of functional impairment/frailty (4.9 ± 0.9) as measured by Functional Ambulation Categories [37], suggesting a need for supervision/assistance on non-level surfaces, whilst 22% required aid on level-surfaces.

Compliance levels were high, with WBV and SIM groups attending 93% and 89% of sessions respectively. Training was not considered a strenuous workout, with participants rating their perceived-exertion levels as 2 (easy) and 1.4 (easy) for WBV and SIM groups, respectively. Participants frequently described WBV-exercise as "*fun to use*" and expressed enjoyment ("*I love it*"). Participants also reported perceived functional-improvements from using the machine, including "*the more I use it, the better I get*", "*found it easier to control walking downhill as a result*", "*feels like you have taken a brisk walk after using it*", "*using the machine has increased my sleep, walking and well-being – I feel more relaxed and confident*", and "*the past month it has felt much easier to walk, even without my stick*".

Table 4.1. Physical Characteristics (mean ± SEM)

Parameter	Overall	WBV Group	SIM Group	CON Group	***p* value** *(between all groups)*
N	117	36	35	46	-
Age (years)	82.45 ± 7.9	79.4 ± 1.1[$]	83.7 ± 1.2	84.3 ± 1.3	**0.012**
Gender	41 M / 76 F	15 M / 21 F	8 M / 27 F	18 M / 28 F	-
Height (m)	1.62 ± 0.09	1.63 ± 0.02	1.61 ± 0.01	1.61 ± 0.02	0.596
Weight (kg)	70.97 ± 14.58	71.42 ± 3.26	72.65 ± 2.59	68.63 ± 3.19	0.626
BMI (kg/m^2)	27.12 ± 5.27	26.67 ± 1.03	28.06 ± 0.94	26.52 ± 1.27	0.596
Functional Ability[#]	4.92 ± 0.93	5.03 ± 0.12	5.09 ± 0.13	4.65 ± 0.17	0.069

[#] Measured using Functional Ambulation Categories outlined by Holden et al (1984)

[$] WBV significantly lower than CON (*p = 0.013*)

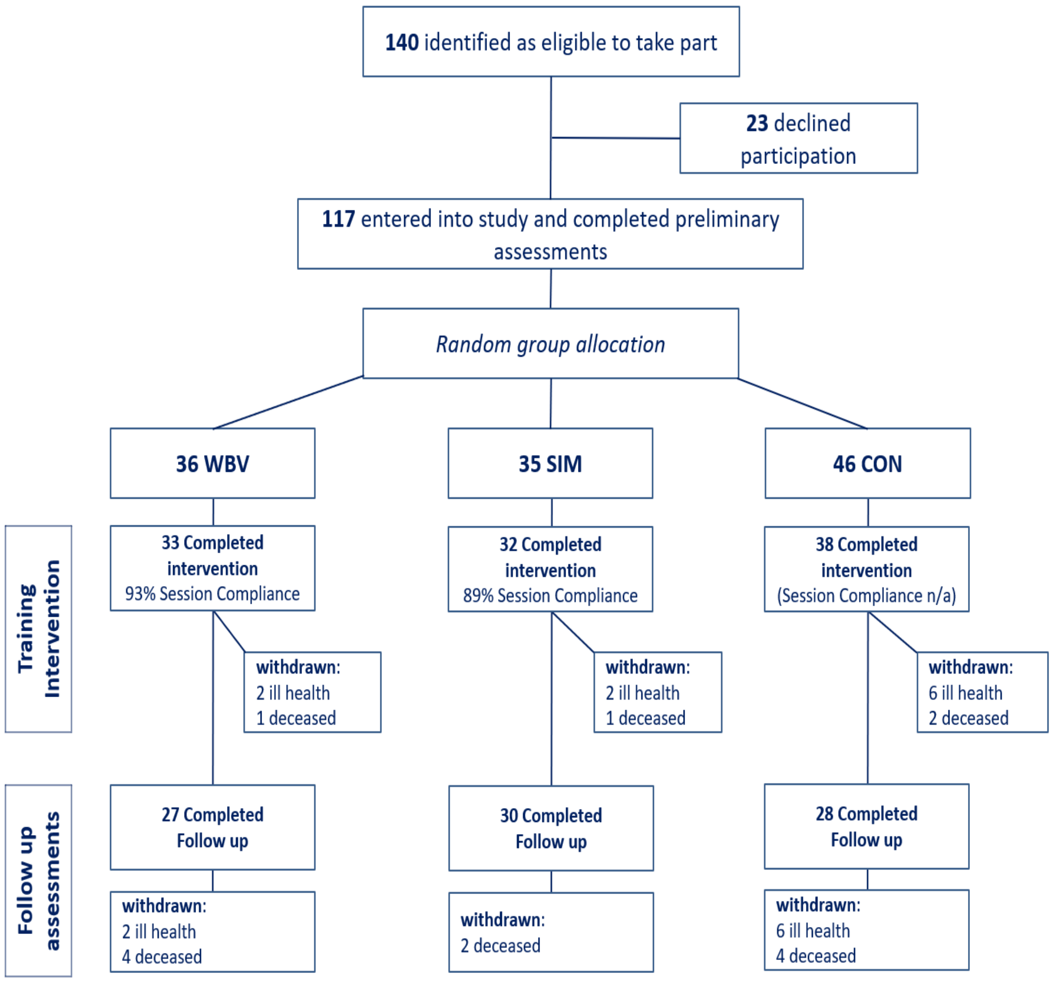

Figure 4.1. Consort diagram.

Functional Assessment Parameters

Figures 4.2 and 4.3 summarise changes in physical function and balance during the study, with statistical-parameters detailed in Table 4.2. Performance in functional tests improved with WBV-training across the intervention period (Figure 4.2, Table 4.2). Specifically, clinically-important improvements of 7.3% and 14.9% were seen in TUG and PWT performance, respectively (Figure 4.2, Table 4.2). Improvements in 10mTW performance trended towards significance after 16-weeks, being associated with clinically-important treatment-effects in comparison with the SIM group at this time (Table 4.2). Participants in SIM and CON groups were slower than baseline for all tests at 8- and 16-weeks (Figure 4.2), with negligible differences between these groups (Table 4.2).

Performance in TUG and 10mTW tests returned to baseline 3-months post-intervention, and within 6-months for PWT (Figure 4.2) for the WBV group. However, clinically-important WBV treatment-effects remained apparent 3-, 6- and 12-months post-intervention for PWT performance (Table 4.2). Moderate-to-large treatment-effects of WBV were also observed for 10mTW performance 3- and 6-months post-intervention, in comparison to SIM-participants (Table 4.2). All other effects of WBV on functional assessment were negligible.

Assessed by PWT score, dynamic-balance during gait was significantly improved with WBV-training compared to baseline (Figure 4.3, Table 4.2). Treatment-effects were observed after 8- and 16-weeks of WBV-training (Table 4.2). Balance remained improved 3-months post-intervention in the WBV-group only (Figure 4.3), displaying moderate-to-large treatment-effects against other groups. Scores returned to baseline within 6-months for WBV-participants, yet treatment-effects were still apparent compared to SIM-participants (Table 4.2). A moderate-effect was observed at 8-weeks only for CON- vs SIM-participants, with all other effects being negligible. All groups returned to equitable levels within 12-months post-intervention.

After 16-weeks of training, Barthel Index scores were on average 5.8% higher than baseline for the WBV group, compared to -0.5% and -6.4% lower for SIM- and CON-participants, respectively (Figure 4.4). Clinically-important treatment-effects of WBV were maintained for the majority of the follow-up period, with treatment-effects between other groups being mainly negligible and of no statistical significance (Figure 4.4; Table 4.2).

Table 4.2. Functional changes associated with 16-weeks of WBV training (Effect Size & *p* value).

	Change from Baseline									
	8 wk		**16 wk**		**3 mo**		**6 mo**		**12 mo**	
	ES	***p***	**ES**	***p***	**ES**	***p***	**ES**	***p***	**ES**	***p***
TUG Time										
WBV vs. SIM	-0.61#	***0.018****	-0.86$	***0.011****	-0.34	*0.312*	0.18	*1.000*	0.36	*0.612*
WBV vs. CON	-0.74#	***0.016****	-1.19$	***0.000†***	-0.38	*0.522*	-0.34	*0.408*	-0.38	*0.201*
SIM vs. CON	0.00	*1.000*	-0.30	*0.487*	-0.06	*1.000*	-0.84$	*0.070*	-0.99$	***0.007†***
10 Timed Walk										
WBV vs. SIM	-0.64#	*0.112*	-0.67#	*0.099*	-0.77#	***0.005†***	-0.50#	*0.165*	-0.40	*0.549*
WBV vs. CON	-0.40	*0.250*	-0.47	*0.112*	-0.33	*0.567*	-0.47	*0.168*	-0.41	*0.216*
SIM vs. CON	0.10	*1.000*	0.03	*1.000*	0.44	*0.121*	0.02	*1.000*	-0.08	*1.000*
PWT Time										
WBV vs. SIM	-0.88$	***0.006†***	-1.04$	***0.006†***	-0.83$	***0.003†***	-0.59#	*0.077*	-0.66$	*0.075*
WBV vs. CON	-0.74#	***0.009†***	-0.74#	***0.007†***	-0.59#	*0.054*	-0.61#	***0.040****	-0.59#	***0.034****
SIM vs. CON	0.06	*1.000*	0.03	*1.000*	0.24	*0.766*	-0.03	*1.000*	-0.04	*1.000*
PWT Score										
WBV vs. SIM	-0.84$	***0.001†***	-1.1$	***0.000†***	-0.81$	***0.003†***	-0.61#	***0.021****	-0.43	*0.177*
WBV vs. CON	-0.37	*0.873*	-0.70#	*0.111*	-0.68#	*0.074*	-0.32	*0.950*	-0.38	*0.515*
SIM vs. CON	0.57#	*0.19*	0.49	***0.043****	0.25	*0.643*	0.39	*0.187*	0.12	*1.000*
Barthel Index										
WBV vs. SIM	0.37	*0.778*	0.80$	*0.074*	0.45	*0.703*	0.66#	*0.390*	0.49	*0.472*
WBV vs. CON	0.53#	***0.026****	0.94$	***0.000†***	0.66#	***0.007†***	0.79#	***0.002†***	0.72#	***0.006†***
SIM vs. CON	0.38	*0.438*	0.55#	*0.086*	0.43	*0.210*	0.46	*0.159*	0.35	*0.298*

Moderate treatment-effect; $ Large treatment-effect;
* Significant difference p < 0.05; † Significant difference p < 0.01;
Effect sizes calculated as per Cohen's d (1988) and interpreted as per Page (2014).

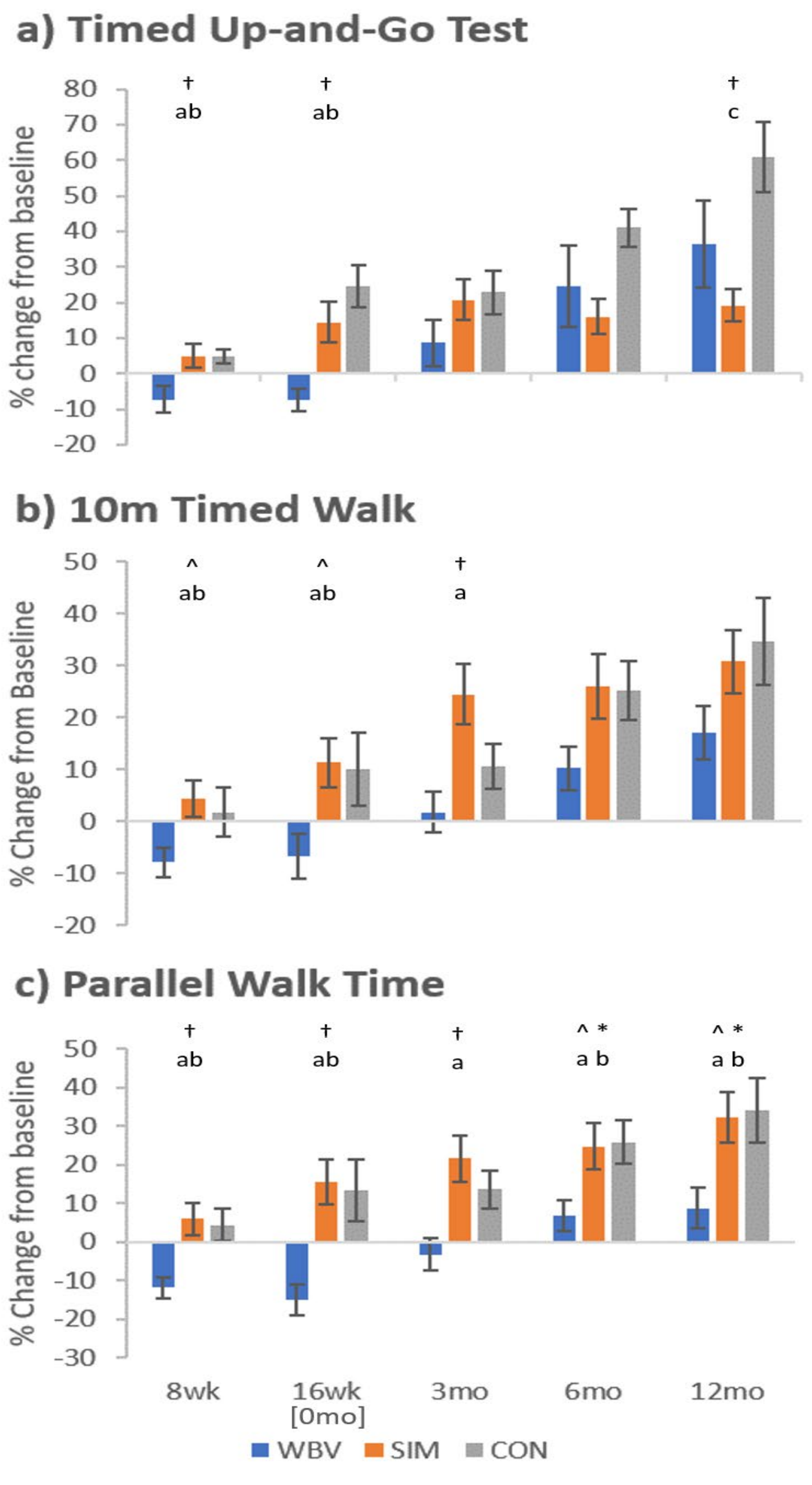

Figure 4.2. Changes in measures of physical function (mean % change ± SEM).

[*p<0.05; †p<0.01; ^p = 0.05-0.08; [a]WBV:SIM difference; [b]WBV:CON difference; [c]SIM:CON difference]

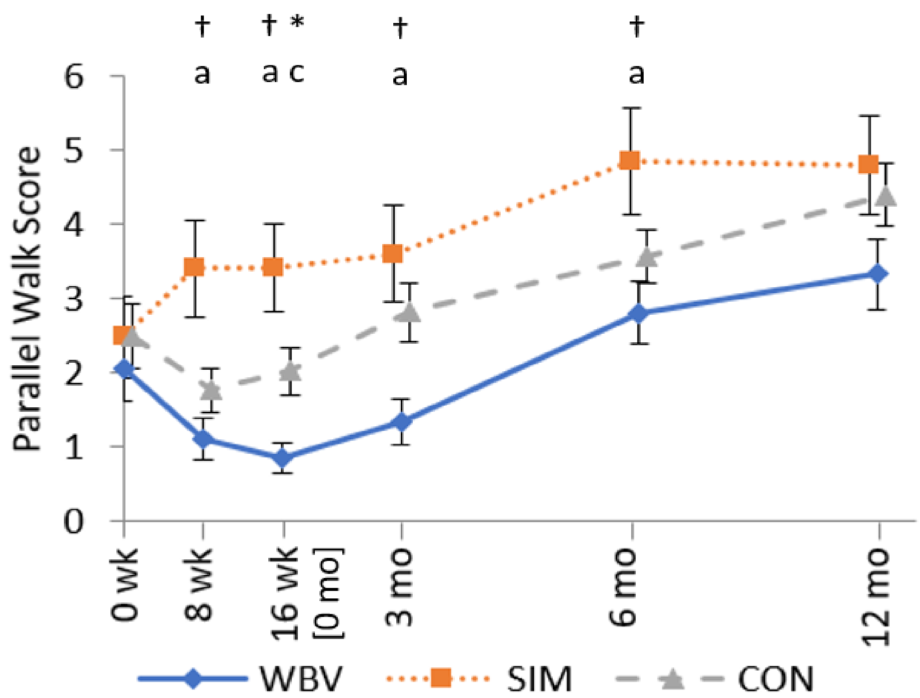

Figure 4.3. Changes in measures of dynamic balance - Parallel Walk Test Score (mean ± SEM).

[*p<0.05; †p<0.01; ^p = 0.05-0.08; [a]WBV:SIM difference; [b]WBV:CON difference; [c]SIM:CON difference]

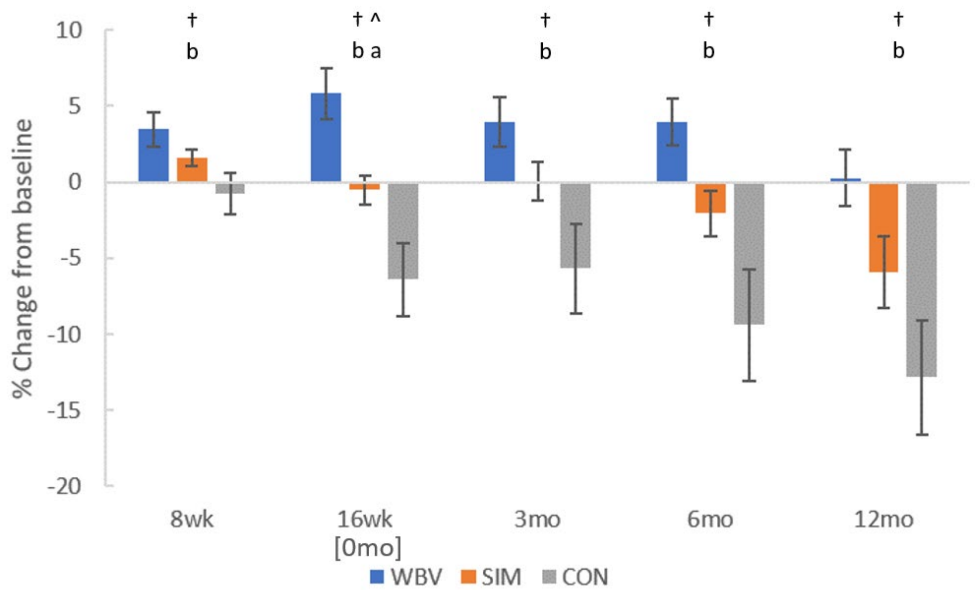

Figure 4.4. Functional independence - Barthel Index Scores (mean % change ± SEM).

[*p<0.05; †p<0.01; ^p = 0.05-0.08; [a]WBV:SIM difference; [b]WBV:CON difference; [c]SIM:CON difference]

4.2.5 DISCUSSION

This study reveals that the frail elderly can benefit from low-level WBV-training. Participants showed significant improvements in balance, lower-limb strength and activities of daily living, which translate into enhanced functionality and independence. Furthermore, the study suggests that such treatment-effects are retained for at least 6-months after WBV-training, identifying a potential therapeutic-window and providing insight into the time-course of detraining.

The functional improvements demonstrated in the current study concur with previous findings suggesting that the frail elderly can benefit from WBV-training [27, 28, 30, 32]. However, the exercise-intensity deployed represents a significant change from previous studies, making the associated improvements particularly noteworthy. Moreover, no discernible placebo-effect was identified for measures of functional-performance, as noted by the lack of significant differences between CON and SIM groups, meaning such improvements can be attributed directly to the WBV-protocol used. Participants in the current study followed a less-intensive WBV-training program (rotational WBV, lower Hz and no concurrent exercise) and were frailer in nature.

Bruyere et al. [27] and Zhang et al. [32] instructed participants to stand/adopt a "partial squat" on the WBV machine, a method replicated here. The absence of additional dynamic-exercise during WBV lessens the need for supervision by an appropriately-qualified individual, decreasing costs. Other programmes, such as the community-based Otago Falls Programme [51-53], were deemed too costly, being labour-intensive and requiring highly-skilled/trained-practitioners yet reaching <2% of the target-population. Consequently, WBV-exercise provides functional improvements utilising an easy-to-master and minimally-demanding form of low-impact exercise, is widely accessible and applicable for frail elderly, and is cost-effective.

The magnitude of treatment-effects elicited in this study are comparable to other studies, for example the 7.3% improvement in TUG time is similar to previously-reported improvements of 9% for community-dwelling [54] and 13.6-18% for frail elderly [27, 28, 30]. The absolute percentage-change is slightly lower for frail elderly in this study, probably due to lower FoV, yet the repeated moderate- and large-sized treatment-effects are of clinical-importance [50]. Merriman et al. demonstrated that one-off bouts of WBV at 2 Hz elicited similar treatment-effects to that of 26 Hz, on both TUG performance and EMG activity of older adults [21], showing that lower-levels of WBV-exercise can still elicit functional benefits. Not surprisingly, the biggest effects of WBV-training have been reported in those with the poorest initial scores, i.e. the frail elderly [55, 56]. The low-level WBV-training used in this study was specifically designed to be comfortable for participants, with rotational WBV minimising energy transfer to the spine and head [57] and frequencies of 5-10 Hz suggested for gentle adaptation in frail populations [13]. Participants clearly found the WBV-training easy to complete, coupling high-levels of compliance with low-levels of perceived-exertion and positive anecdotal-feedback. Meta-analysis studies have indicated larger treatment-effects with vertical WBV of 40-50 Hz [58], whilst utilising low-loading of WBV has been associated with lower levels of muscle stimulation [59] and strength/power gains [31, 60]. None-the-less, the current training-program elicited functional benefits in the frail elderly, showing low-levels of WBV-exercise to be a feasible training-tool for the frail elderly.

The retention of treatment-benefits for at least 6-months post-intervention suggests a potential therapeutic-window, during which time participants could be introduced to 'regular' training options and integrated into more-challenging group-exercise-classes. This agrees with Rogan et al.'s [61] conclusions that WBV has potential for older deconditioned-individuals that need to be 'up-skilled' for regular training. Furthermore, Barthel Index scores were increased for 6-months post-WBV in the current study, suggesting higher levels of independence and thus a lower burden-of-care over this time-span.

Barthel Index scores suggest a possible psychological placebo-effect. At 8-weeks, participants in both training groups showed improvements in this measure, yet by 16-weeks only WBV-participants remained above baseline. Often lonely, the frail elderly can be particularly susceptible to the effects of incidental activity, enhanced social interaction, and intrinsic bias developed from taking part in an exercise-training study [29], which all may contribute to the observed placebo-effect. Unlike previous research comparing WBV to other exercise formats, the inclusion of both SIM and CON groups in this study allows the current researchers to recognise/account for this effect.

