THE SOUTH PACIFIC ISLANDS RESIST DIABETES WITH INTENSE TRAINING (SPIRIT) STUDY

Impact of Progressive Resistance Training and Aerobic Training on Glycaemic Control in Māori and Pacific Islands People with Type 2 Diabetes and Grade III Obesity

A thesis presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Exercise and Sport Science

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2010

ABSTRACT

The purpose of the **S**outh **P**acific **I**slands **R**esist diabetes with **I**ntense **T**raining (SPIRIT) study was to evaluate and compare the effectiveness of two conventional training modalities for improving glycosylated haemoglobin (HbA_{1c}) and related physiological and psychological outcomes in Polynesian adults diagnosed with type 2 diabetes and visceral obesity. Twenty-six adults of self-identified Māori or Pacific Islands descent (20 women, 6 men; 47 ± 8 years; 116.3 ± 27.5 kg; waist circumference 124.0 ± 17.8 cm) were randomised to progressive resistance training (PRT) or aerobic training (AER), 3x/week, for 16 weeks. Nine subjects per exercise group (n = 18) completed the study and were included in per protocol analyses. Within-group ANOVAs revealed that HbA_{1c} remained elevated in PRT and AER after 16 weeks of training (10.7 ± 2.1 to 10.6 ± 2.4%, $P > 0.05$; 8.9 ± 1.9 to 8.8 ± 2.1%, $P > 0.05$, respectively). AER resulted in significant reductions in systolic ($P = 0.006$) and diastolic blood pressure ($P = 0.02$), an increase in skeletal muscle GLUT4 ($P = 0.02$), capillary density ($P = 0.05$), and power output (watts) ($P < 0.001$), while PRT resulted in a significant increase in upper ($P = 0.001$) and lower body strength ($P < 0.001$) and a reduction in hip circumference ($P = 0.05$). Eight (5 AER, 3 PRT) of 18 subjects completed ≥ 75% of available training sessions. Post-hoc analysis on these eight patients revealed a significant reduction in waist circumference ($P < 0.001$). Despite low attendance, many SF-36 QOL domains scores and the Physical Component Summary scores significantly improved in both groups ($P \leq 0.002$). The findings of this doctoral research project suggest that improvement of metabolic outcomes may be delayed or overwhelmed by a combination of low attendance and class III morbid obesity (BMI ≥ 40 kg/m^2). The improvements observed in QOL and muscle outcomes suggest that psychological and myocellular changes may precede

changes in systemic metabolic outcomes. Additional research is required to investigate these hypotheses and overcome barriers to exercise adoption in Māori and Pacific Islands people with morbid obesity and type 2 diabetes.

ACKNOWLEDGMENTS

First and foremost, I am deeply humbled and immensely grateful to all of the SPIRIT study participants who so selflessly volunteered their time and effort to the study. I acknowledge it was difficult to pull away from family, work, and university responsibilities to come to exercise sessions, so I would like to extend a sincere thank you for your sacrifice and commitment to health. I am also grateful to all the family and friends who provided ongoing support and encouragement in motivating participants to attend the exercise sessions. Each and every one of you put the "spirit" in the SPIRIT study.

I would like to gratefully acknowledge my doctoral supervisory committee Drs. Bobby Cheema, Rachel Page, David Rowlands, and Isabelle Lys for their continued guidance and unwavering encouragement over the past four years. Special thanks to Drs. Jeremy Krebs and Murray Leikis (CCDHB) for extending their time and clinical expertise during the course of the SPIRIT study. Thank you to Janet Langbein, Lucretia Teki, and Karen McKeeman for your administrative support from day one and to Marilyn Mabon, Margaret McNeill, Margaret Allison, David Graham, and Andy Hollings for your assistance with lab supplies. A sincere thank you to Prof. Hugh Morton for your assistance with statistical analyses.

I cannot overstate my gratitude to Jan Pearce, Dominic Rogerson, and the dedicated staff at Porirua City Fitness for providing a home for the SPIRIT study exercise sessions. Your support and willingness to accommodate all SPIRIT participants and their families and friends is a clear sign of your genuine commitment and dedication to the health and well-being of the Porirua community.