Although falls were not an outcome of this study, the improved 10mTW test performance suggests increased lower-limb strength [42], which could in-turn lead to a reduction in falls-risk, of which poor leg-strength is a main determinant [62]. Previous researchers have reported WBV-associated increases in muscular-strength in the elderly [15, 23-25]. The proposed mechanism is that the generated sinusoidal vibrations provide mechanical stimuli to α–motor neurons and elicit rapid co-contractions of muscles, comparable to the Tonic Vibration Reflex [16, 63, 64]. Although low-levels of WBV-induced muscle activation and acceleration were deemed unlikely to cause hypertrophy in young healthy-individuals they “may be sufficient in weak and frail people” [59], and indeed muscular hypertrophy changes have been reported in the elderly with WBV-training. Increases in isometric muscle strength have been found in community-dwelling elderly [16, 54, 65] and are related to increases in muscle mass [54, 65]. Similar strength-improvements in the frail elderly with WBV training range from 8% [31] to 52% [32], albeit assessed by varying methods. The challenge of keeping equilibrium during rotational WBV is thought to result in neuromuscular adaptations [66], leading to subsequent improvements in dynamic-balance [28, 61]. The improved PWT scores in this current study suggest that rotational WBV-exercise has an important role in proprioceptive training.

Di Guilio et al. [67] suggested that the tibialis anterior muscle is best linked to an individual’s centre of gravity, and weakness in this muscle/the ankle dorsiflexion group contributes to abnormal gait patterns and slower walking-speeds [68]. Furthermore, high levels of tibialis anterior muscle activation, as opposed to any other muscle/group, have been reported in vertical WBV [69]. Based on our current observations, we agree with the above findings and speculate that the side-to-side motion of rotational WBV may be of particular-importance in improving the sensorimotor function of frail elderly participants, potentially reducing falls-risk. Moreover, such sensorimotor function improvements, coupled with the muscle hypertrophy outlined above, likely contribute towards the timeline for detraining/therapeutic window observed.

Several limitations were identified in the current study. Firstly, we recruited fewer participants than anticipated due to the strict exclusion criteria [36], particularly concerning impaired-cognition, recent-fracture history, and joint-replacement. Nevertheless, our results were both significant and of clinical-importance, whilst this study remains the largest study of WBV effects on frail elderly individuals. The cognitive-ability set-point was important for successful study implementation, but the low cognitive-demand of this exercise protocol makes its use highly-feasible in the cognitively-impaired. Secondly, the overall drop-out rate in the study (27%) was comparable to others reported in frail-elderly research [70], yet the specific rate for the CON group reached 39%. The longitudinal nature of the study coupled with the frail nature of participants meant this was unsurprising, but one must acknowledge that a larger drop-out in the CON group has the potential to bias results in either direction. For example, the PWT scores shown in Figure 4 makes CON participants look better, perhaps because more frail/less able-bodied persons died or dropped-out. A third potential limitation was that participants were not blinded to their treatment-condition, and thus could easily compare their treatment to others. However, controlling for the social interaction associated with exercise sessions may be important for other psychometric assessments (unreported here), hence why WBV- and SIM-groups exercised in mixed-sessions together. As no placebo-effect was identified for measures of physical function, the study design employed was indeed robust. Finally, given the focus on physical function, the lack of a direct-measure of isometric muscle strength could be considered a limitation. However, the authors felt it essential to maximise accessibility so utilised assessments of physical function that were valid, reliable, and directly-applicable to participant's everyday life.

4.2.6 Conclusion

The current study showed that low-level WBV-exercise presents as an easily-accessible exercise for the frail elderly, who would not otherwise engage in physical activity strenuous-enough to gain benefits. Furthermore, the study demonstrated that simple thrice-weekly sessions of limited physical-exertion and time-demand, on both patient and carer, can lead to pronounced improvements in functionality, feasibly reducing falls-risk. For the first time it has been shown that some treatment-benefits were maintained for at-least 6-months post-WBV-training. Moreover, the easily-accessible WBV-training protocol employed was well-received, being fun to participate in, and coupling high-levels of compliance with low-levels of perceived-exertion.

4.3 References

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5. Psychometric Results

5.1 Chapter Overview

The following chapter presents the psychometric results from the current research project, offered in the format of a paper for submission (currently targeting submission to *Experimental Gerontology* Journal). As such, the general method and protocol are restated, but the variables detailed are only the psychological measures. Specifically, the findings and discussion address a primary outcome of the research project, namely the effects of chronic WBV-training on i) the falls-confidence and independence (of which the Barthel Index forms part of this result), and ii) the psychological wellbeing and Quality of Life of the frail elderly. The secondary-outcome regarding the time-line of detraining for these measures is also explored in this chapter.

5.2 PSYCHOLOGICAL EFFECTS OF WHOLE BODY VIBRATION TRAINING IN THE FRAIL ELDERLY

5.2.1 ABSTRACT

Cognitive decline has profound impacts on the wellbeing, confidence, independence and Quality of Life (QoL) of the frail elderly. Exercise can address such declines, however the frail elderly are often unable to exercise conventionally. Whole Body Vibration (WBV) exercise presents as an accessible and effective training-tool for this population, yet very few studies have explored its psychological-benefits for this group.

*One-hundred-and-seventeen male and female pre-screened volunteers (82.5 ± 7.9 years) from residential care-facilities were randomly allocated to a Control (CON), Simulated-exercise (SIM) or WBV-exercise (WBV) group. All participants received regular care, whilst exercise-groups also underwent thrice-weekly training-sessions for 16 weeks. Delivered by overload principle, WBV-exercise began with 5*1-min bouts of rotational-WBV at 6 Hz/2 mm (1:1 min exercise:rest), progressing ad libitum to 10*1-min potentially up-to 26 Hz/4 mm, whilst maintaining knee flexion. Training for SIM participants mimicked exercise stance and duration. Pre- and post-measures for Barthel Index, falls-confidence (ABC-UK) and EURO-QoL-5D were completed.*

Clinically-important moderate- and large-sized treatment-effects were observed in all parameters with WBV-exercise. Whole-Body Vibration training improved Barthel Index and ABC-UK falls-confidence scores by 5.8% and 17.4%, respectively, compared to declines in SIM/CON participants. Psychological beneficial-effects were maintained for up-to 12-months post-intervention. Overall health-related QoL was best maintained by WBV training, in contrast to varying decline in other groups. Further WBV-associated treatment-benefits were observed in Activity, Mobility and Self-Care elements of the EURO-QoL-5D.

Findings demonstrate that 16-weeks of low-level WBV exercise provides sufficient stimulus for the frail elderly to enhance an individual's falls-related confidence, functional-independence and QoL.

5.2.2 INTRODUCTION

Cognitive function declines with age [1], and in the frail elderly is often coupled with the psychological impact of reduced physical capacity and functional independence [2]. Consequently, this population often suffer from a blend of reduced cognition, self-confidence and independence, culminating in increased levels of frailty and decreased Quality of Life (QoL) and mental wellbeing [3]. Exacerbating this, individuals within residential-care exhibit the highest prevalence of falls and associated injury [4], with the fear of falling itself causing severe restrictions in activity and social interaction [5]. So-pronounced are these effects that a fear of falling has been identified as a contributing factor to decreased mobility and increased levels of functional-dependence and falls-risk [6]. When combined, these factors can further negatively impact on an individual's QoL and mental wellbeing [7].

Regular exercise can have pronounced benefits on the cognitive function and psychological wellbeing of older adults aged 60+ years old, increasing cranial blood flow [8] and volume of brain matter [9], and concurrently slowing rates of cognitive decline [10]. Additionally, it can improve levels of self-efficacy, confidence and feelings of control in older adults [11]. These improvements can lead to increasing general health, physical activity and independence, ultimately manifesting as improvements in an individual's health, mental wellbeing and QoL [12]. Enhancing these can have multiple benefits due to the associations with physical and functional decline, cognitive impairment, institutionalisation, frailty, psychological distress and even non-adherence to pharmacotherapy [13].

However, a large proportion of older adults display debilitating degrees of frailty, with a combination of chronic medical conditions, cognitive- and functional-limitations meaning they exhibit poorer health and a higher burden of care. Consequently, they are often unable to exercise conventionally/at the requisite intensity, thus cannot gain such benefits. With as little as 2.4% of older adults meeting the recommended levels of physical activity [14], appropriately designed and easily-accessible exercise programs are needed to maximise exercise compliance, and its associated benefits, in those willing to attempt physical activity.

Whole Body Vibration (WBV) exercise has gained significant traction as a safe and effective training tool in various populations, including athletes [15], sedentary persons [16, 17] and healthy older adults [18-20]. The demands of WBV are minimal for both participant and practitioner, whilst taking part can be as simple as standing on a platform with knees flexed for 1-minute bouts, interspersed with rest periods. Thus, it is an easily accessible form of exercise for those with mobility problems or limited cognitive-ability. The healthy mobile elderly respond well to WBV exercise, with researchers reporting improvements in balance [18, 21-23], physical function [24-27], and muscular strength [17, 28-30], in addition to high-levels of compliance and no adverse effects [16-18]. Research focussing on the use of WBV by the frail elderly residing in residential-care is less prevalent, but improvements in physical function have been reported in this group [31-36]. However, very few researchers have explored if the use of WBV exercise in older adults can produce psychological benefits similar to those reported with conventional exercise.

To-date, only five studies have investigated the effects of WBV exercise on the QoL of community-dwelling older adults, with a further three looking specifically at its effects on a frail elderly population. Two of the studies showed regular sessions of WBV-exercise to significantly improve QoL in community-dwelling older adults [27, 37], with the largest benefits seen in measures of pain and social-activity. However, a lack of control group in either study meant there was no way of specifically attributing those benefits to the WBV-exercise alone, meaning no clear conclusions could be drawn. Only three studies, which included matched-controls, demonstrated successful improvements in community-dwelling older adults' QoL with WBV-interventions, employing 6-, 8- and 12-week WBV interventions [24, 38, 39]. Although these findings have been replicated in older adults living in residential-care, with 6- and 12-week exercise interventions elevating SF-36 and EURO-QoL scores on comparison to matched controls [31, 34], they however utilised WBV at high-intensities of up-to 35 Hz, combining dynamic-exercises with concurrent WBV-exercises in physically- and cognitively-demanding protocols

[31, 34]. Such demands in an exercise-protocol would not be appropriate for the majority of frail older adults, limiting its effectiveness. Lower-frequencies of WBV are less demanding on participants [40], however to-date no researchers have explored if low-level WBV can elicit psychological benefits in the frail elderly.

Increasing confidence and independence can have profound impacts on the frail elderly, yet despite its accessibility, the psychological benefits of WBV-exercise have not been fully explored in this population. Therefore, the current study aims to establish if a low-level, stand-alone WBV-exercise program is a feasible and effective tool for addressing the reduced levels of confidence, mental wellbeing and overall QoL often experienced by frail elderly.

5.2.3 METHODS

Study Design and Participants

Ethical approval for the study was granted by the Health and Disability Ethics Committee of New Zealand (12/NTB/78), and the study has Universal Trial Registration (UTN: U1111-11367-146). Study design and specific participant recruitment procedures are outlined in detail in the FEVER methodology and protocol paper [41]. Following written informed-consent, eligible volunteers from rest home facilities in the Greater Wellington area underwent pre-screening for inclusion-criteria, that is frailty as determined by functional ambulation using a scale of 0-6, where less-than-6 indicates a degree of functional limitation and frailty [42]. Exclusion criteria were: a RUDAS assessment of cognitive function with minimum-score of 20 [43]; a lower-limb/spinal fracture within 12-months; hip- or knee-prosthesis; conditions including peripheral-neuropathy, cancer tumours, diabetic neuropathy; and participation in over 3 hours/week of exercise (detailed in [41]).

Participants were randomly assigned (using a random number computer-generator tool; random.org) to either: i) a Control group (CON), ii) a Simulated-exercise group (SIM), or iii) a WBV-exercise group (WBV). All participants continued to receive access to standard rest home care and activities throughout the study, and in addition participants in the SIM and WBV groups completed 3 exercises sessions a week for 16 weeks. Participants in these two groups exercised together to account for a number of physiological and psychological variables including: demands of the static exercise performed, incidental activity in attending sessions (walking to/from sessions), the social interaction associated with these sessions and any bias due to taking part in a study [44].

Participants in the WBV group stood with isometric knee flexion ≈20˚ (±5˚) whilst receiving 1-minute bouts of WBV, interspersed with 1-minute rest periods. Training load increased gradually over the 16-week intervention according to the overload principle. Participants began with 5 * 1-minute bouts of rotational-WBV exercise and rest (1:1) at 6 Hz / 2.0 mm amplitude (Galileo Fitness Control 0544, Novotec, Germany), increasing the number of bouts/session to 10 * 1-minute bouts of WBV exercise. At this time, progression of Hz and/or amplitude were self-determined by individual participants, up to a potential maximum of 26 Hz / 4.0 mm. Frequency of vibration and amplitude of the WBV-machines used were independently assessed using an accelerometer (Vibsensor, Now Instruments and Software, Inc., CA USA). Participants in the SIM group conducted the same postural stance and rest periods, increasing the number of bouts/session until 10 * 1-minute bouts equivalent to the WBV exercise group. All participants in the WBV and SIM groups were asked to rate their perceived levels of exertion using the OMNI-Vibration Exercise Scale [45] on a weekly basis, with all feedback results monitored by a team of geriatric consultants.

Psychological Parameters Assessment Procedures

Psychological assessment of all participants consisted of short interview-style assessment sessions using the Barthel Index, Activities-specific Balance Confidence UK, and EURO-QoL-5D Questionnaires. Assessments were conducted at 6 time-points throughout the study: at baseline (0 week), after 8 and 16 weeks of the training intervention period, and 3-, 6- and 12-months after completion of the last training session. An interview-style was chosen to avoid bias by lack of comprehension, whilst in order to minimise variation, tests were conducted at a similar time of the day (within 1 hr of the original assessment time) and external factors (such as test order, location, and interviewer) were kept consistent throughout.

The Barthel Index Questionnaire is an ordinal scale used to measure performance in activities of daily living (ADL) [46] as an assessment of daily functionality. It has a high reliability [47], and strong correlation to QoL [48]. Participants were asked all 10 questions in the modified questionnaire [49] as an interview, and were asked to grade the degree in which they were able to conduct a task where appropriate.

Participants' falls- and confidence-related QoL was assessed using the Activities-specific Balance Confidence UK (ABC-UK) scale [50].The ABC-UK questionnaire uses a 16-item scale to ask participants to rate their confidence regarding their balance and ability to remain steady when performing various tasks, from 0% (no confidence) to 100% (completely confident) in multiples of 10% with a combined total acquired. The questionnaire is a valid and reliable tool for detecting differences between fallers and non-fallers [50].

The EURO-QoL 5D [51] is a sensitive, simple and a reliable tool for assessing health-related QoL in this population [52]. Specifically, the EQ-5D-3L version of the questionnaire was used to evaluate participants' health status across five separate health-related QoL dimensions (Mobility, Self-care, Activity, Pain/Discomfort, and Anxiety/Depression) and an overall health status score.

Statistical Analysis

Sample sizes were calculated based on a previous study of WBV effects on the functionality of frail elderly participants, as described in Lark and Wadsworth [41]. Ensuing statistical analyses were conducted using SPSS Version 24 (SPSS, Inc., Chicago, IL, USA). Missing data points were accounted for using 5-step Multiple Imputation (on average 11% of data imputed), in accordance with Sterne et al. [53], and then all data was checked for normal distribution. Treatment effect-sizes were calculated in accordance with the methods outlined by Cohen's d [54], with clinical-importance inferred at Moderate (0.5-0.8) and Large (0.8+) effect-sizes in accordance with Page [55]. Main effects of the training intervention were analysed by repeated measures ANOVA, with specific treatment*time differences identified using subsequent one-way ANOVA and Bonferroni post-hoc tests with significance set at p=0.05. All data is presented as group mean ± standard error of the mean (SEM).

5.2.4 RESULTS

Participants

From an initial 140 potential participants, 117 (mean ± SEM = 82.5 ± 7.9 years) were identified and consented to participate in this study (Figure 4.1, Chapter 4). Participant characteristics are outlined in Table 5.1, with no significant differences found between treatment groups at the onset of the study aside from a difference in mean age between WBV and CON groups (p = 0.012) and in cognitive function between the SIM and CON groups (p = 0.027). Overall, participants displayed a moderate degree of frailty, with degrees of functional- (4.9 ± 0.9) [42] and cognitive-impairment (25.05 ± 3.5) [43] suggesting a need for supervision/assistance, with 22% requiring further forms of supervision/assistance for all forms of ambulation.

No chronic adverse effects were reported by either training group. Both groups exhibited high levels of compliance, attending 93% and 89% of sessions for the WBV and SIM groups, respectively. Training sessions were not experienced as a strenuous workout, with participants rating their perceived exertion levels as 2 (easy) and 1.4 (easy) for WBV and SIM groups, respectively. Participants described the WBV exercise as "*fun to use*" and enjoyed the training ("*I love it*"). Participants also self-reported improvements as a result of using the machine, including "*the more I use it, the better I get*", "*feels like I am improving all the time*", "*using the machine has increased my sleep, walking and well-being – I feel more relaxed and confident*", and "*feeling very good at the moment…it can't just be the machine, can it?*".

Table 5.1. Participant Characteristics (mean ± SEM)

Parameter	Overall	WBV Group	SIM Group	CON Group	***p* value** *(between all groups)*
N	117	36	35	46	-
Age (years)	82.5 ± 7.9	79.4 ± 1.1 $^{\$}$	83.7 ± 1.2	84.3 ± 1.3	**0.012**
Gender	41 M / 76 F	15 M / 21 F	8 M / 27 F	18 M / 28 F	-
Height (m)	1.62 ± 0.09	1.63 ± 0.02	1.61 ± 0.01	1.61 ± 0.02	0.596
Weight (kg)	70.97 ± 14.58	71.42 ± 3.26	72.65 ± 2.59	68.63 ± 3.19	0.626
Cognition ^	25.05 ± 3.53	25.50 ± 0.57	25.86 ± 0.55	23.80 ± 0.52 *	0.017
Functional Ability #	4.92 ± 0.93	5.03 ± 0.12	5.09 ± 0.13	4.65 ± 0.17	0.069

^ Measured using the RUDAS assessment (Storey et al, 2004)
# Measured using Functional Ambulation Categories outlined by Holden et al (1984)
$ WBV significantly lower than CON (*p = 0.013*); * CON significantly lower than SIM (*p = 0.027*).

Psychological parameters

Changes in psychological parameters over the duration of the training intervention and follow-up period are reflected in Tables 5.2-3 and Figures 5.1-3. After 16 weeks of WBV-training, clinically-important treatment effects were shown in markers of functional-independence and falls-related confidence, which were maintained for at least 6 months after finishing the training intervention.

Falls-related confidence increased significantly as a result of WBV-training, in comparison to reductions in both SIM and CON groups (Table 5.2, Figure 5.1). By the end of the 16-week training intervention, WBV participants scored on average 17.4% higher in the ABC Falls-Confidence Questionnaire than at baseline, representing significant treatment-effects vs SIM and CON participants who declined by -4.1 and -16.7%, respectively (Table 5.2). Treatment benefits of WBV remained for falls confidence throughout the follow-up period, with scores being only -2.5% below baseline 12-months post-intervention (Figure 5.1, Table 5.2). In comparison, SIM and CON participant's scores declined by -20.6 and -27.3%, respectively (Figure 5.1). All other treatment effects on falls-related confidence were trivial in size and of no statistical significance (Table 5.2).

Treatment-effects of WBV-exercise were observed on functional independence, with improvements of 5.8% seen in Barthel Index scores after the 16-week intervention, compared to reductions of -0.5% and -6.4% for SIM and CON participants, respectively (Table 5.2, Figure 5.2). Treatment-effects were also observed for SIM vs. CON group comparisons at this time (Table 5.2, Figure 5.2). Effects of WBV-exercise on function remained throughout the follow-up period, being 0.3% above baseline at post-12-months in comparison to reductions of -5.9 and -12.8% for SIM and CON participants, respectively (Table 5.2, Figure 5.2).

Overall health-related QoL was maintained across the 16-week training intervention by WBV and SIM participants, with similar EURO-QoL scores reported at 8- and 16-weeks (Figure 5.3). A clinically-important treatment-effect was observed for WBV vs CON participants at the end of the 16-week intervention, in contrast to negligible effects for other comparisons (Table 5.3). Furthermore, treatment-effects of WBV training were retained after completing the training-intervention in comparison with the CON group (Table 5.3).

Effects on individual elements of the EURO-QoL questionnaire are summarised in Table 5.3. No treatment-effects were apparent between WBV and SIM groups, but clinically-important effects were apparent in comparison to the CON group for various elements. Compared with the CON group, WBV-training had a beneficial-effect on Activity scores after both 8- and 16-weeks of training, and for up-to 6-months post-intervention. A similar treatment-effect was observed for SIM-training vs CON group at 8-weeks, and 3- and 6-months post-intervention, but not after 16-weeks of training. Furthermore, WBV-treatment-effects were observed on Mobility and Self-Care elements, in comparison to the CON group, throughout the duration of the study. No treatment-effects of SIM-training were apparent on Mobility, except for at 8-wks vs CON, and 6-months vs WBV, nor at any-time for Self-Care. Minimal treatment-effects were observed for the Depression and Pain elements for any group, except for SIM vs CON at 16-weeks and 6-months for Depression.

Table 5.2. Psychometric changes associated with 16-weeks of WBV training (Effect Size & *p* value).

	Change from Baseline									
	8 wk		16 wk		3 mo		6 mo		12 mo	
	ES	*p*	ES	*p*	ES	*p*	ES	*p*	ES	*p*
ABC Falls Confidence										
WBV vs. SIM	0.43	*0.319*	0.65#	***0.035****	0.42	*0.269*	0.53#	*0.091*	0.63#	***0.027****
WBV vs. CON	0.49	***0.040****	0.84$	***0.000*†**	0.61#	***0.009*†**	0.74#	***0.001*†**	0.78#	***0.001*†**
SIM vs. CON	0.28	*1.000*	0.47	*0.361*	0.38	*0.663*	0.39	*0.546*	0.29	*0.916*
Barthel Index										
WBV vs. SIM	0.37	*0.778*	0.80$	*0.074*	0.45	*0.703*	0.66#	*0.390*	0.49	*0.472*
WBV vs. CON	0.53#	***0.026****	0.94$	***0.000*†**	0.66#	***0.007*†**	0.79#	***0.002*†**	0.72#	***0.006*†**
SIM vs. CON	0.38	*0.438*	0.55#	*0.086*	0.43	*0.210*	0.46	*0.159*	0.35	*0.298*

Moderate treatment-effect; $ Large treatment-effect;
* Significant difference p < 0.05; † Significant difference p < 0.01;
Effect sizes calculated as per Cohen's d (1988) and interpreted as per Page (2014).

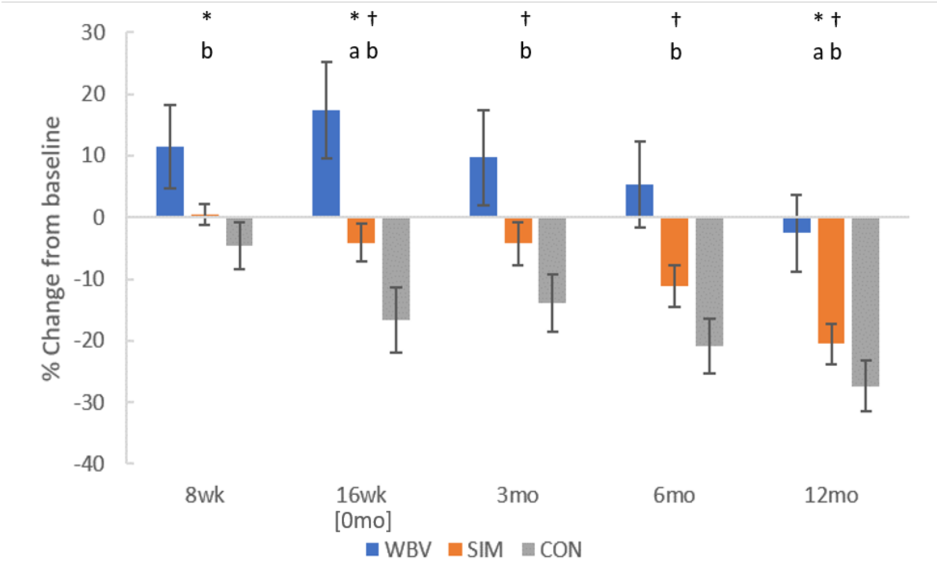

Figure 5.1. Changes in measures of Falls-related Confidence (mean % change ± SEM).

[*p<0.05; †p<0.01; ^p = 0.05-0.08; ᵃWBV:SIM difference; ᵇWBV:CON difference; ᶜSIM:CON difference]

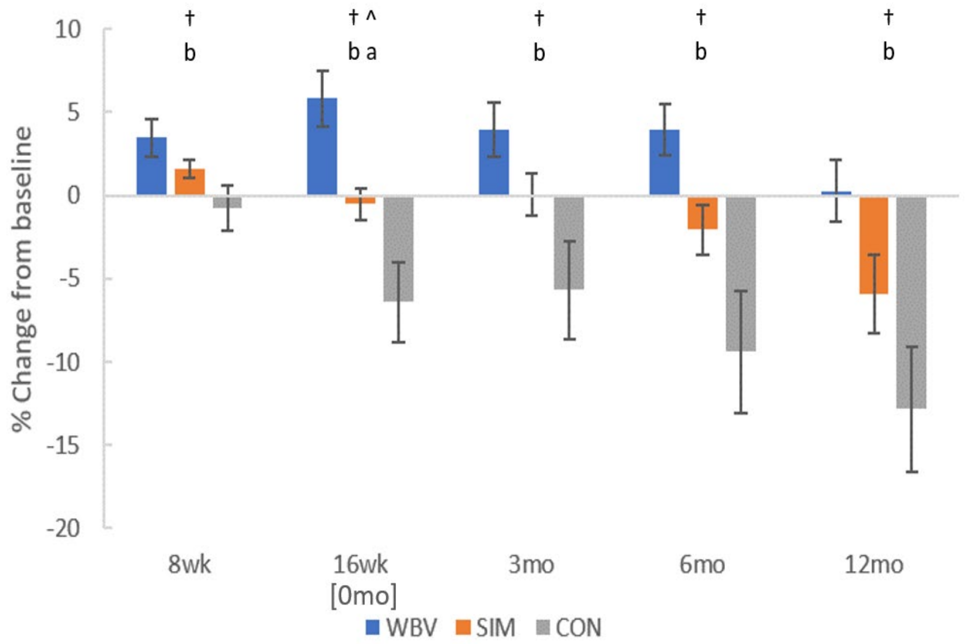

Figure 5.2. Changes in measures of Functional Independence (mean % change ± SEM).

[*p<0.05; †p<0.01; ^p = 0.05-0.08; [a]WBV:SIM difference; [b]WBV:CON difference; [c]SIM:CON difference]

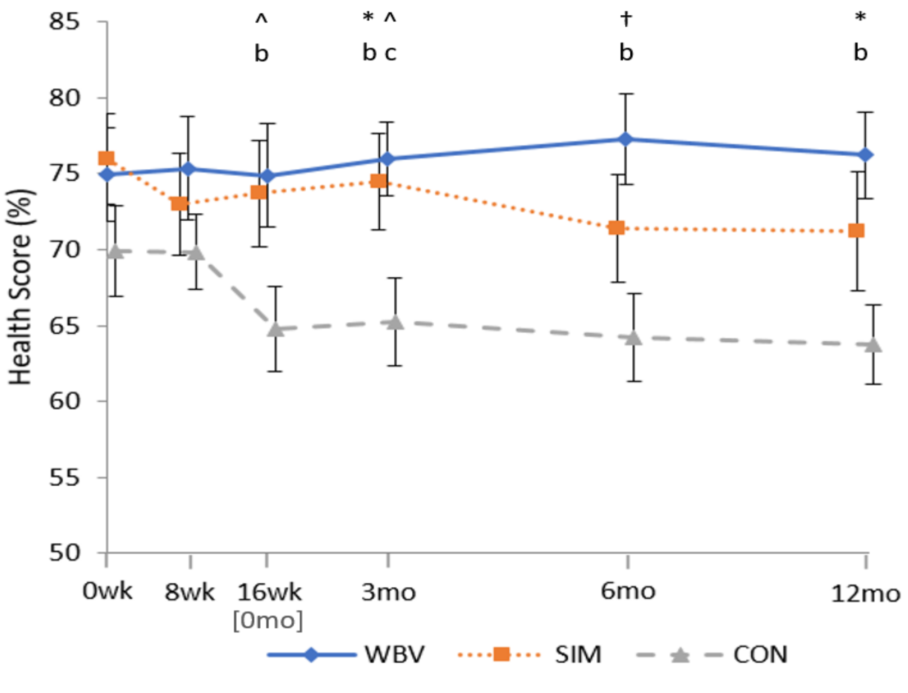

Figure 5.3. Overall health-related Quality of Life (mean ± SEM).

[*p<0.05; †p<0.01; ^p = 0.05-0.08; [a]WBV:SIM difference; [b]WBV:CON difference; [c]SIM:CON difference]

Table 5.3. Psychometric QoL changes associated with 16-weeks of WBV training (Effect Size & *p* value).

	Change from Baseline									
	8 wk		16 wk		3 mo		6 mo		12 mo	
	ES	***p***	**ES**	***p***	**ES**	***p***	**ES**	***p***	**ES**	***p***
EURO-QoL General										
WBV vs. SIM	0.18	*1.000*	0.06	*1.000*	0.09	*1.000*	0.30	*0.616*	0.25	*0.852*
WBV vs. CON	0.30	*0.587*	0.52#	*0.073*	0.64#	***0.025****	0.70#	***0.010***†	0.72#	***0.016****
SIM vs. CON	0.17	*1.000*	0.46	*0.141*	0.48	*0.070*	0.35	*0.314*	0.37	*0.281*
EURO-QoL ACTIVITY										
WBV vs. SIM	0.18	*1.000*	-0.27	*0.409*	0.01	*1.000*	-0.08	*0.673*	-0.13	*0.334*
WBV vs. CON	-0.46#	*0.319*	-0.58#	*0.319*	-0.62#	***0.026****	-0.70#	*0.149*	-0.27	*1.000*
SIM vs. CON	-0.55#	*0.336*	-0.31	*1.000*	-0.59#	*0.263*	-0.55#	*1.000*	-0.14	*0.302*
EURO-QoL DEPRESSION										
WBV vs. SIM	-0.03	*1.000*	0.33	*0.252*	0.21	*1.000*	0.33	*0.444*	-0.09	*1.000*
WBV vs. CON	-0.39	*1.000*	-0.18	*1.000*	-0.02	*0.923*	-0.22	*1.000*	-0.35	*1.000*
SIM vs. CON	-0.38	*1.000*	-0.53#	*0.155*	-0.28	*1.000*	-0.57#	*0.565*	-0.21	*1.000*
EURO-QoL MOBILITY										
WBV vs. SIM	-0.13	*1.000*	-0.32	*0.354*	-0.29	*0.259*	-0.52#	***0.014****	-0.28	*0.167*
WBV vs. CON	-0.46	***0.003***†	-0.49	***0.001***†	-0.48	***0.001***†	-0.49	***0.000***†	-0.39	***0.016****
SIM vs. CON	-0.34	***0.046***^	-0.18	*0.163*	-0.19	*0.188*	0.00	*1.000*	-0.13	*1.000*
EURO-QoL PAIN										
WBV vs. SIM	-0.12	*1.000*	0.00	*1.000*	-0.13	*0.549*	-0.11	*1.000*	0.05	*1.000*
WBV vs. CON	-0.29	***0.003***†	0.07	*1.000*	0.13	*0.706*	-0.14	*0.162*	0.18	*1.000*
SIM vs. CON	-0.17	*0.056*	0.07	*1.000*	0.27	*1.000*	-0.04	*1.000*	0.13	*1.000*
EURO-QoL SELF CARE										
WBV vs. SIM	-0.44	*1.000*	-0.38	*1.000*	-0.35	*0.649*	-0.48	*0.496*	-0.15	*1.000*
WBV vs. CON	-0.58#	***0.020****	-0.40	***0.012****	-0.59#	***0.000***†	-0.56#	***0.003***†	-0.44	***0.011****
SIM vs. CON	-0.16	*0.177*	-0.03	*0.168*	-0.32	***0.029****	-0.13	*0.194*	-0.29	*0.114*

Moderate treatment-effect; $ Large treatment-effect;
* Significant difference p < 0.05; † Significant difference p < 0.01;
Effect sizes calculated as per Cohen's d (1988) and interpreted as per Page (2014).

5.2.5 DISCUSSION

This is the largest study, to-date, providing evidence on the clinical effects of low level WBV exercise on the psychological wellbeing of the frail elderly. The findings show that low-level WBV exercise can elicit clinically-important improvements in falls-related confidence and functional-independence in the frail elderly, significantly increasing their overall Quality of Life. Furthermore, the study-design highlights a psychological placebo-effect of trial participation which has not previously been considered. Finally, it appears that the psychological benefits of WBV-training are retained for at least 6-months after cessation of training, identifying a potential therapeutic window and providing insight to the time-course of detraining.

Employing an easily-accessible WBV-protocol in this study increased falls-related confidence and subsequently helped create a self-fulfilling cycle of mastery, increased confidence, self-esteem and physical activity in frail elderly. As fear of falling is a contributing factor to decreased mobility and increased levels of functional dependence [6], it is reasonable to assume that WBV-exercise increased the likelihood of participants conducting further physical activity, and thus maximising exercise-compliance and associated benefits. Although self-esteem has been shown to increase as a result of both aerobic- and resistance-exercise programs [56], Kressig et al [57] suggested that in order to confer significant health benefits an individual should walk at a pace that is at least moderate. For the frail elderly, such modes and intensities of exercise or physical activity are often not possible. However, the rotational WBV delivered in this study engages muscles alternately as in normal walking motion [58] and has been shown to increase alternating muscle activation accordingly in young adults at a level comparable with brisk walking [59, 60]. Exercise programs for the frail elderly that target improvements in self-esteem and self-efficacy are successful but rare [61], yet in the current study it appeared that the low-level WBV training program utilised can indeed improve both. What is more, empowering frail individuals through exercise is known to also enhance their overall QoL by concurrent increases in psychological parameters such as their confidence, self-esteem, wellbeing and feelings of control [11]. In the current study, benefits in falls-confidence and EURO-QOL markers of Activity, Mobility and Self-Care were retained for at-least 6 months after completing the intervention, suggesting a potential therapeutic window in which to upskill patients, such as that proposed by Rogan et al [62]. During this therapeutic window, participants able to conduct more daily living tasks independently will maintain elevated levels of confidence, self-efficacy and functional independence.

The largest study in this field to-date, the current study-design allows for psychological effects elicited to be accredited directly to WBV exercise by the inclusion of both SIM and CON groups, and having participants exercise in mixed-sessions together. The SIM group accounts for any psychological placebo-effect arising from incidental activity, enhanced social interaction, or intrinsic bias developed from taking part in a study [44], which is not addressed in other WBV studies. The results indicate a placebo-effect of training, particularly for Barthel Index Scores and the Mobility and Activity elements of the EURO-QoL, where treatment-effects were observed in comparison to the CON group. However, WBV-associated treatment-effects were similar or larger in size than SIM-associated benefits. Moreover, WBV-associated benefits were maintained for independence and falls-confidence after the training-intervention ceased, yet in the SIM group they were not, whilst the reported EURO-QoL Mobility and Activity benefits of SIM-training were only present at 8-weeks of training, both having been lost by 16-weeks. These findings indicate that any placebo effects are not sustainable in the long-term, whereas WBV-exercise is able to elicit true, long-lasting psychological benefits.

The beneficial treatment-effects of WBV on overall health-related QoL echo those observed in previous research [24, 34, 38, 39], and were aligned with concurrent treatment-benefits in the Activity, Mobility and Self-Care elements of the EURO-QoL. Importantly, the CON group showed significant natural decline in their overall health-related QoL over the study period (Figure 5.3), emphasising that the WBV training-intervention was successful in improving and maintaining an individual's QoL, and adding further support to the importance of the therapeutic window proposed above. However, treatment-effects on individual elements of the EURO-QoL were only observed when compared to the CON group, not between the 2 training groups (Table 5.3), again supporting the placebo-effect outlined above. Notably though, such effects were much more apparent for WBV-exercise than SIM-training, being observed at-least up-to 6-months post-intervention in all 3 elements, suggesting that the placebo-effect of SIM-training is due to social interaction/study involvement as proposed above. Falls-related confidence and Euro-QoL scores have both been shown in previous literature to correlate closely with Barthel Index scores [36, 40, 63-65]. As seen in figures 5.2 and 5.3, falls-related confidence and Barthel Index scores were both improved in WBV participants in this study, further supporting an overall increased QoL in this group.

The strict inclusion and exclusion criteria for participation in the study [41] somewhat limited participant recruitment. For example, the cognitive ability cut-off coupled with a requirement of no recent fracture history or surgery (within 12-months) greatly reduced the scope of potential participants. The presence of a hip- or knee-prosthesis remains a contraindication to WBV exercise [66], meaning that this safety-measure could not be avoided. Although the sample size was not as large as the authors had originally planned [41], it still represented the largest study into the effects of WBV exercise with this specific population. Secondly, the cognitive cut-off was also employed to ensure participants understood the commitment and time-demands of a long-term study such as this, and to safeguard the validity of cognitive-based assessments utilised (e.g. the Barthel Index Questionnaire). A higher level of cognitive impairment introduces other falls-risk factors [67], so to ensure the safety of all participants a cognitive ability cut-off point was set as a RUDAS score of 20. Nevertheless, the authors do believe, given the achievable benefits of low-level WBV exercise demonstrated here, that with adequate supervision cognitively-impaired persons could also partake in this exercise, and its use as a confidence-building tool in this population is feasible. Retrospectively, a direct-measure of mastery could have enabled thorough identification of psychometric benefits from a mechanistic perspective, however limiting the demands of assessment in this study was a key design element, and the combination of psychometric assessments deployed allows for this link to be theorised. Finally, despite this study employing a short measure of health status (the EURO-QoL 5D), we must consider the possibility that those individuals with some degree of cognitive-impairment may have struggled to interpret some questions, potentially biasing results. Indeed, there has been considerable discussion over the validity of generic health-related QoL measures for people with disabilities, particularly over longitudinal time-frames [68]. However, the EURO-QoL 5D was chosen as it is an easy-to-use assessment tool which has been validated for use in this population [69]. Although developed for self-completion by individuals [70], age impacts on one’s ability to self-complete the EURO-QoL questionnaire [63], so in the current study we administered all questionnaires in an interview to avoid bias by lack of comprehension. Moreover, previous research has employed the EURO-QoL 5D to assess the effects of 8-weeks of WBV exercise on frail elderly participants, resulting in significant improvements [31], suggesting that it was indeed an appropriate assessment tool.

5.2.6 CONCLUSION

The current study showed that low-level WBV-exercise presents as an easily-accessible exercise for the frail elderly, who could not otherwise engage in physical activity strenuous enough to gain benefits. What is more, the study demonstrated that simple thrice-weekly sessions at a low Hz setting and short time-demand, can lead to pronounced, clinically-important psychological benefits beyond that of a placebo effect. Benefits included improved falls-related confidence, functional-independence, and perceived functional-ability in frail elderly individuals. Results suggest a potential therapeutic window in which to build on benefits, as improvements were maintained for at least 6-months after completion of the WBV training. The easily-accessible WBV-training protocol employed was well received, having beneficial effects on participant's Quality of Life and being fun to participate in, particularly as part of a group exercise session, and coupling high levels of compliance with low levels of perceived exertion.

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6. Bone Health Results

6.1 Chapter Overview

The following chapter focuses on the bone health results from the current research project. Presented as a paper for submission (currently being framed for appropriate Sport & Exercise/Gerontology focussed-journals), the findings and discussion address the secondary outcome of the research project pertaining to this parameter, namely that chronic WBV-training can provide sufficient mechanical stimulus to improve the bone health of the frail elderly. Important to consider in any investigation of the health and wellbeing of the frail elderly, Bone Health parameters were included as a sub-section (Part B) in the current project due to their close association with falls-risk in this population, and associated implications with high-rates of mortality from falls. As an arm of the main project, participant numbers were always planned to be much lower than the overall study, yet recruitment was impacted by a plethora of variables (covered in the discussion below) such that researchers chose to only include exercising participants, and not a non-exercising control, deviating from initial plans and addressed in the discussion section.

6.2 EFFECTS OF WHOLE BODY VIBRATION TRAINING ON THE BONE HEALTH OF THE FRAIL ELDERLY.

6.2.1 ABSTRACT

Age-related declines in bone health increase the risk of a fall/fracture, and lower mobility/independence. Conventional weight bearing training counters such declines, but requisite intensities often restrict application in the elderly. Whole Body Vibration (WBV) exercise presents as a safe and effective training tool for the mobile elderly, yet a paucity of research exists on its effects on the bone health of the frail elderly, who could benefit most.

*Twenty male and females (84.5 years ± 1.7) volunteers from residential care-facilities were randomly allocated to undergo Simulated-exercise (SIM) or WBV-exercise (WBV) sessions thrice-weekly for 16 weeks, in addition to regular care. Delivered by overload principle, WBV-exercise began with 5*1-min bouts of rotational-WBV at 6 Hz/2 mm (1:1 min exercise:rest), progressing ad libitum to 10*1-min at up-to potentially 26 Hz/4 mm, whilst maintaining knee flexion. Training* *for SIM participants mimicked exercise stance and duration. Bone health was assessed by changes in serum osteocalcin and vitamin D, urinary pyridinoline/deoxypyridinoline, and bone mineral density (BMD).*

High levels of compliance and ease-of-use were reported, with no adverse effects. No treatment-effects were observed for BMD levels, with both groups demonstrating normal levels of maintenance/age-related decline. Moderate-sized treatment-benefits were observed in osteocalcin levels with WBV-training, but all other biochemical markers remained unaffected by treatment.

Findings suggest that 16-weeks of low-level WBV-exercise provides some stimulus for the frail elderly to increase bone deposition, but at an insufficient extent to enhance BMD levels. However, the treatment elicited no adverse-effects, supporting its safe use in this population when other training goals are the focus.

6.2.2 INTRODUCTION

Characterised by altered composition, bone loss, the thinning of trabeculae/compromised microarchitecture of bone, and ensuing porosity [1], osteoporosis is an exacerbation of the natural age-related deterioration of bone, increasing the risk of a fall and/or a fracture in those aged 65+ years [2]. Indeed, the incidence of fractures is seven-times higher in women aged 80+ years [3], with 70% of this population displaying bone density scores indicative of osteoporosis [4]. Hip fractures are particularly problematic in this population, representing over 50% of all fractures [5], requiring an average hospital stay of 7-21 days, and dramatically increasing the risk of residential-level care, further fractures, and even death within the ensuing 12 months [3]. Consequently, older people's vulnerability and longer recovery periods make falls and associated fractures a particularly serious threat to their survival, health, well-being and independence [6], culminating in financial-burdens being placed on the public health system [7].

Declines in bone health can be attenuated or even reversed with targeted exercise interventions in the elderly. In particular, the mechanical stimuli of weight-bearing exercise and strength-training promote bone turnover and maintenance [8, 9], and researchers have shown resultant associated-benefits in the bone health of osteoporotic older adults [10-12]. However, exercise-intensities of 60-85% of maximal effort are required for such interventions to be successful, restricting their appeal and application within the elderly, leaving as little as 10% of the elderly population conducting such training [13]. The frail elderly residing in residential-care exhibit poorer health and a higher burden of care than even their more-mobile/less-dependent counterparts, being less-able to exercise conventionally, yet make up 1 in 7 New Zealanders aged over 80 years [14]. Consequently, a need exists for an easily-accessible and cost-effective weight-bearing/strength-training exercise program tailored towards this population's specific needs.

Whole Body Vibration (WBV) exercise has gained significant traction as a safe and effective training tool for enhancing muscle strength in various populations, including athletes [15], sedentary persons [16, 17] and older adults [18-20]. Exercise-associated changes in mechanical loading, fluid dynamics and anabolic hormone levels have been proposed as mechanisms for WBV-induced osteogenesis [21]. Indeed, researchers have shown WBV-associated improvements in the bone health of the hip and lumbar spine of healthy/mobile community-dwelling elderly participants [17-20]. However, others have reported no changes [16, 22, 23], or even decline [24] in similar cohorts, somewhat confounding this notion. The demands of WBV exercise can be minimal for participants, making it an easily accessible activity for those with mobility problems or limited cognitive ability. However, there is a paucity of research focussing on WBV exercise in the frail elderly within residential-care who, with the poorest-levels of bone health and the highest rate of falls-related hospitalisation and mortality, would stand to benefit most from such an accessible exercise intervention.

Researchers have shown WBV exercise to be an accessible and effective tool for improving the physical function and muscle strength of frail elderly participants [25-28], yet to-date only one study has investigated the specific effects of WBV exercise on the bone health of the frail elderly within residential-care [29]. Verschueren et al. delivered 6-months of thrice-weekly WBV training at 30 Hz, concurrent with static/dynamic exercises and vitamin D supplementation, to 113 elderly females residing within residential-care facilities, finding significant improvements in dynamic strength and >90% exercise compliance, but reported only a non-significant increase in hip Bone Mineral Density (BMD) [29]. Furthermore, the researchers acknowledged that as few as 18 of the 113 participants suffered moderate-severe frailty, and consequently they were unable to draw any conclusion of the musculoskeletal benefits of WBV exercise in this population group. Considering the research findings conducted with healthy/mobile community-dwelling elderly, WBV exercise does present as a plausible training tool for enhancing bone health. However, it remains unclear if the frail elderly residing in residential-care (at highest risk of falls and associated fractures) can attain sufficient stimulus from WBV exercise to improve their musculoskeletal health.

6.2.3 METHODS

Study Design and Participants

The current study was conducted as a subsection of a wider cohort study, the FEVER study [30]. Ethical approval for the study was received from the Health and Disability Ethics Committee of New Zealand (12/NTB/78), and the study has Universal Trial Registration (UTN: U1111-11367-146). Study design and specific participant recruitment procedures are outlined in the FEVER methodology and protocol paper [30]. Following written informed-consent, eligible volunteers from rest home facilities in the Greater Wellington area underwent pre-screening for inclusion-criteria, that is frailty as determined by functional ambulation using a scale of 0-6, where less-than-6 indicates a degree of functional limitation and frailty [31]. Exclusion criteria were: a RUDAS assessment of cognitive function with minimum-score of 20 [32]; a lower-limb/spinal fracture within 12-months; hip- or knee-prosthesis; conditions including peripheral-neuropathy, cancer tumours, diabetic neuropathy; no indicators of pathologies such as Paget's disease, hypoparathyroidism or diseases resulting in hypercalcaemia; and participation in over 3 hours/week of exercise (fully-detailed in [30]).