I am eternally indebted to all the Pacific and Māori health care professionals and religious leaders who so graciously extended their time, knowledge, and wisdom

in creating and maintaining the SPIRIT study. There is absolutely no question whatsoever that this study could not have been carried out without your support. A heartfelt and sincere thank you to Kitiona (Pacific Health Services and formerly National Heart Foundation) and Teremoana Tauira (Victory Church) not only for your guidance and direction during the SPIRIT study, but also for the genuine warmth of your friendship. Thank you Nick Roskruge, Massey University Māori Policy Advisor for your guidance in the early development stages of the trial. My sincere appreciation to Donna Scandlyn and the Maraeroa Team for inviting me to give a presentation on the Marae. A warm and sincere thank you to Sera Taala-Tapu of CCDHB for making time to meet with me and for connecting the SPIRIT study to the Pacific medical community. Thanks to Ken and Tai Roach of Elim Church for welcoming me into the family and providing guidance during difficult times. Thank you to Tavita Filemoni, Eleni Mason, and Rachel O'Brien of Pacific Health Services for allowing me to speak on the SPIRIT study at the Pacific Diabetes Forum in Lyall Bay. Thank you to Reverends Nove Vailaau and Toko Ine for your support for the SPIRIT study in the Pacific community.

A very warm and sincere thank you to the many general practitioners in the Porirua community for your support and guidance during the SPIRIT study, namely Drs. Kerry Thornbury, Logan McLennan, Sean Hanna, Malini Jayathissa, Ana Goonewardene, Kalyani Wijeweera, Adrian Gilliland, John Rowland, Jim Aubrey, Ket Yung, Bryan Betty, and David Robinson. Special thanks to the practice nurses and administrative support staff at Ora Toa Medical Centres, Maraeroa Marae Health Centre, Titahi Bay Doctors, Whitby Doctors, Ropata Medical Centre, Newlands Medical Centre, namely Lynnaire Matthews, Caroline Roberts, and Nicky Manawati who graciously made themselves available when I needed them. Thanks to the

CCDHB Wellington and Kenepuru Hospital Cardiac Rehab team (Paul Peacock, Christine Murphy, and Janet Dunbar) for being strong exercise advocates and offering guidance at different times during the study. I also gratefully acknowledge all the pharmacies in the Porirua community for your support, namely Waitangirua Pharmacy (Graeme Blanchard), Porirua Pharmacy, Mana Pharmacy, UFS Pharmacy, North City Pharmacy, Titahi Bay Pharmacy, Cannons Creek Pharmacy, Kenepuru Pharmacy, Whitby Pharmacy.

I cannot overstate my gratitude to Stewart Eadie, National Cardiac Care Manager at the National Heart Foundation, for without his support and direction during the early development stages, the SPIRIT study may not have gotten off the ground. Thank you Lisette Jacob of Roche Diagnostics for so willingly donating several Accu-chek glucose meters to the study. A warm and heartfelt thank you to Phil Sheard at University of Otago for your patience and guidance in working with me on the muscle sectioning and immunohistochemistry, and to his wonderful family for welcoming me into their home for the occasional dinner! Thank you to St. John Wakefield, electron microscopist with University of Otago (Wellington) for your assistance with the muscle biopsy processing and for your assistance in locating another cryostat. Thank you to Vivienne Hughes and Russell Cooke of CCDHB Laboratory Services for taking time out to meet with the SPIRIT team and for your expeditious processing of blood samples. Additional thanks to Louise Norris and the team for their delicate nature during the blood draws. A sincere thank you to Sue Newth of CCDHB for helping to organise the exam rooms at Kenepuru Hospital and to the administrative support staff for welcoming SPIRIT study participants upon arrival.

I am extremely grateful for the time and commitment of our exercise leaders

Amy Doyle, Steve French, Moana Jarden-Osborne, Shelley Mather, Bevan Kahui, Mike Ritete, and Mike Toetoe who provided exemplary care and an extremely welcoming atmosphere for all the SPIRIT participants.

DEDICATION

This thesis is dedicated to my loving family Jayne Marie Sullivan, William F. Sukala, Lisa Marie Sukala D'Alessandro, Annemarie D'Alessandro, and Anthony D'Alessandro, and to my life-long friend Michael J. Mattle, his wife Jennifer Jue Mattle, and their beautiful children Justin and Mikayla. Words cannot fully express the gratitude in my heart for your undying support and encouragement over the past four years. Through all the ups and downs, you were always there with just the right things to say. Thank you all for believing in me during what were unequivocally the most difficult and demanding years of my life.

I would also like to dedicate this thesis to my loyal flatmates over the past four years who stood by me through thick and thin and never took it personally when I was mentally and physically exhausted and probably not the easiest person to tolerate! My warmest and sincere thanks to Stuart Moore, Becka Hemmingsen, Braden Crocker, Anita Mills, Ann Bondy, and, of course, the Richard Street family, David Gall, Tamarin Garside, Deanna Sanders, and Libby Riosa.