Detailed as Part B in the methods chapter (Section 3.2, p 55), a subgroup of 20 participants consented to undergo bone health assessments, and were randomly assigned (using a random number computer-generator tool; random.org) to either: i) a Simulated-exercise group (SIM), or ii) a WBV-exercise group (WBV). All participants continued to receive access to standard residential-home care and activities throughout the study, and in addition participants completed 3 exercises sessions a week for 16 weeks. Participants exercised together in mixed-groups, with the SIM group included, rather than a non-exercising control, in order to account for the weight-bearing musculoskeletal- and balance-demands of the study. These demands included the static exercise performed in training, the incidental activity in attending sessions (walking to/from sessions) and frequently rising/sitting during training, as well as the social interaction associated with participation (for psychological parameters not reported in this paper) [33].

Participants in the WBV group exercised by standing with isometric knee flexion ≈20˚ (±5˚) whilst receiving 1-minute bouts of WBV, interspersed with 1-minute rest periods. Training load increased gradually over the 16-week intervention according to the overload principle. Participants began with 5 * 1-minute bouts of rotational-WBV exercise and rest (1:1) at 6 Hz/2.0 mm amplitude (Galileo Fitness Control 0544, Novotec, Germany), increasing the number of bouts/session until 10 * 1-minute bouts of WBV exercise and rest were reached. At this time, progression of Hz and/or amplitude was self-determined by individual participants, up to a potential maximum of 26 Hz/4.0 mm. Frequency of vibration and amplitude of the WBV-machines used were independently-assessed using an accelerometer (Vibsensor, Now Instruments and Software, Inc., CA USA). Participants in the SIM group mimicked exercise stance and duration. All participants were asked to rate their perceived levels of exertion using the OMNI-Vibration Exercise Scale [34] on a weekly basis, at which time they were also given the opportunity to provide feedback on the intervention, with all results monitored by a team of geriatric consultants as an added safety precaution .

Assessment Procedures

Bone health and body composition of participants were assessed using Dual-energy X-ray Absorptiometry (DXA) scans, in addition to further biochemical markers of bone turnover for additional measures of bone health. Assessments were conducted at three time-points throughout the study: at baseline (0 week), after completing the 16-week training-intervention, and 12-months after completion of the training-intervention.

Considered the gold-standard for bone health and body composition assessment, Dual-energy X-ray Absorptiometry (DXA) scans provide valid and reliable measures of bone health at sufficient levels of repeatability to compare changes between repeated assessment points [35]. Bone Mineral Density (BMD) was assessed for the following variables: Whole Body, Lumbar, Neck of Left Hip, and Total Left Hip. All scans were conducted at the same venue (Pacific Radiology, Boulcott Hospital, Lower Hutt NZ), using the same Hologic Horizon A densitometer (Hologic, Inc., Bedford, MA, USA), with the same technician completing all scans for a given participant, with a reported coefficient of variation of 0.66-0.93 [35]. For body composition assessment, participant's Lean Mass, Fat Mass, and Lean Appendicular Mass were also collected. All scans were conducted and interpreted by experts blinded to treatment condition, following the methods outlined in Nowitz & Monahan [35].

Biochemical markers measured for bone turnover consisted of Serum Osteocalcin and Vitamin D, and Urinary Pyridinoline (PYD) and Deoxypyridinoline (DPD) levels. All samples were collected between 6 and 8am, after participants were fasted overnight and before they consumed breakfast. Urine collection was from first- or second-pass urine, and was collected mid-stream, whereas venepuncture blood samples were collected prior to consuming breakfast. Upon collection, blood samples were left to stand for 10 minutes before being centrifuged for 15 minutes at 2500 rpm, after which serum was extracted and subsequently frozen at -80°C until analysis. Levels of total osteocalcin were determined using electrochemiluminescence immunoassays (Cobas, Roche Diagnostics GmbH, Mannheim, Germany), with intra- and interassay coefficients of variation (CVs) for this test being <2.4% and <1.6%, respectively. Serum vitamin D levels were determined using liquid chromatography-tandem mass spectrometry, as per the methods of Lankes et al [36]. After collection, urine samples were also frozen at -80°C until analysis. Urinary PYD and DPD levels were determined using competitive enzyme immunoassay (Aviva Systems Biology, San Diego, CA, USA), with intra- and inter-assay CVs of <4.1% and <5.2% for PYD, and <6.1% and <10.6% for DPD. Conducted by experts blinded to treatment conditions, serum vitamin D and osteocalcin levels were analysed at an accredited pathology laboratory (Canterbury Health, Christchurch, New Zealand), whilst urinary PYD and DPD levels were determined at an accredited university biochemical laboratory (Nutrition Laboratory, Massey University, Palmerston North, New Zealand) by staff independent from the study.

Statistical Analysis

Sample sizes were calculated based on a previous study of WBV effects the lumbar BMD of frail elderly participants, as described in Lark and Wadsworth [30]. Ensuing statistical analyses were conducted using SPSS Version 24 (SPSS, Inc., Chicago, IL, USA). Missing data points were accounted for using 5-step Multiple Imputation (on average 11% of data imputed), in accordance with Sterne et al. [37]. Data was then tested for skewness and kurtosis for normal distribution. Treatment effect-sizes were calculated in accordance with the methods outlined by Cohen's d [38], with clinically-important inference set at >0.5 for moderate- and >0.8 for large-effects, in accordance with Page [39]. Main effects of the training intervention were analysed by repeated-measures ANOVA, and further independent samples t-tests for differences at specific timepoints, with significance set at p=0.05 for all tests. As bone health is influenced by gender, univariate analysis with gender as a covariate were carried out to determine the level of influence on all parameters. All data is presented as group mean ± standard error of the mean (SEM).

6.2.4 RESULTS

Participants

A total of twenty eligible participants (mean age = 84.5 ± 1.7 years) consented to participate in the additional assessments of this subsection of a wider study, and were randomly allocated into one of two parallel treatment groups (Figure 6.1). Participant characteristics are outlined in Table 6.1, with only age demonstrating a significant difference between treatment groups. Overall, participants displayed a moderate degree of functional impairment/frailty, suggesting a need for supervision/assistance on non-level surfaces, with 15% requiring further forms of supervision/assistance for all forms of ambulation. No significant differences existed between groups at baseline assessment of frailty, body composition, or prevalence of osteopenia and osteoporosis (Table 6.1).

No chronic adverse effects were reported by the WBV training group or their counterparts in the SIM group once familiarised with the WBV machine/exercise. Both groups exhibited high levels of compliance, attending 93% and 89% of sessions for the WBV and SIM groups, respectively. Training sessions were not experienced as a strenuous workout, with participants rating their perceived exertion levels as 2 (easy) and 1.4 (easy) for WBV and SIM groups, respectively.

Table 6.1. Participant Characteristics (mean ± SEM)

Parameter	Overall	WBV Group *(n = 8)*	SIM Group *(n = 12)*	***p* value** *between groups*
Age (years)	84.5 ± 1.7	78.8 ± 2.8	88.3 ± 1.3	**0.003**^
Gender	7 M / 13 F	3 M / 5 F	4 M / 8 F	-
Height (m)	1.60 ± 0.02	1.63 ± 0.04	1.58 ± 0.02	0.479
Weight (kg)	69.10 ± 3.13	68.13 ± 6.31	69.75 ± 3.34	0.807
Lean Appendicular Mass (kg/m^2)	6.24 ± 0.23	6.27 ± 0.44	6.21 ± 0.27	0.902
Degree of Frailty#	5.15 ± 0.15	5.00 ± 0.27	5.25 ± 0.18	0.429
% Osteopenic$	15%	12.5%	16.6%	-
% Osteoporotic$	25%	25%	25%	-

Measured using Functional Ambulation Categories outlined by Holden et al (1984)

$ Osteopenia = T-score of -1.0 to -2.5, Osteoporosis = -2.5 or greater; ^ Significant difference at $p < 0.05$

Bone Health Assessment Parameters

Changes in bone health parameters over the duration of the study are summarised in Tables 6.2 and 6.3, and Figure 6.2. Whole-body BMD underwent statistically significant time-dependant changes over the duration of the study, but clinically-meaningful treatment-effects were only observed in serum osteocalcin levels at 12-months post-intervention (Figure 6.2, Table 6.3). All other measures of bone health were not significantly affected by either treatment group.

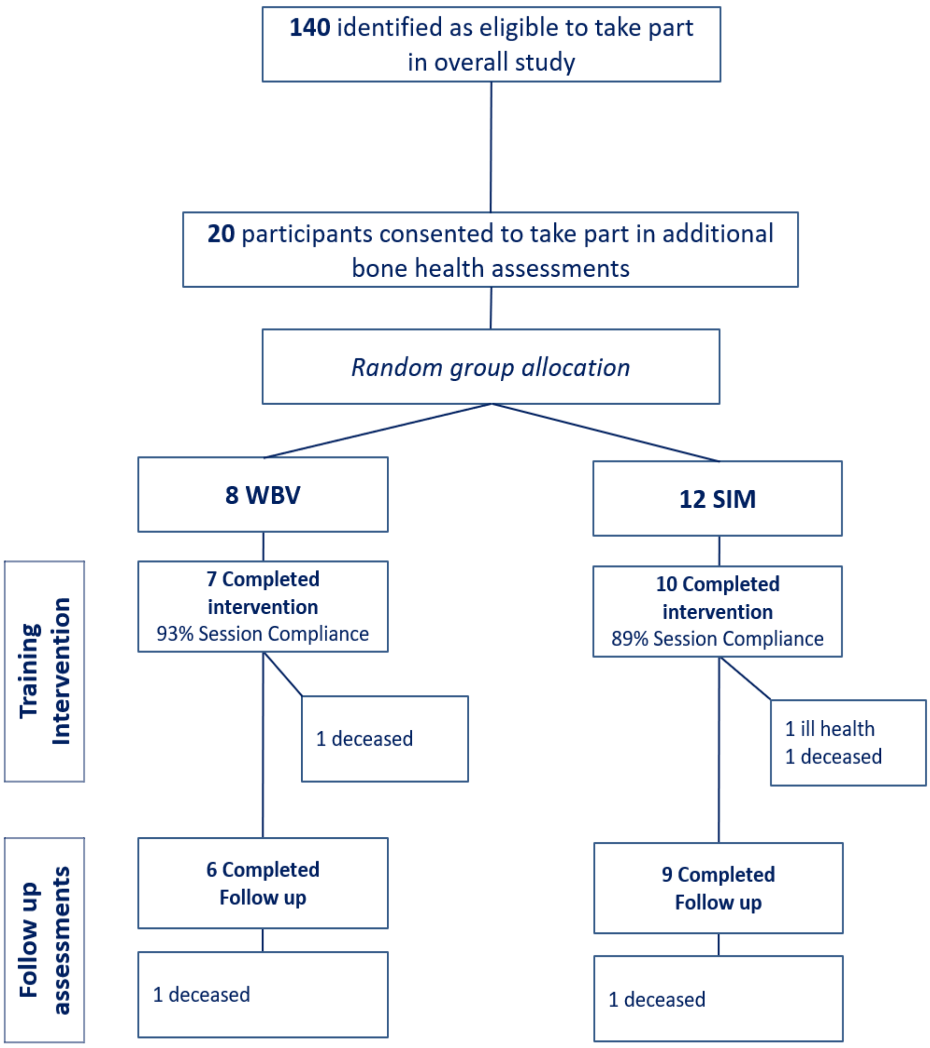

Figure 6.1. Consort diagram (Part B).

Bone Mineral Density levels were unaffected by treatment group, with all treatment-effects being small or trivial in nature and of no statistical significance (Table 6.2). Specifically, Whole Body BMD levels declined over the duration of the study (*p*=0.001), doing so in an equal degree for both groups (Table 6.2). Furthermore, BMD levels at the neck of femur replicated this, also declining over the duration of the study (*p*=0.004) at an equal rate for both groups (Table 6.2). However, BMD levels of the total hip and lumbar spine were unaffected by time (*p*=0.801 and *p*=0.189, respectively) or treatment group (Table 6.2).

Changes in biochemical markers of bone health over the duration of the training intervention and follow-up period are summarised in Table 6.3. In comparison to baseline-levels, a moderately-sized treatment-benefit of WBV-exercise was observed in serum osteocalcin levels 12-months post-intervention (Figure 6.2, Table 6.3), with changes over time and group both approaching statistical significance (*p*=0.073 and *p*=0.057, respectively) for this marker (Figure 6.2). Vitamin D levels were unchanged throughout the duration of the study (*p*=0.583), exhibiting only small/trivial sized-treatment effects of no statistical significance (Table 6.3). Similarly, urinary levels of PYD and DPD also remained unchanged over the duration of the study (*p*=0.095 and *p*=0.282, respectively), with only small/trivial-sized treatment-effects of no statistical significance observed (Table 6.3).

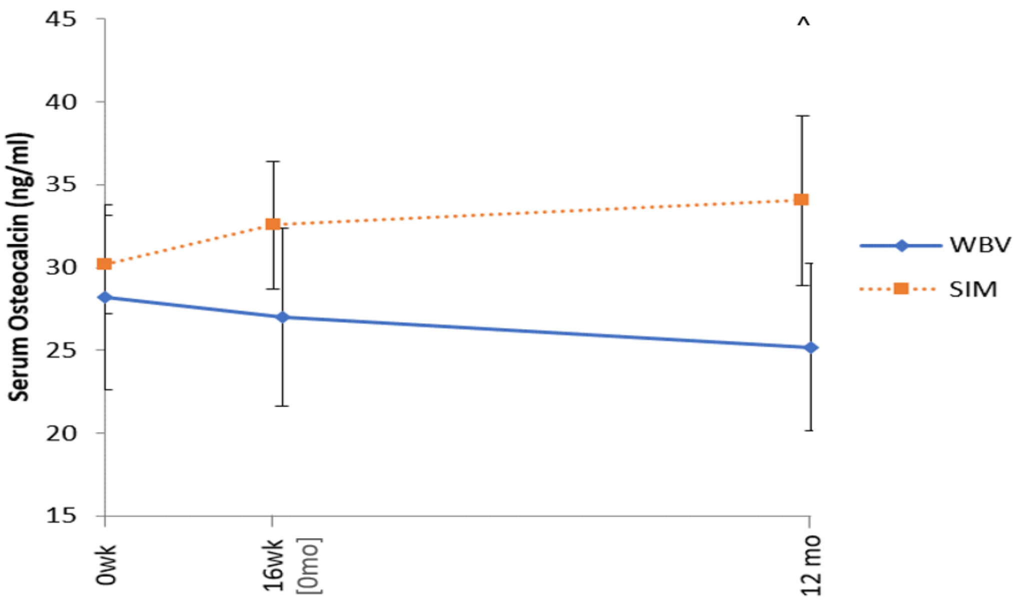

Figure 6.2. Changes in Serum Osteocalcin levels (mean ± SEM).
[*p<0.05; †p<0.01; ^p = 0.05-0.08]

Additional univariate analyses of all markers with gender as a covariate identified a significant-influence of gender for BMD levels in the total hip and lumbar region of the spine, and for urinary PYD levels, but no gender*group effects were observed for any parameter (Tables 6.4 and 6.5). All other covariate analyses identified no significant influence of gender at any time point.

Table 6.2. Bone Mineral Density measures of bone health (mean ± SEM)

Bone Mineral Density measure (g/cm^2)	Values (mean ± SEM)						Effect Size (of WBV treatment)		*p* value^
	WBV			SIM					
	0 wk	*16 wk*	*12 mo*	*0 wk*	*16 wk*	*12 mo*	**16 wks**	**12 mo**	
Whole Body	1.035 ± 0.06	0.994 ± 0.05	0.960 ± 0.05	1.055 ± 0.05	1.046 ± 0.05	1.021 ± 0.05	-0.355 *Small*	-0.396 *Small*	0.239
Neck of Femur	0.659 ± 0.04	0.660 ± 0.04	0.640 ± 0.03	0.623 ± 0.06	0.610 ± 0.06	0.580 ± 0.07	+0.346 *Small*	+0.399 *Small*	0.369
Total Hip	0.776 ± 0.05	0.786 ± 0.05	0.772 ± 0.05	0.754 ± 0.06	0.725 ± 0.05	0.742 ± 0.07	+0.411 *Small*	+0.170 *Trivial*	0.371
Lumbar Spine	1.022 ± 0.08	1.027 ± 0.08	1.041 ± 0.09	1.004 ± 0.05	1.007 ± 0.05	1.017 ± 0.06	+0.098 *Trivial*	+0.111 *Trivial*	0.868

Effect sizes calculated as per Cohen's d (1988) and interpreted as per Page (2014);
^*p* value for time*group (significance set at p < 0.05).

Table 6.3. Biochemical measures of bone health (mean ± SEM)

Marker	Values (mean ± SEM)						Effect Size (of WBV treatment)		*p* value ^
	WBV			SIM					
	0 wk	16 wk	12 mo	0 wk	16 wk	12 mo	16 wks	12 mo	
Serum:									
Osteocalcin (ng/ml)	28.16 ± 5.59	27.01 ± 5.39	25.17 ± 5.06	30.18 ± 2.99	32.55 ± 3.84	34.06 ± 5.13	-0.414 *Small*	-0.599 *Mod*	0.057
Vitamin D (umol/L)	78.73 ± 21.45	84.81 ± 17.15	81.23 ± 12.67	70.60 ± 16.20	68.70 ± 15.10	79.70 ± 17.51	+0.335 *Small*	+0.034 *Trivial*	0.397
Urinary:									
PYD (nmol/L)	184.64 ± 52.20	237.78 ± 84.69	346.12 ± 136.99	214.90 ± 52.61	298.66 ± 46.76	251.63 ± 53.65	-0.361 *Small*	-0.397 *Small*	0.204
DPD (nmol/L)	0.800 ± 0.08	0.860 ± 0.22	1.081 ± 0.18	0.845 ± 0.07	1.111 ± 0.28	1.003 ± 0.12	-0.354 *Small*	+0.197 *Trivial*	0.502

Effect sizes calculated as per Cohen's d (1988) and interpreted as per Page (2014);
^*p* value for time*group (significance set at p < 0.05).

Table 6.4. Univariate analysis for BMD parameters with gender as a covariate.

Parameter	Timepoint	p-value	ETA	Group effect (p-value)
BMD Whole body	0wk	0.231	0.101	0.812
	16wk	0.162	0.135	0.485
	12mo	0.276	0.084	0.451
BMD NoF	0wk	0.070	0.216	0.678
	16wk	0.090	0.192	0.533
	12mo	0.233	0.100	0.491
BMD Hip	0wk	**0.019***	0.334	0.842
	16wk	**0.012***	0.373	0.385
	12mo	0.074	0.211	0.776
BMD Lumbar	0wk	**0.016***	0.328	0.999
	16wk	**0.018***	0.321	0.973
	12mo	**0.015***	0.335	0.950

*p<0.05

Table 6.5. Univariate analysis for biochemical markers with gender as a covariate.

Parameter	Timepoint	p-value	ETA	group effect
OC	0wk	0.781	0.006	0.764
	16wk	0.622	0.018	0.433
	12mo	0.695	0.011	0.260
Vit D	0wk	0.336	0.062	0.743
	16wk	0.283	0.076	0.471
	12mo	0.613	0.018	0.938
PYD	0wk	0.551	0.030	0.687
	16wk	**0.004**†	0.510	0.221
	12mo	0.074	0.290	0.519
DPD	0wk	0.399	0.055	0.737
	16wk	0.937	0.001	0.595
	12mo	0.419	0.051	0.699

*p<0.05; †p<0.01

6.2.5 DISCUSSION

The current study aimed to provide clarity on the clinical effects of long-term, low-level WBV exercise on the bone health of the frail elderly. Changes in serum osteocalcin levels suggest that the current training-protocol delivered stimulus for the frail elderly to enhance rates of bone deposition. The stimulus was, however, not sufficient to address the normal rates of decline exhibited in BMD levels at the neck of femur and whole body. Nevertheless, the results demonstrate that conducting WBV exercise at low-intensities has no detrimental-impact on the bone health of the frail elderly. Consequently, the absence of adverse-effects suggests that the frail elderly can tolerate this easily-accessible level of exercise, making it a safe training tool for this population when other training goals are the focus.

Serum osteocalcin levels have an established inverse correlation with bone health [40-42], and consequently the moderately-sized treatment-benefit observed in this biomarker at 12-months in the current study demonstrates that the WBV-training-protocol utilised can produce clinically-important changes in rates of bone deposition in the frail elderly. Formed by osteoblasts during bone formation and trapped in the ensuing new bone matrix, elevated serum levels of osteocalcin are indicative of slower rates of bone deposition, and thus poorer bone health [40]. What-is-more, short periods of increased fluid flow have been shown to promote the proliferation and survival of osteoblasts [43], underpinning fluid-dynamic-based mechanistic theories of WBV osteogenic-action [21, 44]. Consistent with this, animal-based in-vitro studies have shown WBV to specifically up-regulate osteoblast differentiation, matrix synthesis and mineralization [45]. Viewed in isolation, therefore, the clinically-meaningful reduction in osteocalcin levels shown in the current study supports the notion that WBV training can enhance the bone health of older adults [17-20]. However, this was not reflected in the BMD changes observed, where both treatment groups experienced equitable levels of bone loss, or maintenance, at rates comparable to reported average annual age-related declines [46].

Very little research exists for comparison of WBV-effects on the bone health of the frail elderly, with the sole study to-date reporting only a non-significant increase of 0.75% in hip BMD after 6-months of WBV-exercise with concurrent static and dynamic exercises [29]. That the current study showed maintenance of BMD at the total hip and lumbar regions, in comparison to declines in neck of femur and whole-body BMD levels, echoes the findings of this previous work [29]. However, no treatment effects were observed in any BMD parameter for either training group in the current study. There are a number of possible explanations, chiefly that

Verscheuren et al. delivered vertical WBV exercise at 30-40 Hz in tandem with concurrent exercises, did so for 6 months, and had a larger cohort consisting of WBV-exercise and non-exercising groups [29]. It should be noted that all participants in the current study had the opportunity to engage in other activities of the home, but no treatment-effects were observed. Consequently, the current BMD findings are in agreement with research in community-based/mobile older adults, where it was reported no beneficial training-effect of WBV exercise on BMD [22, 23, 47-49]. Indeed, a recent meta-analysis of 15 studies concluded that “WBV may prevent fractures by reducing falls rate” but “seems to have no overall effect on BMD or microarchitecture” of older adults [50].

The natural age-related loss of BMD is attributed to a drop in mechanical loading on tissue [4], however the level of mechanical stimulus delivered in the current study was not sufficient for the enhanced rates of bone deposition to transpire into increased levels of BMD. Previous researchers have suggested that the mechanics of potential WBV-benefits to bone health are primarily in the upregulation of osteoblast activity, and subsequent secondary down-regulation of osteoclastogenesis [43, 45]. In agreement, the current study demonstrated WBV-associated decreases in levels of osteocalcin, indicative of increased osteoblast activity, coupled with no change in markers of bone resorption (PYD and DPD). An explanation for why no improvements in BMD were observed is that the current study initially deployed rotational WBV at the lowest level (6 Hz), proposed to facilitate gentle adaptation in frail populations [18], and left subsequent progression to be determined ad libitum by individual participants. In accordance with the osteogenic-effects of conventional exercise training [51], both human- and animal-based studies appear to suggest that higher frequencies of WBV are more favourable for eliciting significant bone health benefits, with the largest benefits to-date reported from vertical WBV delivered at 30 Hz for community-dwelling older adults [19], and 40-90 Hz in rat-based models [45, 52]. Furthermore, the smallest reported benefits in older adults are associated with rotational WBV at 12.5 Hz [20], supporting a dose-dependent BMD-effect. Interventions that are shorter in duration have still reported successful effects on BMD, with programs as short as 11-weeks reporting maintenance of BMD levels in older adults [22], thus arresting the natural decline. What-is-more, a recent comprehensive review of 71 studies into the clinical application of vibration therapy in orthopaedic practice concluded that the strongest anabolic signals to bone were achieved with devices delivering low-intensity stimuli at high-frequencies when using vertical displacement [53]. Finally, evidence suggests that muscle activation from WBV-exercise can be maximised by deploying high vibration frequencies (30 Hz) coupled with greater ranges of knee flexion (60°) [54], both of which may be too demanding for the frail elderly. Considering that the forces applied to bone are well-established to be primarily due to muscular contractions [55], the optimal settings described by Ritzmann et al [54] can be said to maximise mechanical stimulus of bone too. Given the frail nature of participants in the current study (and the wider FEVER study of Lark & Wadsworth [30]), the authors specifically designed the WBV-intervention to be as accessible as possible for the frail elderly, with the rotational WBV design employed to minimise energy transfer to the spine and head [56], and the low frequency of vibration (FoV) and simple stance/lack of dynamic exercises both employed to limit workload. However, the semi-squat position utilised has been shown to reduce acceleration by up to 10-times at the knee and hip [57]. Not-withstanding the beneficial treatment-effects of WBV on osteocalcin demonstrated in the current study, in view of the above discussion and the conclusions of Cerciello et al [53], it appears that our gentle approach may also have limited the effectiveness of the protocol for enhancing BMD levels.

The lower-frequency of vibration employed in the current study was a conscious decision made to enhance the participant comfort, ease-of-use, and ultimately the accessibility of WBV exercise for the frail elderly. Indeed, frequencies of 5-10 Hz suggested for gentle adaptation in frail populations [18]. To this end, the protocol deployed can be deemed a large success, scoring highly in levels of compliance, low in ratings of perceived exertion, and eliciting positive functional and anecdotal feedback from the participants involved (reported elsewhere). Moreover, given that the WBV group experienced BMD loss at rates comparable to reported average annual age-related declines [46], and markers of bone resorption (PYD and DPD) were unchanged over time, the authors conclude that the current protocol elicited no adverse effects. In contrast, some previous evidence exists suggesting a negative influence of WBV exercise on the bone health of “healthy” older adults [24], and in comparison, the current lack of detrimental-effects is a positive outcome. Relatively cheap to purchase and easy to administer, WBV exercise is becoming widely-used as a functional training tool for various populations including older adults [19, 58], where enhanced bone health is not the primary training goal. When the enhanced rates of bone deposition are combined with other positive beneficial treatment-effects on functional and psychological parameters (reported elsewhere), the findings suggest that low-level WBV exercise can be a feasible exercise training tool in the frail elderly where enhanced bone health is not the primary training goal. Perhaps the true value of the current protocol in this context lies as a rehabilitation-tool for enhancing an individual’s functional capabilities and confidence such that they are later able to attempt more-demanding weight-bearing exercises for musculoskeletal strength.

The current study is not without limitations that warrant further discussion. Firstly, fewer participants than anticipated were recruited for this study, a subsection of the wider FEVER study [30]. Participant recruitment was limited by the strict exclusion criteria concerning impaired-cognition, specific conditions and/or recent history of a fracture or joint replacement [30], but also participant interest in this arm of the study and the financial costs associated with measures of bone health. Such was this effect that researchers chose to only include exercising participants, and not a non-exercising control, deviating from initial plans [30]. However, when initial sample sizes were calculated based on previously-reported WBV-induced changes in lumbar BMD [19], the resultant group-sizes were doubled from 10 to 20/group in order to account for possible differences in the initial bone health (prevalence of osteoporosis) when compared to the participants in Ruan et al.'s [19] research. As such, the eventual numbers recruited for this sub-section are in-fact close to the calculated size required. Moreover, the sample sizes in the current study reflect those in the work of Gusi et al [18], which demonstrated beneficial effects of 8-months of rotational WBV on the bone health of 28 post-menopausal females. Consequently, whilst the potential of an undetected/underlying detrimental condition to influence results should be acknowledged, the authors can be confident that the sample sizes utilised provided accurate results in the current study. Secondly, the lack of a true non-exercising control group in this study means that we have no "pure" control group with whom to compare rates of BMD loss. As such, one could argue that the true effect of the exercise delivered (isometric squats with or without WBV exercise) remains somewhat unclear. However, given that all participants continued to receive normal care throughout the duration of the current study, comparison with well-publicised average annual age-related declines [46] are valid and justified in order to address this gap. The inclusion of participants from both genders could be viewed as a third limitation, given the associated gender-effects on bone loss and osteoporosis [59]. However, ageing and osteoporosis in older males are both associated with bone loss and increased fracture-rate, mortality and morbidity [59], so it is appropriate to also consider the effects on this specific group. Moreover, whilst there is some evidence that gender differences exist for Osteocalcin [60], there are other studies that showed no such interaction [61]. Regardless of this, data were analysed in the current study by measuring change from baseline of individuals, and then comparing treatment effects, hence exploring within-subject effects and thus negating differences between participants. This approach was essential, as with an already extensive exclusion criteria to then match groups for other parameters such as gender and pre-existing co-morbidities would be wholly infeasible. What-is-more, gender was included as a co-variate for statistical analysis with no significant gender*group interactions identified for any parameter, whilst the incidence of osteoporosis was confined solely to female participants.

Finally, considering that the largest WBV-associated benefits have been reported in those with the poorest levels of bone health and function [16, 62] the specific exclusion criteria pertaining to a recent history of a fracture or joint replacement could to some extent be said to exclude the very individuals who could benefit the most.

6.2.6 CONCLUSION

The current study demonstrated that simple thrice-weekly sessions of low-level WBV-exercise can lead to increased rates of bone deposition, with no change to bone resorption, in the frail elderly. However, the level of stimulus was not sufficient to address the normal rates of decline exhibited in BMD at the neck of femur and whole body. Nevertheless, the beneficial effects on bone deposition evidenced by reduced serum osteocalcin, coupled with an absence of detrimental treatment-effects, shows that the frail elderly can tolerate this easily-accessible level of exercise, making it a safe training tool for this population when other training goals are the focus.

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7. Cardiovascular Health Results

7.1 Chapter Overview

The following chapter focuses on the cardiovascular health results from the current research project. Presented in a paper format for journal submission (currently under preparation for *Experimental Gerontology* or the *Journal of Health and Sports Science*), the general methodology and protocol are as previous chapters, but the measurement of the specific cardiovascular variables is presented in more detail than the methodology chapter. As such, findings and discussion address the secondary outcome of the research project pertaining to this parameter, namely that chronic WBV-training will not adversely affect the cardiovascular health of the frail elderly. Initially included as a safety-precaution to monitor the effects of WBV-training, the paper also discusses novel beneficial effects identified in the current project.

7.2 EFFECTS OF WHOLE BODY VIBRATION TRAINING ON THE CARDIOVASCULAR HEALTH OF THE FRAIL ELDERLY.

7.2.1 ABSTRACT

Age-related declines in vascular health and physical-function limit the application of conventional exercise-training in the frail elderly. Whole-Body Vibration (WBV) exercise is an accessible form of strength-training for the frail elderly, but its effects on vascular health are unclear and thus its safe use in this population remains uncertain. Therefore, this study investigated WBV-exercise effects on the vascular health of the frail elderly.

*One-hundred-and-seventeen males and females (82.5 ± 7.9 years) from residential-care-facilities were randomly allocated to Control (CON), Simulated-exercise (SIM) or WBV-exercise (WBV) groups. Participants received their regular-care, whilst WBV- and SIM-groups also underwent thrice-weekly exercise sessions for 16 weeks. Delivered by overload principle, WBV-exercise began with 5*1-min bouts of rotational-WBV at 6 Hz/2 mm (1:1 min exercise:rest), progressing to 10*1-min at up-to 26 Hz/4 mm, maintaining knee-flexion. Training for SIM participants mimicked exercise stance and duration. Vascular health was assessed by pre- and post-measures of Augmentation Index (AIx), Mean Arterial Pressure (MAP), Resting Heartrate (rHR), and Systolic (SBP) / Diastolic (DBP) Blood Pressures.*

Significant reductions of 23.3% and 16.7% were observed in AIx after 8- and 16-weeks, respectively, of WBV-exercise. Additionally, there was a strong-trend towards significant-reductions 3-months post-intervention for this group/parameter. Further clinically important treatment-effects on MAP, SBP and DBP were also demonstrated with WBV-exercise, but no treatment-effects were observed for other groups.

Chronic low-level WBV-exercise elicited clinically-important improvements in the vascular health of frail elderly participants, decreasing arterial stiffness and BP. It therefore presents as a safe and effective training-tool for addressing age-related health declines in this population.

7.2.2 INTRODUCTION

Age-associated declines in health are markedly prevalent in older adults [1]. Of primary concern are decreases in cardiovascular health, and concurrent increased risks of cardiovascular disease, coronary artery disease, and ultimately mortality [2]. Arterial stiffness increases with age and is an independent risk factor for cardiovascular disease [3] and systolic hypertension [4]. In particular, elevated arterial stiffness increases the likelihood of atherosclerosis [4], left ventricular failure [5, 6] and myocardial ischemia [7, 8], making it an important measure of vascular health in older adults.

Displaying low functional status, poor vascular health, and a high-incidence of chronic disease, no group can feasibly benefit more from exercise than the elderly [9], yet paradoxically such factors also significantly limit their ability to exercise conventionally. Whole Body Vibration (WBV) exercise has gained prominence as an accessible and effective training-tool in various populations including older adults [10-12]. However, few studies to-date have investigated the effects of WBV exercise on arterial stiffness. Considering the characteristically poor vascular health displayed by this group [13], caution must be shown with this population when prescribing any exercise. This is especially pertinent when, although not unanimous, there are some reports that resistance exercise may increase arterial stiffness [7, 14, 15] , increasing the risks of cardiovascular disease outlined above. As an effective strength-training alternative to resistance training [16, 17], until otherwise established it is prudent to speculate that WBV-exercise may likewise increase arterial stiffness in compromised individuals.

Exploration into the effects of WBV on vascular health are reporting some promise. Methodologies are mixed, having predominantly considered the acute-effects on a limited amount of younger- and older-participants, but researchers have consistently delivered WBV of between 20-40 Hz. Acute reductions in systemic arterial stiffness have been reported in young healthy adults [18], with significant decreases observed up-to 40 minutes following 10*1-minute sets of static squats combined with WBV [19, 20]. The acute-effects of WBV exercise on older adults are relatively unknown, yet passive vibration delivered directly to the legs did improve the arterial stiffness of 11 older post-stroke patients [21]. The chronic-effects of WBV exercise on arterial stiffness have only been explored by two research groups, with beneficial effects reported in young- and postmenopausal-obese females after 6, 8 and 12 weeks of dynamic-exercise sets performed whilst receiving WBV [22-24]. Interestingly, researchers reported strong correlations between decreased arterial stiffness and increased leg muscle strength [22, 24], yet there is no way to attribute these benefits directly to either the WBV exercise or the dynamic-exercise sets performed. A further study delivering 3-months of WBV with no concurrent exercises to mobile middle-aged and elderly men, aged 61.9 years-old, reported beneficial decreases in their arterial stiffness, although this did not reach statistical significance between groups [25]. Despite the early promise of these findings, the effects on the arterial stiffness of less-mobile, frail elderly are unknown.

Whole Body Vibration exercise is also associated with acute shifts in fluid dynamics [26, 27], vasodilation of capillaries [28] and resultant increased peripheral circulation [29] at a variety of intensities. However, with reported increases in peripheral blood flow in-excess of 50% with acute bouts of WBV exercise [26, 27], this vasodilation of lower-limb vessels, and ensuing erythema, could potentially lead to pooling of blood and subsequent orthostatic intolerance [30]. Improved endothelial function and arterial stiffness may exacerbate this risk, where resultant reductions in wave reflection back to the heart could further decrease myocardial strain and central blood pressures. Such potential orthostatic intolerance may result in episodes such as dizziness, postural vasovagal syncope, or postural tachycardia syndrome, simultaneously increasing the risk of injury from a sudden-fall and reducing an individual's independence and quality of life [30]. Although the acute-effects of WBV exercise on vascular health show some promise, the chronic-effects remain unknown. As such, effective and safe clinical applications of WBV-exercise cannot be derived for frail elderly whilst concerns around localised-erythema and orthostatic intolerance exist.

Generally reporting the poorest levels of vascular health [13], yet showing the largest reported WBV-associated benefits in other measures [31, 32], the frail elderly stand to gain the most from the deployment of such exercise programs. Accessibility of exercise is essential to this population, and WBV-exercise presents as an easily-accessible training-tool, yet to-date no-one has explored the chronic-effects of low-level WBV on their vascular health. Therefore, this study aimed to investigate any potential vascular changes associated with chronic WBV-exercise in the frail elderly, in order to determine if it is a safe exercise with regards to their vascular health.

7.2.3 METHODS

Study Design and Participants

Ethical approval for the study was granted by the Health and Disability Ethics Committee of New Zealand (12/NTB/78), and the study has Universal Trial Registration (UTN: U1111-11367-146). The FEVER methodology and protocol paper [33] fully-outlines study design and participant recruitment procedures. Following written informed-consent, eligible volunteers from rest home facilities in the Greater Wellington area underwent pre-screening for inclusion-criteria, that is frailty as determined by functional ambulation using a scale of 0-6, where less-than-6 indicates a degree of functional limitation and frailty [34]. Exclusion criteria were: a RUDAS assessment of cognitive function with minimum-score of 20 [35]; a lower-limb/spinal fracture within 12-months; hip- or knee-prosthesis; conditions including peripheral-neuropathy, cancer tumours, diabetic neuropathy; and participation in over 3 hours/week of exercise (fully-detailed in [33]).

Eligible volunteers gave written informed consent, and subsequently underwent pre-screening for exclusion criteria including a RUDAS assessment of cognitive function, recent fracture history, and participation in more than 3 hours of exercise a week at the time of recruitment (detailed in).

Continuing to receive access to standard residential-care and activities throughout the study, participants were randomly assigned (using a random number computer-generator tool; random.org) to: i) a Control group (CON), ii) a Simulated-exercise group (SIM), or iii) a WBV-exercise group (WBV). Participants in the SIM and WBV groups exercised together 3-times a week for 16 weeks. The SIM group was included to account for any possible placebo effect brought about by the cardiovascular-demands of study participation, both in the static exercise performed in training and in the incidental activity in attending sessions (walking to/from sessions) and frequently rising/sitting during training, as well as the social interaction and attention associated with participation.

Training Protocol

Participants in the WBV group exercised by receiving 1-minute bouts of WBV, whilst standing with isometric knee flexion ≈20˚ (±5˚), interspersed with 1-minute rest periods. Training load increased gradually over the 16-week intervention according to the overload principle. Participants began with 5*1-minute bouts of rotational-WBV exercise and rest (1:1) at 6 Hz/2.0 mm amplitude (Galileo Fitness Control 0544, Novotec, Germany), increasing until 10*1-minute bouts of WBV exercise and rest were reached. Progression of Hz and/or amplitude were then self-determined by participants, up to a potential maximum of 26 Hz/4.0 mm. Frequency of vibration and amplitude of the WBV-machines used were independently-assessed using an accelerometer (Vibsensor, Now Instruments and Software, Inc., CA USA). Participants in the SIM group mimicked exercise stance and duration. All participants in exercise-training groups were given the opportunity to provide comments on a weekly basis, which were monitored by geriatric consultants.

Cardiovascular Assessment Procedures

The vascular health of all participants was assessed by monitoring changes in Systolic/Diastolic Blood Pressure, Mean Arterial Pressure, Augmentation Index, and Resting Heartrate. All assessments were conducted at 6 time-points: baseline (0 week), after 8- and 16-weeks of the training intervention, and 3-, 6- and 12-months post-intervention for follow-up. To minimise variation, tests were conducted within 1 hr of the original assessment time, with all measurements collected from the same arm whilst participants were seated, having been so for at least 10-minutes prior. After familiarisation at baseline, duplicate readings were collected for each assessment, and an average value calculated.

Measures of vascular health were collected using the PulseCor R7 Cardioscope (PulseCor, Auckland, New Zealand), a validated form of assessment of Pulse Wave Analysis (PWA) [36, 37]. Measurements were collected as previously described [38], and Resting Heartrate (rHR), Systolic- (SBP) and Diastolic-Blood Pressures (DBP) were directly measured. Systolic and Diastolic BP are reported in order to reflect changes in peripheral vasculature, as the effects of WBV are predominantly localised within the lower-limbs. An effective indicator of aortic stiffness and arterial compliance that is widely-used in PWA [39], the Augmentation Index (AIx) was mathematically-derived from pulse pressure readings using the following equation:

Augmentation Index = (augmentation pressure/pulse pressure) * 100).

Mean Arterial Pressure (MAP) was calculated using the established formula: MAP ≈ DBP + [(SBP-DBP)/3] [40].

Statistical Analysis

Statistical analyses were conducted using SPSS Version 24 (SPSS, Inc., Chicago, IL, USA). Missing data points were accounted for using 5-step Multiple Imputation (on average 15% of data imputed), in accordance with Sterne et al. [41]. Data was then tested for skewness and kurtosis for normal distribution. Treatment effect-sizes were calculated in accordance with the methods outlined by Cohen's d [42], with clinical-importance inferred at Moderate (0.5-0.8) and Large (0.8+) effect-sizes in accordance with Page [43]. Main effects of the training intervention were analysed using repeated-measures ANOVA, with specific treatment*time differences identified using subsequent one-way ANOVA and Bonferroni post-hoc tests. As AIx is influenced by HR and gender, and the equation involves blood pressure, univariate analysis with MAP, gender and rHR as covariates [44] were carried out to determine the level of influence on AIx for frail elderly. Additional paired-samples t-tests were used to identify within-group changes for AIx and SBP. All data is presented as group mean ± standard error of the mean (SEM) with significance at $p \leq 0.05$.

7.2.4 RESULTS

Participants

From a potential 140 eligible individuals, 117 participants consented to participate (Figure 4.1, Chapter 4). Participant characteristics for each group are outlined in Table 7.1, with no significant differences found between groups at the onset, aside from the mean age of WBV and CON groups (p = 0.013). Participants displayed a moderate degree of functional impairment/frailty (4.9 ± 0.9), as measured by Functional Ambulation Categories [34], with no differences between groups. Compliance levels were high throughout the training intervention, with WBV and SIM groups attending 93% and 89% of sessions respectively.

Table 7.1. Participant Characteristics (mean ± SEM).

Parameter	Overall	WBV Group	SIM Group	CON Group	***p* value** *(between all groups)*
N	117	36	35	46	-
Age (years)	82.45 ± 7.9	79.4 ± 1.1 [$]	83.7 ± 1.2	84.3 ± 1.3	**0.012**
Gender	41 M / 76 F	15 M / 21 F	8 M / 27 F	18 M / 28 F	-
Height (m)	1.62 ± 0.09	1.63 ± 0.02	1.61 ± 0.01	1.61 ± 0.02	0.596
Weight (kg)	70.97 ± 14.58	71.42 ± 3.26	72.65 ± 2.59	68.63 ± 3.19	0.626
SBP (mmHG)	137.9 ± 2.0	137.6 ± 2.8	137.1 ± 3.5	138.7 ± 3.8	0.442
DBP (mmHG)	75.9 ± 1.1	76.4 ± 1.7	77.9 ± 2.2	73.9 ± 1.7	0.463
Functional Ability [#]	4.92 ± 0.93	5.03 ± 0.12	5.09 ± 0.13	4.65 ± 0.17	0.069

[#] Measured using Functional Ambulation Categories outlined by Holden et al (1984);
[$] WBV significantly lower than CON (*p = 0.013*).

Cardiovascular parameters

Figures 7.2-7.4 summarise the changes in cardiovascular health observed in this study, with the effects of the 16-week training intervention detailed in Tables 7.2 and 7.3. Cardiovascular health improved with WBV training, with participants in the WBV group showing clinically-important reductions in blood pressure and arterial stiffness across the intervention period (Figures 7.1 and 7.2). Significant treatment-effects were lost within 3-months of ceasing WBV-training.

Clinically-important treatment-effects of WBV-training were apparent in AIx in comparison to both other conditions (Figure 7.1, Table 7.2). Similar reductions were also observed in MAP after 8-weeks of WBV-training, but not at 16-weeks (Table 7.2). Likewise, clinically-important treatment-effects were observed in both SBP and DBP for WBV vs CON after 8-weeks only, trending towards statistical-significance vs SIM participants at the same time-point (Figure 7.2, Table 7.2). Differences between SIM and CON group-effects were negligible and of no clinical-importance/significance throughout the intervention-period.

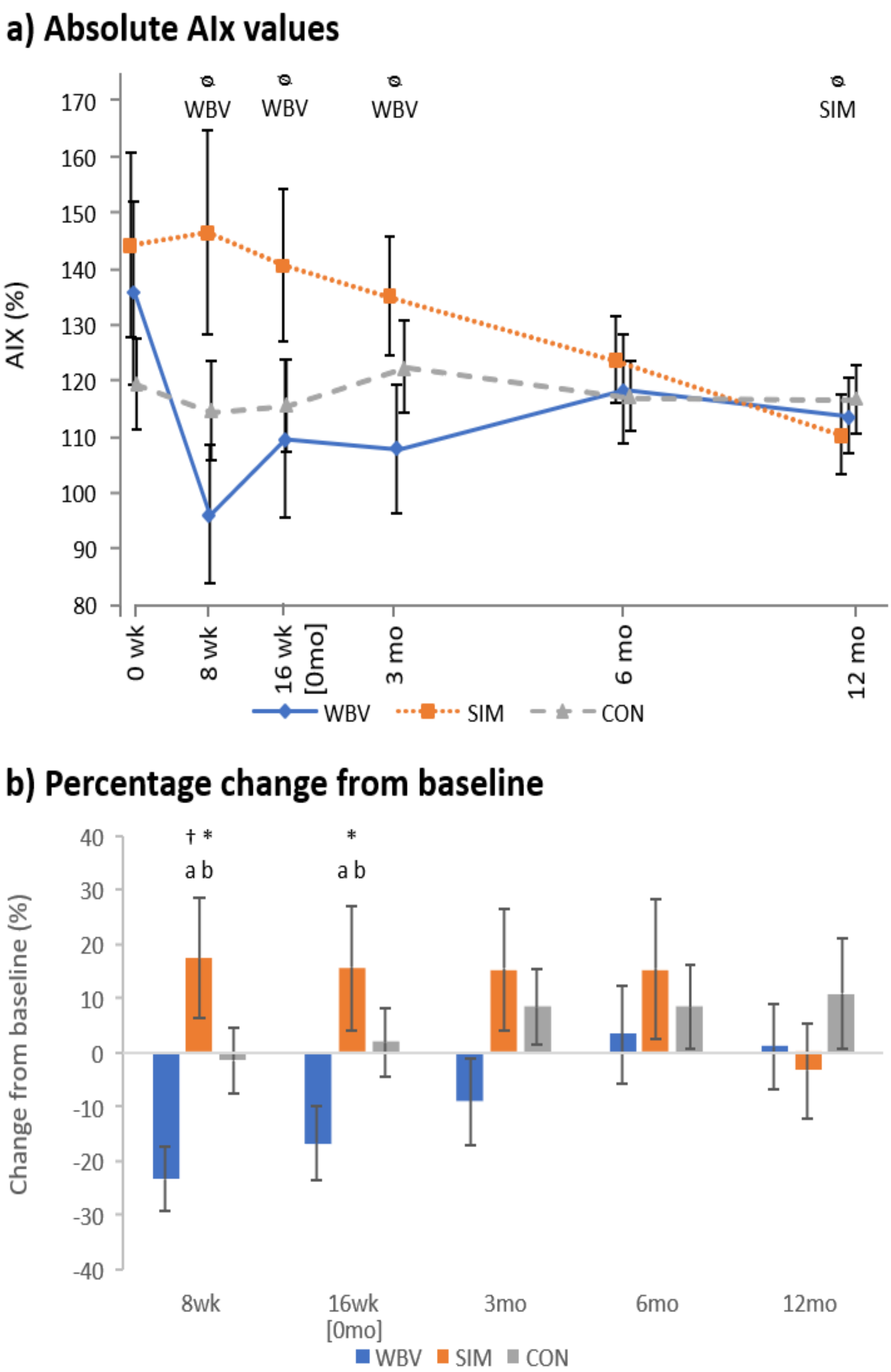

Figure 7.1. Changes in AIx, both in a) raw data (mean ± SEM), and b) percentage-change from baseline (mean % change ± SEM). [*p<0.05; †p<0.01; ^p = 0.05-0.08; [a]WBV:SIM difference; [b]WBV:CON difference; [c]SIM:CON difference; [ø]significantly below baseline level]

Table 7.2. Cardiovascular changes associated with 16-weeks of WBV training (Effect Size & *p* value).