IN MEMORIAM

In loving memory of Nikotemo Lopa (24 September 1964 – 27 May 2009), an inspiring man of great humility who represented the spirit of the SPIRIT study and touched the lives of all with whom he came into contact.

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LIST OF ACRONYMS

1RM	1 Repetition Maximum
ACSM	American College of Sports Medicine
AER	Aerobic exercise
AHA	American Heart Association
ANOVA	Analysis of Variance
β-blocker	beta blocker
BMI	Body Mass Index
BSA	Bovine Serum Albumin
CONSORT	Consolidated Standards of Reporting Trials
CRP	C-Reactive Protein
CV	Coefficient of Variation
DBP	Diastolic Blood Pressure
DEXA	Dual Energy X-ray Absorptiometry
FFA	Free Fatty Acids
GLUT4	Glucose Transporter 4^{th} isoform
GOX	Glucose Oxidation
HbA_{1c}	Haemoglobin A_{1c} (glycated haemoglobin)
HDL	High Density Lipoprotein
HOMA-β	Homeostasis Model Assessment beta cell function
HOMA2-IR	Homeostasis Model Assessment Insulin Resistance (v.2)
HRR	Heart Rate Reserve
LDL	Low Density Lipoprotein
MET	Metabolic Equivalent
NOX	Non-oxidative glucose metabolism
OCT	Optimal Cutting Temperature embedding medium
PBS	Phosphate Buffered Saline
PRT	Progressive Resistance Training
QOL	Quality of Life
RMANOVA	Repeated Measures Anova
RPE	Rating of Perceived Exertion
SBP	Systolic Blood Pressure
SF36	Medical Outcomes Trust Short-Form 36 questionnaire
SPARC	Sport and Recreation New Zealand
SPIRIT	South Pacific Islands Resist diabetes with Intense Training
VLDL	Very Low Density Lipoprotein
VO_2	Volume Oxygen consumed
WRS	William R. Sukala

CHAPTER 1

Introduction

1.1 Introduction

Type 2 diabetes has become a public health epidemic in New Zealand, with the Polynesian population (i.e. Māori and Pacific Islands people) being the most severely affected ethnic group. Currently, the prevalence of diagnosed type 2 diabetes in Māori and Pacific Islands people (~8.0%) is nearly double that compared to New Zealanders of European origin (~4.3%) [1]. Polynesian people also have significantly reduced life expectancy [2] due to the development of diabetes-related comorbidities such as obesity [3], vascular disease [4-6], hypertension [7], and macro-[8] and microvascular complications [9, 10]. It has been predicted that by 2020, the disparity in diabetes prevalence could increase to nearly four-fold, where 17% of Polynesian versus 4.5% of European New Zealander adults will have type 2 diabetes [11].

The aetiology of this gap in health status remains unclear. A selective evolutionary adaptation for efficient fat storage in Polynesian people has been suggested which, in past centuries, might have afforded protection against famine and the harsh climatic conditions of the South Pacific [12]. However, this previously protective physiological mechanism has become a health liability in a modern backdrop of food overabundance and physical inactivity. While this "thrifty gene" hypothesis [13] remains controversial [14], there is clear evidence to suggest that the incidence of obesity and related comorbidities (e.g. type 2 diabetes and cardiovascular disease) increases sharply in Polynesian people exposed to industrialisation on their home islands or when they move to more affluent nations such as New Zealand [15].

1.2 Historical accounts of physical activity in the South Pacific

The westernisation of Polynesian culture and resultant health impairments are relatively recent, occurring primarily over the past several decades, and do not reflect

the natural historical state of the Polynesian people. Centuries ago, French explorer Louis de Bougainville, struck by the lean bodies of the Tahitian people, commented "I never saw men better made. I thought I was transported into the Garden of Eden [16]." Other explorers such as Cook, Magellan, and Quirós also marvelled at the "tall, muscular, and well-proportioned people" of the South Pacific [16].

The seminal work of Professor John Macmillan Brown published in 1907 [17] addresses the origins of Polynesian people, highlighting evidence of historical migration patterns through Indonesia, Asia, and eventually to the South Pacific Islands. A defined pattern of habitual, daily physical activity emerges within the dialogue of Māori culture, customs, arts, war, hunting, gathering, agriculture, and fishing habits [17]. Brown provides references to the construction of canoes manually carved out from entire trees, and epic canoe voyages from outer islands to New Zealand [17]. Descriptions of war rituals appear to refer to *kapa haka*, or traditional Māori song and dance. It is clearly evident that a lifestyle of perpetual physical activity was required by the Māori people prior to colonisation, not with a conscientious focus on health maintenance *per se*, but instead for daily survival, traditional rituals, arts and culture, and inter-island travel.

In 1939, Dr. Weston Price [18] commented on the "splendid physiques" and "great physical endurance" of the few Māori men and women who, up to that point in history, remained uninfluenced by westernisation. Price noted that "few primitive races have developed calisthenics and systematic physical exercise to so high a point as the primitive Māori." Song and dance are performed by all until "the entire village is swaying in unison to the same tempo….with the result that these people maintain excellent figures to old age [18]." Sadly, these reports from early European explorers [16] and Drs. Brown [17] and Price [18] stand in stark contrast to current obesity and

non-communicable disease trends in the South Pacific.

1.3 Current obesity trends in New Zealand

Obesity is an established risk factor for type 2 diabetes. The incidence of obesity is particularly high and continues to increase amongst the Polynesian people of New Zealand [3, 19, 20]. In a study of 534 South Auckland adults aged 40-79 years, obesity defined as Body Mass Index (BMI) ≥ 31.0 kg/m^2 was present in 63% of Māori and 69% of Pacific Islands people compared to 26% of New Zealand Europeans [3]. This elevated prevalence of obesity was associated with a higher prevalence of type 2 diabetes [3].

The obesity epidemic is also on the rise in Polynesian children. Turnbull *et al.* [19] found obesity to be significantly higher among children of Pacific Islands (overweight = 35.0%; obese = 15.0%) and Māori origin (overweight = 24.7%; obese = 15.3%) versus those of European descent (overweight = 18.2%; obese = 5.7%). The authors implicated the classic hallmarks of "modern westernisation," including excessive television viewing, computer use, and video game play [19]. The disparities in obesity among children have been corroborated by Tyrell *et al.* [20]. The authors reported a prevalence of obesity of 24.1% in Pacific Islands children and 15.8% in Māori (15.8%) children. By contrast, the prevalence of obesity in children of European origin was only 8.6% ($P < 0.0001$).

These trends in childhood obesity are now beginning to translate into diagnoses of type 2 diabetes in Polynesian teenagers and an early onset of diabetes-related complications [9, 21]. For example, in a study which included 28 younger subjects (< 30 years) with type 2 diabetes, McGrath *et al.* [9] reported that the average age of type 2 diabetes diagnosis was just 19.1 years. Of the subjects enrolled, 86% were obese and

62% suffered from microalbuminuria or nephropathy. Scott *et al.* [21] have determined that obesity is prevalent among 100% of young people with type 2 diabetes, irrespective of race. The authors also found that microalbuminuria, a risk factor for the development of diabetic nephropathy [22], was more common among Māori and Pacific Islands people (43.8%) as compared to New Zealanders of European descent (17%).

1.4 Current physical activity levels in New Zealand

Physical inactivity is a significant risk factor for a vast array of chronic diseases including type 2 diabetes, obesity, cardiovascular disease, and metabolic syndrome. The updated American College of Sports Medicine (ACSM) and the American Heart Association (AHA) guidelines for physical activity and health [23] recommend a minimum of 30 minutes of accumulated moderate-intensity physical activity at least five days per week, or 20 minutes of vigorous activity at least 3 times per week to maintain or enhance health status. A recent Sport and Recreation New Zealand (SPARC) survey of 4443 adults aged 16 and over [24] reported that 53.5% of Māori, 52.6% of Pacific Islands, and 48.9% of New Zealand European respondents met these guidelines. Māori and Pacific Islands people also reported similar or higher participation rates in organised sports compared to other ethnic groups. However, these data were based on self-report, which may be unreliable.

A study in the United States objectively measuring physical activity levels of 6329 adults *via* accelerometer found that less than 5% of subjects achieved 30 minutes of activity per day [25]. Another study of 1114 adults found that for subjects who met the recommended guidelines, only 1% accumulated the recommended 30 minutes in bouts of at least 10 minutes [26]. Moreover, it has been suggested that those who meet the daily requirements but maintain a sedentary lifestyle for the remainder of the day

(i.e., during work hours) may actually negate the benefits of physical activity and remain at risk for health problems. For example, in a study of 4064 Australian adults who performed 150 minutes per week of physical activity, a significant positive association was observed between television viewing time and several important metabolic risk factors, including waist circumference, systolic blood pressure, fasting 2-hour plasma glucose, triglycerides, and high-density lipoprotein cholesterol in [27]. Additional New Zealand-based research is required using objective measures (i.e., accelerometers, inclinometers, GPS technology) to quantify physical activity levels relative to key cardiometabolic risk factors. This would provide a more accurate representation of inactivity-linked health impairments across the general population, including Māori and Pacific Islands people, and allow for greater understanding of any potential ethnic-specific disparities.