	Change from Baseline									
	8 wk		**16 wk**		**3 mo**		**6 mo**		**12 mo**	
	ES	***p***	**ES**	***p***	**ES**	***p***	**ES**	***p***	**ES**	***p***
SBP										
WBV vs. SIM	-0.47	*0.053*	-0.19	*0.446*	0.00	*0.985*	0.08	*0.750*	0.06	*0.816*
WBV vs. CON	-0.53#	***0.021****	-0.36	*0.121*	-0.21	*0.372*	-0.08	*0.719*	-0.06	*0.782*
SIM vs. CON	-0.09	*0.696*	-0.24	*0.307*	-0.22	*0.35*	-0.14	*0.549*	-0.11	*0.633*
DBP										
WBV vs. SIM	-0.46	*0.06*	-0.11	*0.646*	-0.04	*0.851*	-0.17	*0.483*	0.01	*0.982*
WBV vs. CON	-0.67#	***0.004*†**	-0.17	*0.446*	-0.16	*0.617*	-0.16	*0.471*	-0.09	*0.684*
SIM vs. CON	-0.28	*0.234*	-0.36	*0.128*	-0.08	*0.742*	0.00	*0.998*	-0.09	*0.691*
MAP										
WBV vs. SIM	-0.62#	***0.012****	-0.03	*0.910*	-0.05	*0.833*	-0.07	*0.761*	0.02	*0.939*
WBV vs. CON	-0.81$	***0.001*†**	-0.35	*0.135*	-0.22	*0.356*	-0.15	*0.525*	-0.11	*0.635*
SIM vs. CON	-0.23	*0.32*	-0.39	*0.116*	-0.16	*0.487*	-0.15	*0.725*	-0.11	*0.632*
RH										
WBV vs. SIM	0.04	*0.860*	0.09	*0.715*	-0.12	*0.615*	-0.22	*0.363*	-0.25	*0.305*
WBV vs. CON	0.16	*0.467*	-0.12	*0.589*	-0.07	*0.749*	0.15	*0.497*	0.00	*0.990*
SIM vs. CON	0.13	*0.570*	-0.22	*0.338*	0.04	*0.854*	0.37	*0.106*	0.22	*0.345*
AIX										
WBV vs. SIM	-0.88$	***0.002*†**	-0.65#	***0.020****	-0.47	*0.080*	-0.20	*0.449*	0.11	*0.697*
WBV vs. CON	-0.66#	***0.013****	-0.52#	***0.050****	-0.42	*0.108*	-0.11	*0.684*	0.19	*0.466*
SIM vs. CON	0.40	*0.137*	0.28	*0.296*	0.14	*0.600*	0.13	*0.631*	-0.27	*0.298*

Moderate treatment-effect; $ Large treatment-effect;
* Significant difference p < 0.05; † Significant difference p < 0.01;
Effect sizes calculated as per Cohen's d (1988) and interpreted as per Page (2014).

Statistically-significant reductions from baseline-levels were seen in SBP, being 9.4 and 7.0 mmHg lower after 8- and 16-weeks of WBV-training, respectively (Table 7.3, Figure 7.2). Strong-trends were still observed 3- and 6-months post-intervention. No significant reductions were observed in either SIM or CON groups during the training-intervention period, although SBP was significantly-lower than baseline levels 6- and 12-months post-intervention in SIM participants.

All treatment-effects were lost upon ceasing WBV-training, with the exception of a strong-trend towards significance for the retention of the observed effects of WBV-training on AIx 3-months post-intervention (Figure 7.1, Table 7.2). Furthermore, no significant-effects were observed on rHR at any time in the duration of the study (Figure 7.3, Table 7.2).

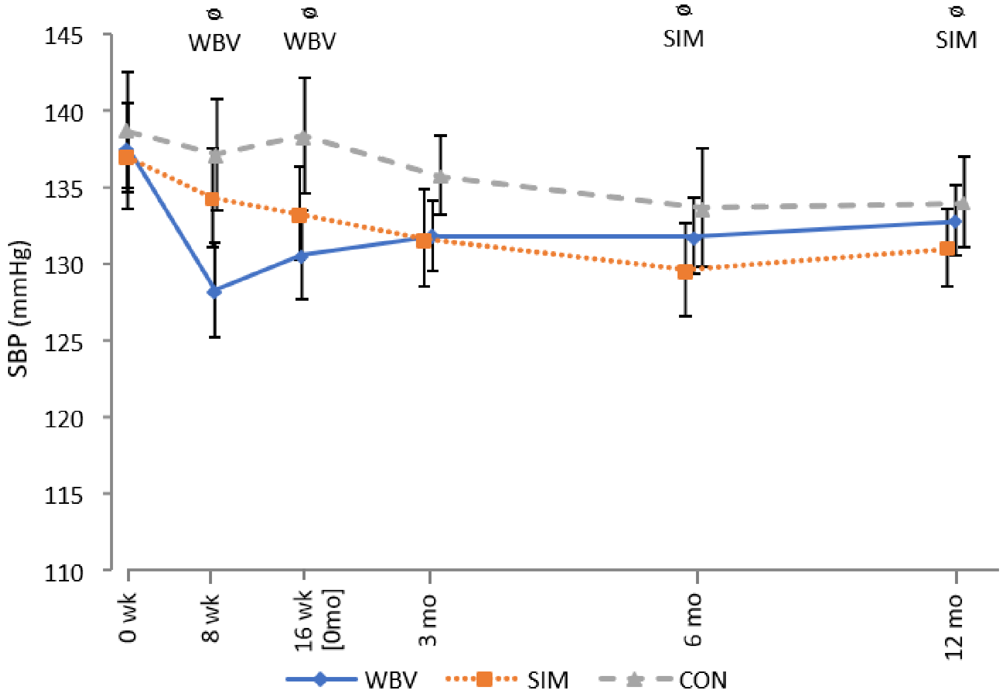

Figure 7.2. Changes in Systolic BP (mean ± SEM). [ᵊsignificantly below baseline level]

Table 7.3. Absolute change in SBP values from baseline (mmHg).

Timepoint *paired to baseline*	**WBV** Mean (± SEM)	Sig. (*p* value)	**SIM** Mean (± SEM)	Sig. (*p* value)	**CON** Mean (± SEM)	Sig. (*p* value)
8-wk	9.4 ± 2.8	***0.002***†	2.7 ± 2.2	*0.221*	1.6 ± 2.2	*0.481*
16-wk	7.0 ± 3.3	***0.042******	3.8 ± 2.1	*0.085*	0.3 ± 3.0	*0.913*
3-mo	5.7 ± 3.0	*0.062*	5.4 ± 2.7	*0.054*	2.9 ± 3.2	*0.361*
6-mo	5.8 ± 2.9	*0.052*	7.4 ± 3.1	***0.023******	5.1 ± 4.0	*0.208*
12-mo	4.8 ± 3.0	*0.118*	5.9 ± 2.9	***0.049******	4.6 ± 3.5	*0.189*

* Significant difference $p < 0.05$; † Significant difference $p < 0.01$;

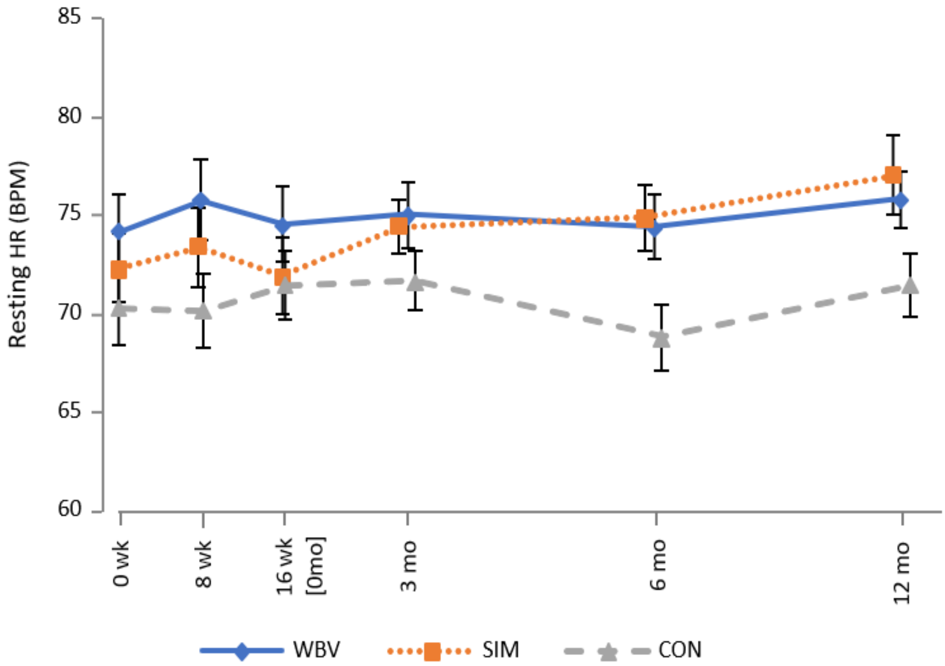

Figure 7.3. Changes in Resting Heartrate (mean ± SEM).

Additional univariate analyses of AIx with rHR, gender and MAP as covariates only identified a significant-influence of MAP at 8 wks (eta = 0.043; $p = 0.027$) for WBV vs SIM. All other covariate analyses identified no significant influence of MAP or rHR on AIx at any time point.

7.2.5 DISCUSSION

The current study reveals that chronic WBV-training is not only safe to conduct but can also have beneficial effects on the vascular health of the frail elderly. In comparison to other treatment groups, participants showed significant, clinically-important improvements in Systolic Blood Pressure, Mean Arterial Pressure and Arterial Stiffness as a result of 16-weeks of low-level WBV-training. Treatment-effects were lost within 3-months of completing the exercise-intervention, providing insight into the time-course of detraining.

Characteristic increases in SBP and arterial stiffness contribute to the increased likelihood of cardiovascular events in older adults [45], making the reported reductions in both parameters in the current study of particular clinical importance. Increased arterial stiffness increases pulse pressure, and subsequently SBP [46], as part of a vicious cycle in which higher SBP concurrently accelerates arterial stiffness [47]. As such, the reductions of ≈9 mmHg in SBP reported in the current study are of clinical importance [48] and reflect improvements in arterial stiffness. Moreover, the lack of change in rHR data reveals that the benefits observed are due to arterial-compliance effects, and not merely changes in rHR. This is an important distinction to make as rHR is inversely related to, and is a recognised determining factor of, AIx [44, 49]. This is confirmed by significant effects being evident with MAP as a covariate at 8 weeks, but not rHR. Consequently, chronic low-level WBV can be utilised as a safe exercise-tool for the frail elderly. Possibly more important is the demonstrable reduction in two important risk factors for cardiovascular disease (SBP and AIx), indicating potentially-significant vascular health benefits for this population.

It was feared that acute shifts in fluid dynamics due to increased peripheral circulation of the lower limbs could bring about orthostatic intolerance and drops in systolic and diastolic BP that could in-turn increase the risk of a fall [30]. Clinically-important reductions in diastolic BP were observed with WBV exercise in comparison to the CON group, and approached significance vs the SIM group, yet at an average of 3 mmHg the magnitude of this reduction was far below the drops of 10 mmHg found to elicit orthostatic intolerance and its consequences [50]. Although systolic BP did significantly decrease during the training period, it was concurrent with a systemic decrease in arterial stiffness, indicating that not only was vasodilation of peripheral lower limb capillaries but also other mechanisms operating. As well as theoretically reducing SBP, such localized vasodilation and increased blood flow may lead to increased shear stress on the arterial wall, leading to improved endothelial function [51]. This is supported by previous research whereby acute vibration sessions have independently been associated with both increased levels of the potent-vasodilator nitric oxide [52] and reductions in endothelin-1, a vasoconstrictor [53]. This in-turn may decrease wave reflection back to the heart, measured by AIx [54], theoretically increasing the risk of orthostatic intolerance [30], yet no adverse effects were observed. Although this provides a plausible mechanism for the acute-effects of WBV on vascular health, research into the chronic-effects is limited. To standardise measures in the current study, vascular health was assessed, and benefits observed, at stand-alone assessment sessions, not during/directly-following WBV exercise. The results suggest that the current chronic WBV-training intervention caused no adverse effects on vascular health and the observed effects were real and long-lasting, perhaps being elicited by additional mechanisms that warrant some discussion.

Skeletal muscle mass and arterial compliance both decline with age [8, 55], whilst the underlying mechanisms interrelate [56], suggesting that that the two conditions are not just co-morbid factors, but rather interact with each other. Indeed, inverse-relationships have been demonstrated between skeletal muscle and arterial stiffness in both healthy adults [57] and older adults [56, 58-60], whilst high muscle-strength has been shown to reduce the mortality risk in older adults [61]. Furthermore, the mechanical stimulation provided by WBV is greatest in the lower limbs [62], making specific inverse-relationships between arterial stiffness and leg muscle-mass [58-60] particularly pertinent when considering the current findings.

Although ageing-related pathways have an important impact on angiogenesis [63, 64], exercise-induced skeletal muscle growth and concurrent angiogenesis presents as a plausible reason for the effects on BP and arterial compliance observed in the current study. In fact, exercise has been shown to enhance virtually all angiogenic-steps impaired by ageing [64]. Of particular interest, metabolic stress from one-off bouts of endurance exercise has been shown to increase upregulation of vascular endothelial growth factor (VEGF) [65], an important angiogenic growth-factor [66-68] responsible for triggering most mechanisms activating and regulating angiogenesis [69]. Moreover-, this response is unaffected by the ageing process [70], whilst the super-imposition of vibrations further elicits VEGF-expression [71]. A second angiogenic coactivator is peroxisome proliferator-activated receptor-γ coactivator 1α (PGC-1α), which in-turn elicits an upregulation of VEGF [72]. Both can thus be deemed viable mediators in exercise-induced angiogenesis in skeletal muscle [65, 73]. Importantly, some evidence exists to suggest that WBV exercise can upregulate these factors [73, 74]. A one-off bout of combined WBV+resistance exercise with sustained vascular occlusion activated both PGC-1α and VEGF in 8 young men [73], whilst repeated-bouts of physiotherapy+WBV increased levels of PGC-1α, but not VEGF, in 49 COPD patients [74]. Interestingly, although a one-off 3-minute bout of WBV-exercise did not significantly increase VEGF levels of 10 young males the authors speculated that this effect may become clinically relevant under pathological conditions [75]. Findings of this present study suggest that the frailty of the current participants may have some bearing, although without direct measurement of PGC-1α and/or VEGF, or even markers of muscle hypertrophy, one can only speculate at this mechanism via associated improvements in functionality and inferred muscle-strength (reported in Chapter 4).

Whole-Body Vibration exercise also has other purported benefits that could be at least in-part responsible for the improved vascular health reported in this study. It is well-established that androgens, and in particular testosterone, regulate muscle mass and strength [76, 77], but conversely low testosterone levels have also been reported with arterial stiffness [59, 78]. As well as increases in muscle-mass of both healthy [16, 17, 79] and frail elderly [80, 81], WBV-training has reportedly increased circulating levels of testosterone [82, 83] and other anabolic hormones including Growth Hormone [82, 84], adrenaline and noradrenaline [85]. While predominantly reported in young adult males [82, 84, 85], some potential exists in older adults aged 66-85 year olds, where insulin-like growth factor 1 was elevated by acute WBV exercise, but Growth Hormone and Testosterone levels were unchanged [86]. In tandem with the mechanisms discussed above, increased circulating levels of anabolic hormones provides further plausible mechanistic explanation for the combined anabolic effects of WBV on muscle (reported elsewhere) and vascular health reported in the current study.

Significant beneficial-effects on SBP were observed at 8-weeks with vibration training, which remained below baseline levels but did not further improve following the second 8-weeks of the training-intervention. The authors believe that this lack of a continued effect/improvement in the second-half of the intervention can be attributed to the study-design, specifically due to the minimal progression of the WBV-stimulus. Participants started by receiving only 5*1-minute bouts of WBV, interspersed with 1-minute rest periods, and the initial progression was additional 1-minute bouts of WBV at pre-determined intervals, until 10*1-minute bouts were conducted all at the same amplitude. However, further progression was dictated ad libitum by participants, who could increase Hz and/or amplitude as desired, and most did not choose to progress beyond 7-8Hz/4mm. This lack of continued increases in stimuli may be responsible for the reduction of effect-size observed in the latter-half of the intervention. Intensity is known to be a key determinant of successful exercise-training programs, for example the ACSM recommends exercise-intensities of 60-85% of 1 repetition maximum for improving muscle strength and mass in older adults [87, 88]. Moreover, the ACSM also state that progression is necessary in order to stimulate further adaptation toward a specific training goal(s) [89]. The decision to allow participants to self-determine their progression (in the latter-half the intervention) was made with safety, compliance, and self-efficacy/mastery in mind, yet it may also have limited the training effect in this stage. Additional structured-progression of WBV intensity across the latter-half of the intervention may have elicited further beneficial effects on BP.

When considering AIx changes from baseline, two notable outliers in the SIM group were identified. In comparison with others in this group, these participants exhibited increases in their AIx, in-excess of 100% higher than at baseline. Were these outliers to be removed from consideration, SIM and CON group changes in AIx become more equitable, both showing little change from baseline in accordance with a reported plateau in this measure after 60 years of age [13]. However, it is worth noting that WBV-associated AIx training effects were observed against both SIM- and CON-groups, and were still moderately-sized vs CON-participants. Therefore, the authors are confident that the beneficial-effects of WBV-exercise on AIx are real, and appropriately reported.

The current study may be somewhat limited by a smaller than anticipated sample-size, however it should be acknowledged that this was calculated with a functional-measure as the primary outcome [33]. Nonetheless, our findings were of both statistical- and clinical-significance, whilst the sample size compares favourably to others investigating the chronic effects of WBV on vascular health of stroke survivors [22]. Secondly, the use of AIx as an indicator of arterial stiffness has been debated [49, 90], with Pulse Wave Velocity and/or Central Pressure Augmentation being proposed as gold-standard assessments of arterial stiffness [49]. However, the Pulse Wave Analysis methods followed in the current study represent a reliable [91, 92] and widely used technique for evaluating AIx and systemic arterial stiffness [44], whilst the non-invasive nature lends itself well to work with frail populations. What-is-more, the authors recognised the influence of MAP and HR on AIx, including both as covariates in statistical analysis as per recommendations [44].

7.2.6 CONCLUSION

In conclusion, the current research shows that WBV exercise can play a part in enhancing the vascular health of the frail elderly, reducing their arterial stiffness and systolic blood pressure, which may reduce their likelihood of a cardiovascular event. Specifically, the findings demonstrate that chronic low-level WBV is safe for the frail elderly to complete, highlight the importance of continued progression during training-periods, and reveal a timeline of detraining. The study's novel findings offer insight into the potential mechanisms for clinically-important vascular health benefits that can be obtained from WBV-training in patients with poor cardiovascular health.

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8. DISCUSSION

8.1 Overall Discussion

The current research revealed that the frail elderly can achieve clinically-meaningful benefits from 16-weeks of low-level WBV-training. Summarised in figure 8.1 below, participants exhibited significant improvements in balance, lower-limb strength, falls-related confidence, functional-independence and vascular health. These clinically-important treatment-effects translated into improvements in functionality, independence and QoL. Moreover, some treatment-effects were retained for up-to 6-months after WBV-training, identifying a potential therapeutic window and providing insight into the time-course of detraining. Furthermore, the research highlighted a previously overlooked psychological placebo-effect of trial participation. Finally, there was some suggestion that the current protocol enhanced rates of bone deposition, however this was not substantial enough to address declines in BMD. None-the-less, the absence of vascular adverse-effects demonstrates that the frail elderly can tolerate this easily-accessible form of exercise, making it a safe and effective training tool for this population when functional, psychological or health training goals are the focus.

This research project set out to develop and evaluate an easily-accessible form of exercise for the frail elderly. Measuring against parameters such as cost-effectiveness, ability to reach a large-proportion of the frail elderly population, safety, ease-of-use, and ultimately effectiveness, the current WBV-training protocol delivered on each point. Costing as little as $16,000 NZD, machines compare favourably to either 1:1 physiotherapy-based programs (such as the Otago Falls Program [1]) or hospitalisation for fall/fractures (at an average of 21-days at $800/day ≈ $16,800 without surgical costs [2]). Participants consistently rated the WBV-exercise as fun and easy to do, whilst concurrently reported no adverse effects and showed compliance rates in-excess of 90%. This ease-of-use, coupled with very minimal long-term maintenance/running costs and the lack of requirement for a qualified exercise-professional to run sessions means that the current WBV-protocol presents the ability to reach large sections of the frail elderly cohort cost-effectively, yet still offering attainable clinically-meaningful benefits (Figure 8.1).

In order to maximise accessibility in the frail elderly population, the ensuing WBV training-protocol differed from previous research [3-8] by deploying rotational WBV-exercise at a low-level (beginning at 6 Hz) with no concurrent exercise requirements, meaning that the overall demands/intensity were considerably lower. Consequently, the resultant improvements are of particular-significance. Fatigue, a loss of motivation, and perceived physical-limitations are all key determinants of physical inactivity in older adults [4, 9, 10]. Considering the high-levels of compliance exhibited in the current study, one can conclude that the minimally-demanding form of exercise addresses these key determinants of exercise avoidance, successfully demonstrating the easily-accessible nature of the protocol used. Participant's consistently low levels of perceived exertion, coupled with an array of positive anecdotal feedback (Appendix I), adds further support to this conclusion. What-is-more, the mastery experience provided by physical activity interventions [11] serves to enhance participant's self-efficacy, addressing another key determinant of exercise-avoidance.

The many complex interrelationships behind the observed results are depicted in figure 8.1. As discussed below, functional and psychological performance are not autonomous, rather they are co-dependent in determining an individual's levels of independence and self-sufficiency. Moreover, factors defining an individual's physical function can also influence their vascular health, and vice-versa, potentially also shaping bone health. Figure 8.1 shows how WBV exercise can positively influence many of these determining-factors, resulting in the associated benefits observed in the current research.