The outcomes of the SPARC physical activity survey [24] are interesting in light of current disease trends and statistics in New Zealand [1]. If Polynesian people are active to an equal or greater extent than New Zealand Europeans [24], then a comparatively lower incidence of obesity and associated comorbidities might be expected. However, an alternative hypothesis could be that established physical activity guidelines [23] may be insufficient to maintain or enhance health in this ethnic cohort given their historical propensity to habitually high levels of physical activity [16-18]. Therefore, it could be suggested that greater doses of physical activity (i.e., frequency, intensity, or duration) may be required to improve and maintain health in Polynesian people.

Empirical investigations have demonstrated that physiological disparities exist between ethnic groups. The degree of insulin resistance and pancreatic β-cell function have been shown to vary between ethnic groups, including African-American and Sub-

Saharan African [28], Afro-Caribbean [29], Middle-Eastern [30], Māori [31], Asian-Indian [29, 32], and European-Caucasian subjects [28-31, 33], giving rise to the possibility that the physiological response to an exercise prescription might also vary according to ethnicity.

1.5 The efficacy of prescribed exercise training in type 2 diabetes

Numerous reviews [34-39] and meta-analyses [40-42] underscore the value of exercise for improving glycaemic control and associated health outcomes in people with type 2 diabetes. Three recent meta-analyses which evaluated the impact of aerobic exercise only [40, 41], resistance training only [41], or a combination of both [41, 42] found that both forms of exercise can significantly reduce glycosylated hemoglobin, enhance insulin sensitivity, reduce body fat, reduce visceral adipose tissue, and reduce systolic and diastolic blood pressure, even without significant reductions in body mass [40-42]. However, the majority of the 13 to 28 studies included in these reviews were carried out in predominantly European-Caucasian subjects. A number of ethnic exercise studies, most of which were published after these reviews, have been conducted in other high-risk populations such as diabetic Asian-Indian [43-45], African [46, 47], Hispanic [48], Middle-Eastern [49], and Chinese [50] subjects (reviewed in detail in Chapter 2). However, no structured supervised clinical exercise trials to date have been conducted in Polynesian New Zealanders with type 2 diabetes.

1.5.1 Polynesian lifestyle interventions

Though no clinical exercise trials have been conducted in Māori and Pacific Islands people with type 2 diabetes, four lifestyle interventions [51-54] with obese and non-diabetic Polynesian subjects offer useful information which may help guide the

development of more rigorous training studies.

In a four-month uncontrolled pilot study by McAuley *et al.* [52], 31 obese Māori men and women (BMI 34.2 ± 6.1 kg/m^2) received dietary advice, attended cooking classes, and were provided with general exercise guidelines plus four supervised exercise sessions with the aim of improving insulin sensitivity, a prominent risk factor for the development of type 2 diabetes and cardiovascular disease. Insulin sensitivity measured via euglycaemic insulin clamp significantly improved. The subjects also experienced statistically significant reductions in body mass index (−1.1 kg/m^2), total (−2.0 kg) and truncal fat mass (−1.1 kg), waist circumference (−7 cm), and systolic blood pressure (−7 mmHg) [52].

In a two-year prospective non-randomised controlled lifestyle intervention [54] which included the results of an earlier investigation [53], 516 Samoan and Tongan church congregants received diabetes awareness education, cooking demonstrations, and light aerobic exercise sessions with the aim of reducing diabetes risk factors. Simmons *et al.* [54] reported a significant increase in exercise participation (+22%), stabilisation of weight gain (no change), and a reduction in waist circumference (−4 cm) in Samoan participants receiving 24 months of diabetes awareness, nutrition education, and culturally appropriate exercise sessions (i.e., church-based and included traditional dance movements) compared to a non-intervention control church (all $P \leq 0.05$). In Tongan congregants, exercise participation, body weight, and waist circumference remained unchanged after two years and was attributed to lower participation rates and perceived "usefulness" of the intervention [54]. Diabetes knowledge as assessed by the diabetes knowledge and behaviour questionnaire [55] increased significantly in both Samoan (+46%) and Tongan intervention groups (+19%) compared to their respective control groups, but more so in the Samoan church group who experienced greater health

benefits [54].

In a one-year non-randomised controlled weight management intervention in 471 obese Samoan church members (BMI $\geq$ 34.3 kg/m^2), Bell *et al.* [51] reported a statistically significant increase in the number of participants who were categorised as vigorously active (+10%), a reduction in body weight (−0.4 kg), and a trend toward reduction in systolic blood pressure (−10 mmHg) in the experimental group. Although the absolute change in body weight was small (0.4 ± 0.3 kg) the authors noted that even small reductions or stabilisation in weight in this high-risk population may substantially reduce the risk of developing cardiovascular disease and type 2 diabetes.

A number of methodological and reporting limitations of these lifestyle intervention trials [51-54, 56] must be considered. Firstly, exercise prescriptions and compliance data were not clearly described. In the church studies, subjects engaged in "sitting exercises, low-impact aerobics, walking, and sports" [53] or "walking groups and aerobics classes" [51], but no specific information regarding exercise frequency, intensity, or duration was provided. This introduces problems for replication of these studies, the application and practical utility of findings, and the development of exercise prescription guidelines to minimise diabetes risk and enhance health status in this population. McAuley *et al.* [52, 56] prescribed the 1990 American College of Sports Medicine guidelines for cardiovascular exercise [57] and provided heart rate monitoring instructions to their subjects, but did not mention levels of attendance or compliance to these guidelines. There were also inconsistencies in the testing methods employed by the researchers and the reported results. For example, the authors stated that subjects performed a one-mile walk test to assess aerobic fitness, but the published data were based on a modified Bruce treadmill protocol [52, 56]. Thus, exercise prescription reporting limitations described herein introduce difficulty in making any statements of a

dose-response relationship [51, 53, 54]. Secondly, randomisation of subjects to a control group has proven difficult in these lifestyle intervention trials. For example, McAuley *et al.* [52] intended to carry out a randomised controlled trial, but this was not feasible due to the close proximity and sharing of information between participants potentially randomised to different groups. Furthermore, a control group was deemed unethical since participants stated they knew they were at high-risk for developing diabetes and should therefore be afforded a potentially beneficial treatment [52]. Bell *et al.* [51] and Simmons *et al.* [53] recruited large numbers of church congregants which, by nature of the communal setting, made it difficult to conceal the intervention from the control groups. In fact, one control group initiated their own exercise program because they were upset about not receiving the intervention [53]. Moreover, ministers and church members sometimes participated in opposing churches' meetings which may have compromised the integrity of the control due to sharing of study-related information and experiences [51]. Lastly, the combination of treatment modalities provided (i.e., diet and exercise education, exercise classes) makes it difficult to determine the extent to which these results could be attributed solely to the exercise component. This does not necessarily invalidate the findings of these lifestyle interventions [51-54], but instead provides impetus for further research which may eventually elucidate the isolated effect of a variety of exercise prescriptions on important health outcomes in this cohort. Future exercise trials addressing these limitations are necessary and important for the establishment of clinical exercise guidelines for Māori and Pacific Islands people with type 2 diabetes.

1.6 Statement of purpose

The purpose of this doctoral research project was to:

1) Conduct the first supervised clinical exercise trial in Māori and Pacific Islands people with type 2 diabetes; and

2) Evaluate the impact of structured high-intensity progressive resistance training and aerobic exercise on glycaemic control and associated physiological, anthropometric, and psychological outcome measures.

Relevant blood and muscle outcome measures related to glycaemic control and insulin sensitivity were assessed and included haemoglobin A_{1c}, fasting plasma glucose, insulin, and serum free fatty acids, C-reactive protein, adiponectin, GLUT4 content, and capillary density. Homeostasis model assessment and the McAuley Index wer used for determining insulin resistance, and C-peptide was measured as an indicator of pancreatic β-cell function. Anthropometric measurements included body mass index, waist circumference, and bioelectrical impedance analyses to determine fat and lean muscle mass, all of which are relevant to identifying composition-mediated metabolic improvements. Blood pressure and blood lipid profile including total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides were assessed due to the higher cardiovascular risk observed in individuals with type 2 diabetes.

The **S**outh **P**acific **I**slands **R**esist diabetes with **I**ntense **T**raining (SPIRIT) study was accomplished through extensive cultural consultation with Māori and Pacific Islands community leaders for a period of 18 months before enrolling the first subject. In fact, the title of the SPIRIT study was developed in partnership with cultural leaders and was particularly relevant to many participants with a strong religious faith. Physicians, nurses, diabetes educators, and affiliated researchers at different universities provided technical advice and ongoing guidance from inception of the trial to its completion.