The improvements in functionality and ambulatory performance are indicative of lower-limb strength gains [12, 13], providing rationale for not only the observed functional gains but also those reported in psychological-parameters and vascular health. If these muscular- and strength-benefits are focussed on the muscles of the lower-limbs, then improvements in proprioception can be expected as muscles in this region, such as the tibialis anterior and gastrocnemius, are key to retaining balance and posture [14]. Indeed, the highest levels of muscle activation from WBV-exercise are reported in the tibialis anterior [15], whilst the specific challenge of keeping equilibrium on a rotational WBV platform is thought to result in neuromuscular adaptations [16] and subsequent improvements in dynamic balance [4, 17]. Moreover, strength gains have been shown to enhance a person's perceived-ability to avoid a fall [18], being strongly correlated with mobility, balance, and self-esteem improvements in older adults whilst concurrently reducing their levels of anxiety and depression [19]. Indeed, the very action of exercise-participation by those in residential-care has been shown to foster feelings of success and achievement [20], building a sense of mastery and empowering such frail individuals by increasing their confidence, self-esteem, wellbeing and feelings of control [21]. Finally, skeletal muscle has been shown to have an inverse-relationship to arterial stiffness, a key vascular health measure in older adults [22, 23]. The increased leg-muscle strength evidenced indirectly in the current study is probably due to muscle hypertrophy, which in-turn has led to the observed-reductions in arterial stiffness. This idea is supported by Sanada et al.

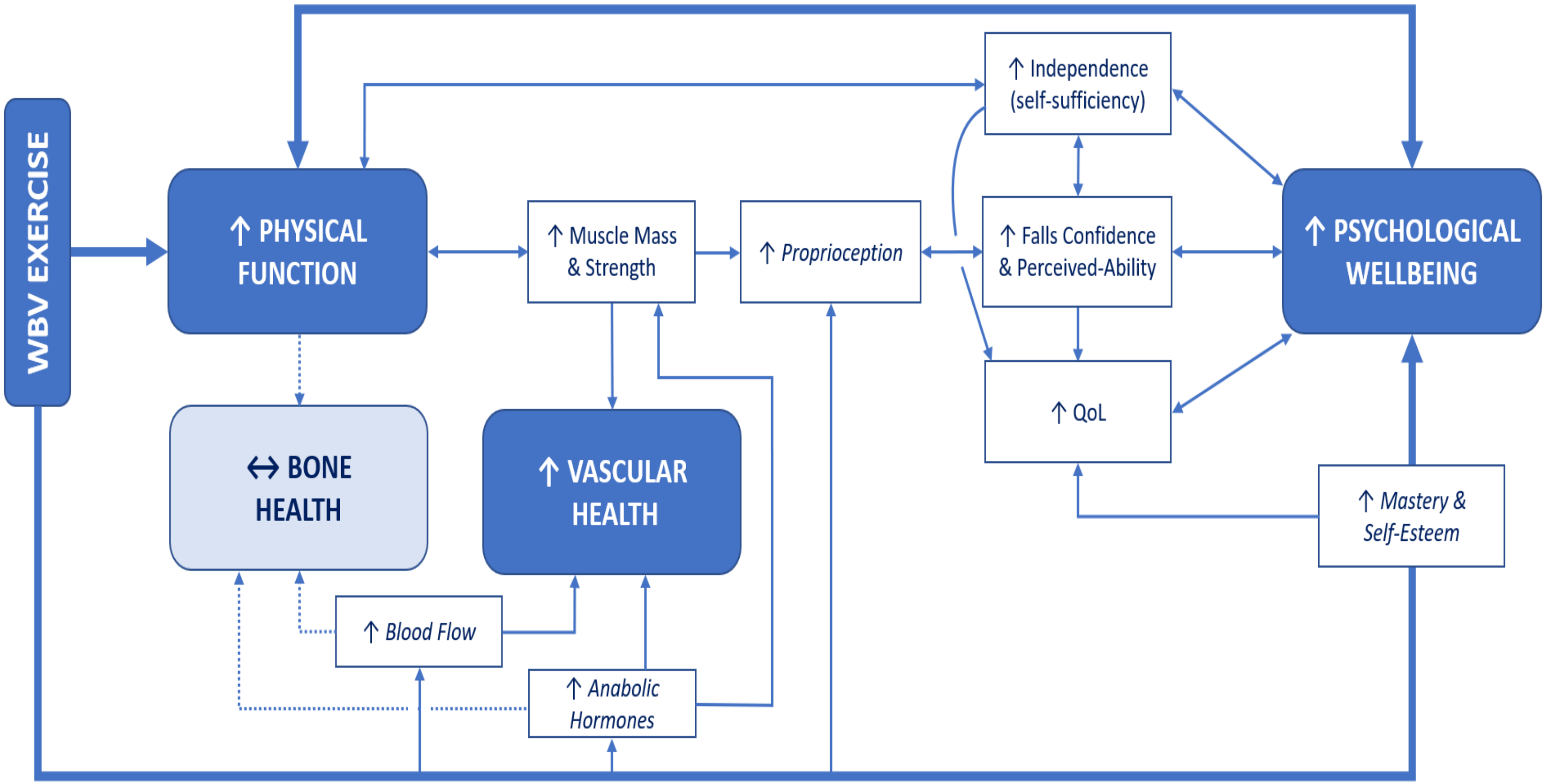

Figure 8.1. Summary of results exhibited in the current study, and the potential mechanisms involved (*proposed mechanisms are shown in italics*).

[24] who reported an inverse-relationship between arterial stiffness and leg muscle mass in sarcopenic older adults, a population comparable to the frail elderly participants in the current study. Of interest given this inverse-relationship, researchers have reported WBV-associated improvements in lower-limb strength of the frail elderly residing within residential-care [7, 8], whilst training-programs combining WBV-exercise with concurrent exercises have independently reported beneficial effects on the arterial stiffness [25, 26] of older adults. Therefore, the current reported-improvements, coupled with previously-reported WBV-induced increased levels of muscle activation [27], muscle mass [28], and mid-calf area [29], provide credible support for the Tonic Vibration Reflex, and associated muscle hypertrophy, as a plausible mechanistic action of the low-level WBV exercise.

It is most likely that the combined improvement in muscle-strength and improved falls-confidence are developed in a self-fulfilling cycle of mastery, increasing frail elderly participant's confidence, self-esteem and physical function via WBV-training (as presented in Figure 8.1). The accessibility of the low-level WBV-program is therefore key to its success, as it provides frail elderly patients with a practicable opportunity for exercise-participation, fostering feelings of success and achievement [20], building a sense of mastery [21], and increasing the likelihood of compliance and further physical activity in this group. In turn, the high-rates of compliance allow for sufficient WBV-training to take place that improvements in muscle-strength are elicited over-time, further improving an individual's perceived-ability to avoid a fall [18]. What-is-more, in the current study improvements in falls-confidence and EURO-QOL markers of Activity, Mobility and Self-Care are retained for at-least 6 months after completing the intervention. Associated functional improvements are also retained for at-least 3 months, identifying a potential therapeutic window in which levels of confidence, perceived-ability and actual physical-ability are all elevated. Initially proposed by Rogan et al. [30], such a therapeutic window can be used to introduce participants to 'regular' training options and integrate them into more-challenging group exercise classes, further continuing the self-fulfilling cycle. This highlights the potential for WBV-exercise to "up-skill" older deconditioned individuals, increasing their levels of independence and thus lowering their burden of care. However, falls-risk can actually increase should a mismatch of confidence and physical function/balance coordination occur [31], suggesting that the combination of enhanced muscle-strength and improved falls-confidence provided in the current study is essential.

Potentially contributing towards the muscle hypertrophy discussed above, WBV exercise has been shown to increase circulating levels of testosterone [32, 33] and other anabolic hormones including Growth Hormone [32, 34], known regulators of muscle mass and strength [35, 36].

These hormones have also been reported to correlate-inversely with arterial stiffness [22, 37], have anabolic effects on osteoporotic bone [38], and have been associated with improvements in the balance and physical function of older men [39]. The current research reports WBV-associated improvements in physical function, balance and arterial stiffness, and as such exercise-induced skeletal muscle growth and concurrent angiogenesis present as plausible reasons for these observed effects. However, no observable-benefits were seen in BMD. Without direct measures of hormonal serum-concentrations, or associated growth-factors, one can only speculate at the involvement of this hormonal mechanism.

Shifts in fluid dynamics, and the increased shear stresses associated with enhanced blood flow, are postulated mechanisms behind previously-reported osteogenic actions of WBV-exercise [40-42]. These may also provide some explanation of the reduced arterial stiffness observed in the current research, as the vibrations delivered by WBV exercise are proposed to directly influence endothelial function and arterial compliance. The greatest WBV-effects on blood circulation are observed in the lower extremities [43], yet to-date it is unclear if effects are either intensity- or dose-dependent. If they are, this could provide some explanation as to why improvements were not observed in BMD in the current research, where perhaps the shear-stresses generated were enough to influence endothelial function/arterial compliance, and even osteoblast activity as evidenced by osteocalcin levels, but not BMD. Whole-Body Vibration has been reported to deliver intensities similar to brisk walking [15, 44], with this being especially true for rotational WBV [45], yet conversely brisk walking has been shown not to stop bone loss in older adults [46], with high-intensity walking needed to enhance BMD levels [47]. Moreover, a recent comprehensive meta-analysis of 15 studies and almost 2000 participants concluded that WBV-training can reduce falls-risk but not enhance BMD levels [48], supporting the notion that perhaps attenuated bone loss should not have been an expected outcome from the current study. What is evident for the first time, however, is that chronic low-level WBV-exercise can reduce arterial stiffness, a key risk factor for cardiovascular disease in this population [49, 50].

8.2 Limitations

Limitations of the current research are addressed in the specific results sections but are summarised here. Firstly, fewer participants than anticipated were recruited, due in-large to strict exclusion criteria [51], particularly concerning impaired-cognition, recent fracture history, and joint replacement. Each exclusion-criteria was valid in its inclusion in the study design, either as a patient safety-measure, to protect the integrity of assessment-measures, or a combination of the two. Nevertheless, the current researchers believe, given the achievable benefits of low-level WBV exercise demonstrated here, that with adequate supervision cognitively-impaired persons in-particular could also partake in this exercise, and its use as a confidence-building tool in this population is feasible. The prevalence of hip- and knee-prostheses is vast [52], particularly in those over 80-years-old [52], yet current safety-recommendations are for individuals with such prostheses to avoid WBV exercise [16], hence it was an exclusion criterion in the current research. In addition, the lack of tracking of individual data around comorbidities, medications and falls rate could be deemed a factor limiting the breadth of results. Although collecting such data would allow for more complete patient profiles, it would not have changed recruitment inclusion/exclusion criteria nor results but would have significantly increased input from retirement-facility staff. A final limiting-factor for participant recruitment in this research is that of exercise avoidance. Amongst a plethora of barriers, older adults in residential-care frequently cite perceived physical-limitations, fatigue and loss-of-motivation as reasons for low-levels of compliance or total exercise avoidance [10, 53, 54]. When faced with such obstacles, the appeal of volunteering for a 16-week long exercise-intervention trial is understandably daunting, no matter how easily-accessible the exercise may appear to be. Similarly, although the overall drop-out rate reached 27%, this was both comparable to previous research in the frail elderly [55] and not unexpected given the longitudinal nature of the study coupled with the frail nature of participants. Finally, the lack of tracking of medications and co-morbidities across the time-course of the study could also be viewed as a further limitation. However, as this study measured change from baseline of individuals, and then compared treatment effects, it is looking at within-subject effects and thus negates any potential differences between participants. This approach was essential, as with an already extensive exclusion criteria to then match groups for co-morbidities would be fully infeasible. Nevertheless, despite these limitations the current results were both significant and of clinical-importance, whilst this research remains the largest study of WBV effects on frail elderly individuals.

8.3 Future Research

Findings from the current research have revealed a number of potential avenues for future research in this field. Firstly, the beneficial effects observed on vascular health are the first to be demonstrated with chronic WBV training in the frail elderly, and suggest potential for its use in addressing this important risk factor of cardiovascular events. Future research in this field could therefore continue to explore this application of WBV-exercise in other population groups with poor vascular health, e.g., Peripheral Arterial Disease or recovering from a Stroke. The effects of WBV on Stroke patients has been initially explored, with 2 recent comprehensive reviews both simultaneously acknowledging some positive results but calling for further research to ascertain the efficacy of WBV exercise in this population [56, 57]. Furthermore, future research should investigate the effects of WBV exercise on anabolic hormones and/or growth factors to identify the mechanisms behind this effect. For example, although levels of PGC-1α and VEGF, important factors stimulating angiogenesis, have been shown to increase with one-off and repeated-bouts of WBV exercise [58, 59], the magnitude of chronic training on these factors is unclear.

A second potential avenue of interest for future exploration is the effects of WBV-training on Parkinson's Disease (PD). Characterised by postural instability and ensuing disruptions to gait, mobility, falls-risk and independence [60], researchers have attempted to apply the purported functional benefits of WBV training to elicit improvements in individuals with PD, with some promising results. Showing some benefit to postural stability from acute bouts [60, 61] and short-term training interventions [62], the lack of properly-controlled chronic-interventions coupled with the possibility of a placebo effect [63] suggests the need for further research in this field. With a similar study design to the current research, both utilising low-frequencies of WBV and a sham-WBV control group, direct comparison with the work of Kaut et al. [62] is warranted. Although chronic in nature, with participants receiving a maximum of 48 sessions of WBV over 16 weeks, the current research also reported improved balance as a measure of functional improvements. Moreover, 5 individuals with PD were amongst the frail elderly participants in this study, and anecdotal evidence from researchers and carers suggested that considerable improvements in function were elicited in these individuals when receiving WBV-training, with carers in-particular noting the functional improvements displayed in some individuals. What-is-more, the current protocol elicited benefits in confidence and function, both of which are independently linked to falls-risk in PD patients [64], suggesting it has noteworthy potential for use in PD patients. Given that there currently remains insufficient evidence to prove or refute the effectiveness of WBV training on PD when compared to another active intervention or placebo [65, 66], further research in this field is warranted. As a result of randomisation, no individuals with PD were in the CON group in the current study, however the study-design, and ensuing comparison with both an active- and non-active placebo, could add some clarity towards the effects of low-level WBV on patients with PD in future.

A recent meta-analysis investigating the reported-effects of WBV-exercise on falls and fractures in 15 studies, encompassing 1837 elderly males and elderly/postmenopausal females, concluded that the impact of WBV on fractures requires further exploration [48], and this highlights a final direction for future work. Interestingly, much like the current research, the analysis of Jepsen et al. found WBV training to reduce falls rate yet have no impact on BMD [48]. Although not directly-measured in the current research, a reduction in falls can be inferred from improvements in functionality and falls-confidence, both important determinants of falls-risk [19, 67]. Consequently, future research should look to address this gap in the literature highlighted by Jepsen et al. [48], as well as further exploring the effects of WBV exercise on bone health at a molecular/biochemical-level to clarify possible dose-response effects. Furthermore, in restricting the use of WBV-exercise in those with hip/knee prostheses and/or cognitive impairment, one is removing individuals who may benefit hugely from the functional- and psychological-benefits associated with WBV exercise, and thus those who could garner significant reductions in their falls- and fracture-risk from its use. Consequently, future research is needed to review the contraindications placed on these specific population-subgroups within the frail elderly. Safe-use of WBV-exercise in either of these populations could have profound impacts on their rate of falls and fractures, and thus their burden of care. Moreover, such a review could help to establish and steer guidelines for expanding the safe use of WBV within residential-care.

8.4 Conclusion

This research demonstrates that low-level WBV exercise presents as an effective and easily-accessible exercise for the frail elderly that can be appealing and fun to participate in, particularly as part of a group exercise session. Moreover, simple thrice-weekly sessions, of limited physical exertion and time-demand on patient and carer, can lead to pronounced improvements in the functionality, psychological wellbeing, and vascular health of frail individuals, increasing their levels of independence and QoL whilst theoretically reducing their risk of falling and the likelihood of cardiovascular events. In particular, the exercise program used in this study demonstrates potential as a rehabilitation tool for enhancing the ability and confidence of frail elderly patients, enabling them to later take part in more challenging rehabilitation exercises, and opening the door for continued improvement. In addition to reflecting the safe use of low-level WBV exercise, the study's novel findings on vascular health offer insight into the benefits that can be obtained from WBV-training in patients with poor cardiovascular health, and thus have potential implications for many other patient-groups, not just the frail elderly. Although rates of bone deposition were increased, the levels of stimulus were not sufficient to address normal age-related BMD decline. Nevertheless, the absence of detrimental treatment-effects shows that the frail elderly can tolerate this easily-accessible level of exercise. In conclusion, the WBV exercise-program used in this study adds significant weight to a growing body of work in this field, supporting the proposal of low-level WBV as an effective and accessible exercise-tool for the frail elderly.

8.5 References

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9.2 Appendix B: Ethical Approval Documentation

Health and Disability Ethics Committees

Health and Disability Ethics Committees
Ministry of Health
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15 April 2013

Mr Daniel Wadsworth
Massey University
Private Bag 756
Wellington
6140

Dear Mr Wadsworth

Re:	**Ethics ref:**	**12/NTB/78**
	Study title:	Physiological, psychological and functional changes with Whole Body Vibration Exercise in the Frail Elderly.

I am pleased to advise that this application has been *approved* by the Northern B Health and Disability Ethics Committee. This decision was made through the HDEC-Full Review pathway.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Northern B Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.

2. Before the study commences at *any* locality in New Zealand, it must be registered in a WHO-approved clinical trials registry (such as the Australia New Zealand Clinical Trials Registry, www.anzctr.org.au).

3. Before the study commences at *a given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

Non-standard conditions:

4. The committee are happy to grant approval for the main study to proceed, on the understanding that pQCT tests are not performed until the committee is provided with confirmation that the radiologist is appropriately qualified.

After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Participant access to ACC

The Northern B Health and Disability Ethics Committee is satisfied that your study is not a clinical trial that is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Participants injured as a result of treatment received as part of your study may therefore be eligible for publicly-funded compensation through the Accident Compensation Corporation (ACC).

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Raewyn Sporle
Chairperson
Northern B Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted

Document	*Version*	*Date*
Protocol: Protocol Document, including Blood & pQCT SOP, GP Health Screening Form and Correspondence with the Kai Arahi at Massey University	1	22 November 2012
Survey/questionnaire: Questionnaires to be used in the study	1	22 November 2012
PIS/CF: Participant Information Sheet & Consent Form	1	22 November 2012
Participant Recruitment Poster	1	22 November 2012
CVs for other Investigators: CV for Lead-Supervisor, Dr. Sally Lark	1	22 November 2012
Evidence of scientific review: Evidence of Discussion at College of Science Research Seminar	1	22 November 2012
CV for CI: CV for Co-ordinating Investigator (CI)	1	22 November 2012
Application		
Response to Request for Further Information		
Covering Letter: 12NTB78_HDEC Revisions Cover Letter.docx		20 March 2013
Survey/questionnaire: New Zealand (English) EQ-5D-3L.docx		
PIS/CF: PISCF_HDEC_DWadsworth.doc	2	24 January 2013
RUDAS_AdminScoringGuide.pdf		
Survey/questionnaire: WBV Monitoring Questionnaire.docx		

Appendix B
Statement of compliance and list of members

Statement of compliance

The Northern B Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the *Standard Operating Procedures for Health and Disability Ethics Committees*, and with the principles of international good clinical practice (GCP)
- is approved by the Health Research Council of New Zealand's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990
- is registered (number 00008715) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*
Mrs Raewyn Sporle	Lay (the law)	01/07/2012	01/07/2015
Mrs Maliaga Erick	Lay (consumer/community perspectives)	01/07/2012	01/07/2014
Mrs Mary Anne Gill	Lay (consumer/community perspectives)	01/07/2012	01/07/2015
Mrs Kate O'Connor	Non-lay (other)	01/07/2012	01/07/2015
Mrs Stephanie Pollard	Non-lay (intervention studies)	01/07/2012	01/07/2015
Dr David Stephens	Lay (consumer/community perspectives)	01/07/2012	01/07/2014
Dr Paul Tanser	Non-lay (health/disability service provision)	01/07/2012	01/07/2014
Ms Kerin Thompson	Non-lay (intervention studies)	01/07/2012	01/07/2015

http://www.ethics.health.govt.nz

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31 January 2014

Mr Daniel Wadsworth
Massey University
Private Bag 756
Wellington 6140

Dear Mr Wadsworth

Re:	**Ethics ref:**	**12/NTB/78/AM01**
	Study title:	Physiological, psychological and functional changes with Whole Body Vibration Exercise in the Frail Elderly.

I am pleased to advise that this amendment has been *approved* by the Northern B Health and Disability Ethics Committee. This decision was made through the HDEC Expedited Review pathway.

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

R.A. Sporle

Mrs Raewyn Sporle
Chairperson
Northern B Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted

Document	Version	Date
PIS/CF: PIS/CF amended to include reference to collection of a urine sample (paragraph 3 on page 3)	2	02 December 2013
Post Approval Form	AM01	02 December 2013
Covering letter	1	15 January 2014
PIS/CF	3	15 January 2014
Response to Request for Further Information		15 January 2014

Appendix B
Statement of compliance and list of members

Statement of compliance

The Northern B Health and Disability Ethics Committee:

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- is registered (number 00008715) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*
Mrs Raewyn Sporle	Lay (the law)	01/07/2012	01/07/2015
Mrs Maliaga Erick	Lay (consumer/community perspectives)	01/07/2012	01/07/2014
Mrs Kate O'Connor	Non-lay (other)	01/07/2012	01/07/2015
Mrs Stephanie Pollard	Non-lay (intervention studies)	01/07/2012	01/07/2015
Dr Paul Tanser	Non-lay (health/disability service provision)	01/07/2012	01/07/2014
Ms Kerin Thompson	Non-lay (intervention studies)	01/07/2012	01/07/2015

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31 January 2014

Mr Daniel Wadsworth
Massey University
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Dear Mr Wadsworth

Re:	**Ethics ref:**	**12/NTB/78/AM02**
	Study title:	Physiological, psychological and functional changes with Whole Body Vibration Exercise in the Frail Elderly.

I am pleased to advise that this amendment has been *approved* by the Northern B Health and Disability Ethics Committee. This decision was made through the HDEC Expedited Review pathway.

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Mrs Raewyn Sporle
Chairperson
Northern B Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted

Document	Version	Date
Post Approval Form	AM02	02 December 2013
Covering letter	1	15 January 2014
Response to Request for Further Information		15 January 2014

Appendix B
Statement of compliance and list of members

Statement of compliance

The Northern B Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the *Standard Operating Procedures for Health and Disability Ethics Committees*, and with the principles of international good clinical practice (GCP)
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- is registered (number 00008715) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*
Mrs Raewyn Sporle	Lay (the law)	01/07/2012	01/07/2015
Mrs Maliaga Erick	Lay (consumer/community perspectives)	01/07/2012	01/07/2014
Mrs Kate O'Connor	Non-lay (other)	01/07/2012	01/07/2015
Mrs Stephanie Pollard	Non-lay (intervention studies)	01/07/2012	01/07/2015
Dr Paul Tanser	Non-lay (health/disability service provision)	01/07/2012	01/07/2014
Ms Kerin Thompson	Non-lay (intervention studies)	01/07/2012	01/07/2015

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18 February 2016

Mr Daniel Wadsworth
Massey University
Private Bag 756
Wellington 6140

Dear Mr Wadsworth

Re:	**Ethics ref:**	**12/NTB/78/AM03**
	Study title:	Physiological, psychological and functional changes with Whole Body Vibration Exercise in the Frail Elderly.