1.7 Thesis chapters overview

The thesis is divided into six chapters as follows:

1.7.1 Chapter 1: Introduction

Chapter 1 summarises physical activity and non-communicable disease trends in New Zealand, examines Polynesian diabetes prevention and weight management lifestyle interventions, provides a rationale for structured exercise trials in Māori and Pacific Islands people with type 2 diabetes, including the current Ph.D project.

1.7.2 Chapter 2: Systematic review of exercise intervention trials in high-risk ethnic populations with type 2 diabetes

Chapter 2 presents a systematic review of clinical exercise studies in populations disproportionately afflicted with type 2 diabetes. To date, no other reviews have evaluated the impact of structured exercise on glycaemic control and associated cardiometabolic outcomes in high-risk ethnic groups. This is likely due to the fact that studies included in this systematic review were published relatively recently, over the past eight years. Findings from studies in other ethnic cohorts suffering similar health burdens to Polynesian people may expose gaps in the exercise literature and yield useful insights for developing targeted exercise regimens to combat the growing type 2 diabetes problem in Polynesian New Zealanders.

1.7.3 Chapter 3: Cultural considerations, methodology, and implementation of a randomised trial of exercise training in New Zealand Māori and Pacific Islands people

Chapter 3 describes the study design and experimental methodology of the

doctoral research project with details regarding cultural consultation with Māori and Pacific church and community leaders, as well as medical and technical advice from general practitioners, endocrinologists, diabetes educators, and associated hospitals, health clinics, and public health organisations. The chapter also discusses the methodology for data collection and analysis of specific metabolic, anthropometric, haemodynamic, muscle biopsy, and health-related quality of life outcomes measures.

1.7.4 Chapter 4: Metabolic, anthropometric, haemodynamic adaptations in New Zealand Māori and Pacific Islands people after 16 weeks of high-intensity progressive resistance training and aerobic exercise

Chapter 4 presents results and discussion for metabolic, anthropometric, haemodynamic, and muscle biopsy outcome measures for the SPIRIT study.

1.7.5 Chapter 5: effect of exercise training on quality of life

Chapter 5 presents results and discussion for health-related quality of life assessed *via* Medical Outcomes Study Short-Form General Health Survey (SF36 version 1) [58].

1.7.6 Chapter 6: Conclusion

Chapter 6 presents an overall discussion of the SPIRIT study, summarises key findings, project limitations, and provides recommendations for future exercise trials in Māori and Pacific Islands people with type 2 diabetes.

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CHAPTER 2

Systematic Review of Exercise Intervention Trials in High-Risk Ethic Populations with Type 2 Diabetes

2.1 Introduction

According to the International Diabetes Federation, the prevalence of diabetes in 2010 is estimated at 285 million cases. This number is projected to rise to 438 million by 2030 [1]. Clearly, the greatest disease burden will be experienced by individuals diagnosed with type 2 diabetes as this form of the disease accounts for approximately 90% of cases.

Empirical evidence shows that the prevalence of type 2 diabetes is elevated in many ethnic cohorts as compared to those of Caucasian-European origin [2-4]. A recent European consensus statement of evidence-based guidelines for the prevention of type 2 diabetes has included ethnicity as a non-modifiable risk factor, with the authors citing a higher prevalence of the disease amongst individuals of Hispanic, Afro-Caribbean, and Asian-Indian descent compared to Caucasians [2]. In a prospective 20-year investigation of 78,419 apparently healthy women in the United States, the relative risk of developing diabetes was one and a half to three times higher in Asian-, Hispanic-, and African-Americans compared to Caucasians before and after adjusting for differences in BMI [3]. Further, in a telephone survey of 184,450 Americans [4], 11.1% of African-American and 8.9% of Latino-American respondents reported a diagnosis of diabetes versus only 6.6% of Caucasians respondents. Results from the 2006/2007 New Zealand Health Survey revealed the prevalence of diabetes to be 5.8% in Maori, 10.0% in Pacific peoples, and 6.5% in Asian respondents compared to 4.3% in European New Zealanders [5]. Though Maori and Pacific men have been shown to have more fat free mass than New Zealand men of European origin [6], there is also evidence of a greater tendency toward central obesity [7, 8] which may partially explain the relative higher prevalence of type 2 diabetes.