I am pleased to advise that this amendment has been *approved* by the Northern B Health and Disability Ethics Committee. This decision was made through the HDEC Expedited Review pathway.

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Kate O'Connor
Chairperson
Northern B Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted and approved

Document	Version	Date
PIS/CF: Amended PIS/CF to reflect the further information request of the committee (dated 21 Jan 2016)	4	01 February 2016
Covering letter: Cover letter for current amendment	3	08 January 2016
Post Approval Form	1	-
Response to Request for Further Information	1	-

Appendix B
Statement of compliance and list of members

Statement of compliance

The Northern B Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the *Standard Operating Procedures for Health and Disability Ethics Committees*, and with the principles of international good clinical practice (GCP)
- is approved by the Health Research Council of New Zealand's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990
- is registered (number 00008715) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*
Mrs Maliaga Erick	Lay (consumer/community perspectives)	01/07/2012	01/07/2018
Mr John Hancock	Lay (the law)	14/12/2015	14/12/2018
Mrs Phyllis Huitema	Lay (consumer/community perspectives)	19/05/2014	19/05/2017
Dr Nora Lynch	Non-lay (health/disability service provision)	01/07/2015	01/07/2018
Miss Tangihaere Macfarlane	Lay (consumer/community perspectives)	19/05/2014	19/05/2017
Mrs Kate O'Connor	Lay (ethical/moral reasoning)	01/07/2012	01/07/2018
Mrs Stephanie Pollard	Non-lay (intervention studies)	01/07/2012	01/07/2018
Mrs Leesa Russell	Non-lay (intervention studies), Non-lay (observational studies)	14/12/2015	14/12/2018

Unless members resign, vacate or are removed from their office, every member of HDEC shall continue in office until their successor comes into office (HDEC Terms of Reference)

http://www.ethics.health.govt.nz

9.3 Appendix C: RUDAS Questionnaire

RUDAS Assessment

Item 1 – Memory

Grocery List

1. I want you to imagine that we are going shopping. Here is a list of grocery items. I would like you to remember the following items which we need to get from the shop. When we get to the shop in about 5 minutes time I will ask you what it is that we have to buy. You must remember the list for me.

   Tea
   Cooking Oil
   Eggs
   Soap

   Please repeat this list for me (Ask person to repeat the list 3 times). (If person did not repeat all four words, repeat the list until the person has learned them and can repeat them, or, up to a maximum of five times.)

Item 2 - Body Orientation

Body Orientation

2. I am going to ask you to identify/show me different parts of the body. *(Correct = 1, Incorrect = 0)*.

Once the person correctly answers 5 parts of this question, do not continue as the maximum score is 5.

(1) show me your right foot	1
(2) show me your left hand	1
(3) with your right hand touch your left shoulder	1
(4) with your left hand touch your right ear	1
(5) which is (point to/indicate) my left knee	1
(6) which is (point to/indicate) my right elbow	1
(7) with your right hand point to/indicate my left eye	1
(8) with your left hand point to/indicate my left foot	1

..../5

Item 3 - Praxis

Fist / Palm

3. **I am going to show you an action/exercise with my hands. I want you to watch me and copy what I do. Copy me when I do this . . .** (i.e. demonstrate - put one hand in a fist, and the other hand palm down on the table or your knees and then alternate simultaneously.) **Now do it with me. I would like you to keep doing this action at this pace until I tell you to stop** - approximately 10 seconds or 5 – 6 sequences. (Demonstrate at moderate walking pace).

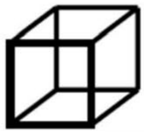
Score as:

Normal	= 2	*(very few if any errors; self-corrected; progressively better; good maintenance; only very slight lack of synchrony between hands)*
Partially Adequate	= 1	***(noticeable errors with some attempt to self-correct; some attempt at** maintenance; poor synchrony)*
Failed	= 0	*(cannot do the task; no maintenance; no attempt whatsoever)*

..../2

Item 4 - Drawing

Visuo-Constructional Cube Drawing



4. Please draw this picture exactly as it looks to you (Show cube on back of page).
(Yes = 1; No = 0)

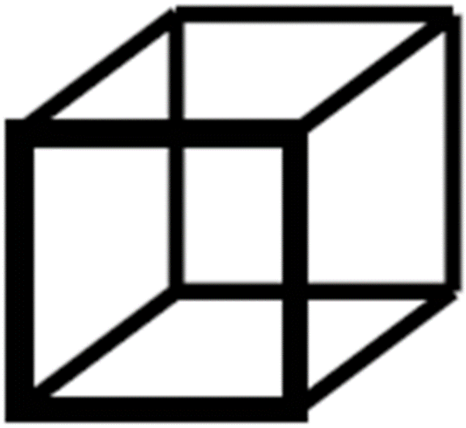
Score as:

(1) Has person drawn a picture based on a square? 1

(2) Do all internal lines appear in person's drawing? 1

(3) Do all external lines appear in person's drawing? 1

..../3



Item 5 - Judgement

Judgement - Crossing the Street

5. You are standing on the side of a busy street. There is no pedestrian crossing and no traffic lights. Tell me what you would do to get across to the other side of the street **safely**. (If person gives incomplete answer use prompt: "Is there anything else you would do?") Record exactly what patient says and circle all parts of response which were prompted.

....

....

Score as:

Did person indicate that they would look for traffic? 2
(YES = 2; YES PROMPTED = 1; NO = 0)

Did person make any additional safety proposals? 2
(YES = 2; YES PROMPTED = 1; NO = 0)

..../4

Item 1 – Memory

Memory Recall (Item 1 Revisited - 4 Grocery Items)

1.® We have just arrived at the shop. (Can you remember the list of groceries we need to buy? (Prompt: If person cannot recall any of the list, say "The first one was 'tea'."

(Score 2 points each for any item recalled which was not prompted.)

Circle 'Tea' if used as a prompt and score as 0 out of 2)

Tea	2
Cooking Oil	2
Eggs	2
Soap	2

..../8

Item 6 - Language

Language Generativity – Animal Naming

6. I am going to time you for one minute. In that one minute, I would like you to tell me the names of as many different animals as you can. We'll see how many different animals you can name in one minute. (Repeat instructions if necessary). Maximum score for this item is 8. If person names 8 new animals in less than one minute there is no need to continue.

1. …………………………………	5. …………………………………
2. …………………………………	6. …………………………………
3. …………………………………	7. …………………………………
4. …………………………………	8. …………………………………

…./8

9.4 Appendix D: Barthel Index Questionnaire

BARTHEL ADL INDEX

PATIENT'S NAME:

HOSPITAL NUMBER:

		DATE						
BOWELS	0 = Incontinent 1 = Occasional accident (1 per week) 2 = Continent							
BLADDER	0 = Incontinent or catheterised & unable to manage 1 = Occasional accident (max 1 x per 24 hours) 2 = Continent for over 7 days							
GROOMING	0 = Needs help 1 = Independent, face, hair, teeth, shaving.							
TOILET USE	0 = Dependent 1 = Needs some help but can do something. 2 = Independent (on and off, dressing, wiping).							
FEEDING	0 = Unable 1 = Needs help cutting, spreading butter etc. 2 = Independent.							
TRANSFER	0 = Unable 1 = Major help (1-2 people, physical). 2 = Minor help (verbal or physical). 3 = Independent							
MOBILITY	0 = Immobile 1 = Wheelchair independent including corners etc. 2 = Walks with help of 1 person (verbal or physical). 3 = Independent (but may use any aid, eg. stick).							
DRESSING	0 = Dependent 1 = Needs help but can do half unaided. 2 = Independent							
STAIRS	0 = Unable 1 = Needs help (verbal, physical, carrying aid). 2 = Independent up and down.							
BATHING	0 = Dependent 1 = Independent							
	TOTAL							

9.5 Appendix E: ABC-UK Falls Confidence Questionnaire

How confident are you that you can maintain your balance and remain steady when you….	/10
• Walk around the house?	
• Walk up or down stairs?	
• Bend over and pick up a slipper from the floor at the front of a cupboard?	
• Reach for a small tin of food from a shelf at eye level?	
• Stand on your tip-toes and reach for something above your head?	
• Stand on a chair and reach for something?	
• Sweep the floor?	
• Walk outside the house to a parked car?	
• Get into or out of a car?	
• Walk across a car park to the shops?	
• Walk up or down a ramp?	
• Walk into a crowded shopping centre where people walk past you quickly?	
• Are bumped into by people as you walk through the shopping centre?	

• Step onto or off an escalator while holding onto the handrail?	
• Step onto or off an escalator while holding onto parcels such that you cannot hold onto the handrail?	
• Walk outside on a slippery pavement?	

9.6 Appendix F: EURO-QOL 5-D Questionnaire

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety/Depression

I am not anxious or depressed ❑

I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

SAMPLE

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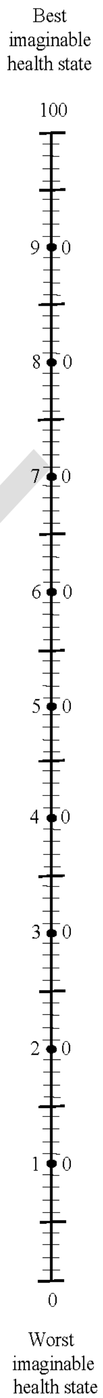
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



SAMPLE

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9.7 Appendix G: WBV Monitoring Questionnaire

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UNIVERSITY OF NEW ZEALAND

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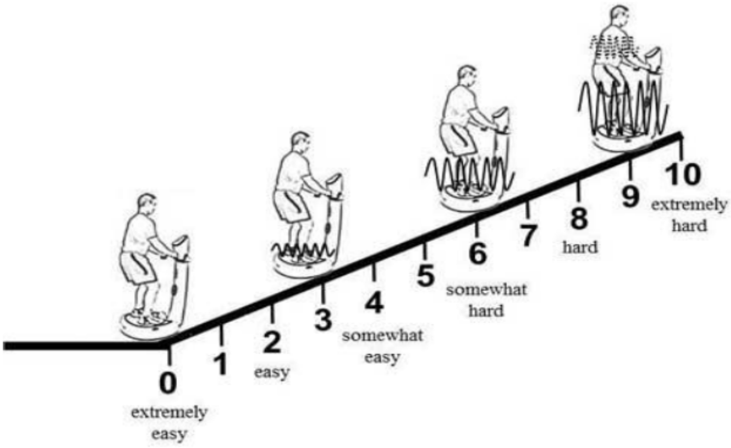
WBV Exercise Monitoring Questionnaire

Participant Name:	**Study Code:**
WEEK:	**Group:** WBV

Please answer the following questions. This questionnaire is designed to help the investigators monitor the effects of WBV exercise on you as you complete the exercise intervention. Results will be collated and made available to a team of geriatric consultants from CCDHB, who will monitor the potential for harm as the study progresses. Please ring the correct answer (YES or NO) and fill in the spaces when asked. If you have any problems with the questions then please ask the investigator for clarification. Your answers will be kept strictly confidential.

1.	Did you feel any discomfort while exercising on the Whole Body Vibration Machine? If yes, please detail these:	YES	NO
2.	Did exercising on the machine make you feel unwell?		
	a) Today	YES	NO
	b) On previous occasions	YES	NO
3.	Do you have any other comments regarding your use of the machine? *(continued over the page)*		

4.	Using the scale below, please rate how hard you found exercising on the machine today: 

Above image reprinted from the Journal of Sports Science & Medicine, Vol 11, Marin, P., et al., Reliability and validity of the OMNI-vibration exercise scale of perceived exertion, p. 438-443, Copyright (2012), with permission from the JOURNAL OF SPORTS SCIENCE AND MEDICINE.

9.8 Appendix H: Galileo WBV Device Technical Data

Training in this research was conducted on WBV machines produced by Novotec (Germany). Specific technical data for the machines are detailed below.

Model: Galileo Fitness Control 0544 (Novotec, Germany)	
Type numbers	8N057410, 8N057411
Medical device	No
Certificate	CE
Hand rail	Yes
External control	Mounted on hand rail
Internal control	Yes
Remote control	Yes
Frequency range (from/to)	5..36 Hz
Amplitude (from/to)	0..+/-5,2 mm
Stroke	0..10,4 mm
Max. acceleration	27,1 g
Dimensions base unit (l/w/h)	780 x 615 x 138 mm
Dimensions footplate (l/w)	580 x 370 mm
Overall dimensions (l/w/h)	780 x 880 x 1300 mm
Weight base unit	42 kg
Total weight	64 kg
Max. load (body weight)	200 kg
Power consumption	800 VA
Categorisation	professional
Wobbel function	Yes
Galileo® Smart Coaching	Yes
Tower with control panel incl. key switch	Dimensions: 730 x 880 x 1300 mm, Weight: 22 kg

Source: https://www.galileo-training.com/de-english/products/p35/galileo-fit.html

9.9 Appendix I: Anecdotal Participant Feedback

Participants were given the opportunity each week to record their feedback on the WBV training session. These comments are listed below.

- ↑ Sleep, relaxed, confidence, walking, well-being
- Sore knee 30 mins after first time only; feels safe - make sure to help on/off
- enjoying it
- Feels exercise in thighs; Questioned the use straight after lunch (but wants it at this time in order to go out after!)
- Feels like you have exercised/brisk walk after using
- Advance quicker!
- helps with incontinence, breathing better, relief
- increased warmth
- can feel the difference if you change stance (i.e. don't bend knees you can feel it in your head)
- wants more (harder?)
- lost weight since using; helping incontinence
- nice to have increased strength, very grateful
- doesn't feel it is doing him any good
- Knees feel 100% better, no pain
- maybe uneven vibration as 1 leg longer than other!!
- Sore neck & shoulder
- The more you use it, the better it gets
- slight discomfort in quads
- comments regarding use straight after meal
- wants to keep going for as long as possible; increased motivation & walking
- has found downhill-walking easier
- Found it easier to control walking down a steep slope
- Feels that she is improving; lost weight (0.75kg); better leg movement, no knee cramps, will miss it!
- increased knee bend = more comfort
- Increased use = better it gets; miss it when gone
- time passed quickly when talking!!
- discomfort 1st time, but used to it now. Likes to go for a walk after
- good length of time on the machine

- energised/restless legs
- funny sensation!
- none
- nervous about using the machine
- Good feeling, I like it!
- Joints are feeling better as a result
- Legs feel tired at end
- using the machine increased an already present stomach ache
- Felt a good effect in circulation of legs on occasions
- funny sensation
- minute long enough
- Legs feel tired at end
- wants to progress - doesn't feel like much exercise!
- felt a little dizzy at end
- quite good
- slight knee discomfort at end
- Legs feel tired at end
- none
- would like to increase freq. Feels no effect on body
- Thinks it is a good exercise tool, but "exhausting"
- felt good, not unwell
- Legs feel tired at end
- tempted to increase - wants more!
- "does what it is meant to do"; appreciates help
- doesn't notice the benefit; enjoying higher Hz
- Feels positive towards machine; felt an increase in motivation to complete exercise
- feeling unsteady due to age; feels better difference since increasing Hz; still not challenging
- Feeling tired after workouts
- gets a bit tired of the commitment to the study
- Would like to increase Hz again!
- felt unsteady on feet today - wonders if it is machine?
- can feel the effect of moving out to position #3
- wonders about the repetitive nature? And relevance? Would like to see some info on benefits to the elderly

- does not mind the machine - quite likes exercising on it
- Hoping it will increase balance & strength; slight dizziness after first session
- Increased "energy buzz" from it
- Feel it working the legs, but quick to recover
- Quite easy to do
- Feel it working in the knees
- none
- Feels very good at the moment - can't just be the machine?!
- Felt it in Left Leg on Monday, fine for other sessions
- Feels the knees working hard
- curious about progressing feet out
- none
- Can feel the difference of progressing from #1-2; making her feel good!!
- Noticing the difference of moving from #1-2 (pelvic area & hamstrings - not uncomfortable)
- feel it working more on #3; past month has felt much easier to walk, even without stick
- pretty straightforward to use
- more aware of movement (feet @ #2)
- Feel it more on #3
- Feel it more @ top of hip/waist and tingle in legs at #3
- Feels improving all the time (feet @ #3)
- Going up to level 4 a bigger transition than others (feet @ #4)
- feels unrelated inflamed muscle when using WBV
- waiting to notice any changes!
- feel bones moving when knees together
- feels a little puffed out today
- Feels better for using it - loosens up
- Foot position #2 - working more
- bit wobbly; hopeful it will help; feels blood increase flow
- relaxed sensation
- easy to use
- felt good; getting more used to the sensation
- shakes up food a little after lunch! Getting easier though…
- used to it now - doesn't bother me

- "not bad"
- fun to use
- sleeping better
- felt harder today - a little shaky after
- less stressful than when first started (used to it)
- fun to use (feet #2)
- easy to use (feet #2)
- enjoying the experience (speed 7Hz, feet #2)
- feels good
- Pleased to be using it
- Fun
- Felt tingle in legs, cramp at night after first session - linked?
- enjoying it
- helped back
- helping with evening toilet (incontinence/pelvic muscles)
- enjoyable & fun
- Improved energy & balance; less asthma?
- feel more energetic
- legs ached yesterday - linked?
- Feeling benefits re incontinence & easier to get up
- Good - I love using it!!
- None - use it or lose it!!
- after Friday's session felt a sore leg (muscle ache) - to keep an eye on this
- didn't sleep well the night after (no cramp this time!)
- feeling well
- warm feeling in feet
- feels lovely - I'm enjoying it!
- fully happy with it - no problems!
- leg feeling good now
- finding it easier to go up stairs
- Love it, it's fun!
- Fantastic, not a problem, "anyone can do it"
- good fun
- no problems
- ankles maybe a little swollen last night - linked? (been away)

9.10 Appendix J: Statement of Contribution forms

DRC 16

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STATEMENT OF CONTRIBUTION
DOCTORATE WITH PUBLICATIONS/MANUSCRIPTS

We, the candidate and the candidate's Primary Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of candidate:	Daniel Wadsworth
Name/title of Primary Supervisor:	Dr Sally Lark
Name of Research Output and full reference:	
Physiological, psychological and functional changes with whole body vibration exercise in the elderly: FEVER methodology and protocols	
In which Chapter is the Manuscript /Published work:	Chapter 3 & Appendix
Please indicate:	
• The percentage of the manuscript/Published Work that was contributed by the candidate:	75%
and	
• Describe the contribution that the candidate has made to the Manuscript/Published Work:	
With guidance and advice from Dr Lark: devised protocols, researched and composed rationale all elements of the publication.	
For manuscripts intended for publication please indicate target journal:	
Candidate's Signature:	Daniel Wadsworth Digitally signed by Daniel Wadsworth Date: 2019.03.21 14:01:56 +10'00'
Date:	21/03/2019
Primary Supervisor's Signature:	Dr Sally Lark Digitally signed by Dr Sally Lark Date: 2019.03.22 08:26:31 +13'00'
Date:	22/03/19

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Name of candidate:	Daniel Wadsworth
Name/title of Primary Supervisor:	Dr Sally Lark
Name of Research Output and full reference:	
EFFECTS OF WHOLE BODY VIBRATION TRAINING ON THE PHYSICAL FUNCTION OF THE FRAIL ELDERLY	
In which Chapter is the Manuscript /Published work:	Chapter 4
Please indicate:	
• The percentage of the manuscript/Published Work that was contributed by the candidate:	75%
and	
• Describe the contribution that the candidate has made to the Manuscript/Published Work:	
With guidance and advice from Dr Lark the candidate devised protocols, completed data collection and analysis, and researched/composed the manuscript.	
For manuscripts intended for publication please indicate target journal:	
Archives of Physical Medicine and Rehabilitation	
Candidate's Signature:	Daniel Wadsworth Digitally signed by Daniel Wadsworth Date: 2019.03.21 14:01:56 +10'00'
Date:	21/03/2019
Primary Supervisor's Signature:	Dr Sally Lark Digitally signed by Dr Sally Lark Date: 2019.03.22 08:42:52 +13'00'
Date:	22/03/19

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Name of candidate:	Daniel Wadsworth
Name/title of Primary Supervisor:	Dr Sally Lark
Name of Research Output and full reference:	
PSYCHOLOGICAL EFFECTS OF WHOLE BODY VIBRATION TRAINING IN THE FRAIL ELDERLY	
In which Chapter is the Manuscript /Published work:	Chapter 5
Please indicate:	
• The percentage of the manuscript/Published Work that was contributed by the candidate:	75%
and	
• Describe the contribution that the candidate has made to the Manuscript/Published Work:	
With guidance and advice from Dr Lark, the candidate devised protocols, completed data collection and analysis, and researched/composed the manuscript.	
For manuscripts intended for publication please indicate target journal:	
Geriatrics & Gerontology International	
Candidate's Signature:	Daniel Wadsworth Digitally signed by Daniel Wadsworth Date: 2019.03.21 14:01:56 +10'00'
Date:	21/03/2019
Primary Supervisor's Signature:	Dr Sally Lark Digitally signed by Dr Sally Lark Date: 2019.03.22 08:43:40 +13'00'
Date:	22/03/19

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Name of candidate:	Daniel Wadsworth
Name/title of Primary Supervisor:	Dr Sally Lark
Name of Research Output and full reference:	
EFFECTS OF WHOLE BODY VIBRATION TRAINING ON THE BONE HEALTH OF THE FRAIL ELDERLY	
In which Chapter is the Manuscript /Published work:	Chapter 6
Please indicate:	
• The percentage of the manuscript/Published Work that was contributed by the candidate:	65%
and	
• Describe the contribution that the candidate has made to the Manuscript/Published Work:	
With guidance and advice from Dr Lark & Dr Nowitz, the candidate devised protocols, completed/managed data collection and sample analysis, conducted statistical analysis and researched/composed the manuscript.	
For manuscripts intended for publication please indicate target journal:	
Archives of Physical Medicine and Rehabilitation / Osteoporosis International	
Candidate's Signature:	Daniel Wadsworth Digitally signed by Daniel Wadsworth Date: 2019.03.21 14:01:56 +10'00'
Date:	21/03/2019
Primary Supervisor's Signature:	Dr Sally Lark Digitally signed by Dr Sally Lark Date: 2019.03.22 08:45:09 +13'00'
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Name/title of Primary Supervisor:	Dr Sally Lark
Name of Research Output and full reference:	
EFFECTS OF WHOLE BODY VIBRATION TRAINING ON THE CARDIOVASCULAR HEALTH OF THE FRAIL ELDERLY	
In which Chapter is the Manuscript /Published work:	Chapter 7
Please indicate:	
• The percentage of the manuscript/Published Work that was contributed by the candidate:	70%
and	
• Describe the contribution that the candidate has made to the Manuscript/Published Work:	
With guidance and advice from Dr Lark, the candidate devised protocols, completed data collection, conducted statistical analysis, and researched/composed the manuscript.	
For manuscripts intended for publication please indicate target journal:	
European Journal of Applied Physiology	
Candidate's Signature:	Daniel Wadsworth Digitally signed by Daniel Wadsworth Date: 2019.03.21 14:01:56 +10'00'
Date:	21/03/2019
Primary Supervisor's Signature:	Dr Sally Lark Digitally signed by Dr Sally Lark Date: 2019.03.22 08:46:06 +13'00'
Date:	22/03/19

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