Environmental factors are believed to contribute to the increased risk of type 2

diabetes in some ethnic groups. A greater prevalence of the disease is observed in ethnic groups that migrate from rural to more urbanised and sedentary "obesogenic" regions [9]. Moreover, the prevalence of type 2 diabetes in high-risk ethnic groups increases dramatically with immigration to industrialised westernised nations [9]. For example, in the United States, the prevalence of diabetes is at least 12 times greater among African-Americans versus those residing in continental Africa [9]. Moreover, Pima Indians living in the state of Arizona have a diabetes prevalence of 54% and 37% for men and women, respectively, compared to only 6% and 11% among those living in northwestern México who still maintain their traditional lifestyle habits [9].

Although environmental factors play an aetiological role in the development of type 2 diabetes, interethnic variance in diabetes prevalence observed among different ethnic groups sharing a similar environment may also indicate a biological mechanism for this difference. The progression from normal glucose tolerance to impaired glucose tolerance and eventually to type 2 diabetes is accounted for by the degree of insulin resistance and pancreatic β-cell secretion of insulin [10]. Interethnic variations in these factors may contribute to the disparate prevalence of type 2 diabetes relative to Caucasians. In Sweden, Middle-Eastern immigrants were shown to have an earlier age of onset (43 ± 10 vs. 55 ± 12 years, $P < 0.001$) and stronger first-degree family history of type 2 diabetes as compared to Swedish-Caucasian participants (61% vs. 47% reported first-degree relative with diabetes, $P = 0.02$) [11]. While both groups were insulin resistant, the Middle-Eastern subjects exhibited more severe pancreatic β-cell dysfunction as measured by homeostasis model assessment of β-cell function (HOMA-β) (1.7 [0.1–9.1] vs. 2.7 [0.1–59.0]; $P = 0.01$). The United Kingdom Prospective Diabetes Study Group [12], evaluated clinical and biochemical outcomes in 5098 subjects (82% Caucasian, 10% Asian-Indian, and 8% Afro-Caribbean) with type 2

diabetes. Insulin sensitivity was highest in Afro-Caribbean (27%), followed by Caucasian (23%), and Asian-Indian (19%) subjects. However, β-cell function was most impaired in Afro-Caribbean subjects compared to Asian-Indians and Caucasians (28, 35, and 45% of normal, respectively). In another study, Goran *et al.* [13] reported that African-American and Hispanic children were more insulin resistant than Caucasian children after controlling for adiposity and, despite similar levels of insulin resistance, relied on different compensatory mechanisms (i.e., differences in β-cell insulin secretion, hepatic insulin clearance) to maintain euglycaemia. In a New Zealand study of 111 subjects evaluating racial differences in type 2 diabetes risk, at any BMI or total or truncal fat mass, Māori women were more likely to be insulin resistant than New Zealand Europeans [14]. These differences persisted even after adjustment for age, smoking, and glucose levels.

Taken as a whole, the interethnic variation in the pathophysiological mechanisms leading to hyperglycaemia and eventually to type 2 diabetes may be influenced by both lifestyle and underlying genetic factors mediated by a westernised environment.

2.2 Rationale for prescribed exercise in individuals with type 2 diabetes

The current trident of diabetes prevention and treatment consists of a combination of medication, diet, and exercise, with the latter garnering considerable empirical support in recent years. Numerous reviews [15-20] and meta-analyses [21-23] underscore the value of prescribed exercise for improved glycaemic control (assessed by HbA_{1c}) and associated health outcomes in people with type 2 diabetes. Meta-analyses of controlled clinical trials have shown that prescribing aerobic exercise training (AER), progressive resistance training (PRT), or a combination of both for five

weeks to two years can reduce HbA_{1c} by 0.6 to 0.8% [21-23], fasting insulin by 7 to 31%, visceral adiposity by 4 to 15%, waist circumference by 0.8 to 2%, and systolic and diastolic blood pressure by 1.3 to 5.6 mmHg. However, the studies included in these reports [21-23] were carried out in predominantly (80 to 93%) European-Caucasian participants.

Given the current disparities in health status between ethnic groups and empirical evidence that insulin sensitivity, insulin resistance, and pancreatic β-cell function vary by race [9, 11, 12, 14], the physiological response to similar doses and modalities of exercise may also vary according to ethnicity. A number of exercise intervention trials published in the last decade have investigated and reported on the exercise response in disproportionately afflicted ethnic populations with obesity and type 2 diabetes. Thus far, studies have been conducted in diabetic Hispanic [24], African [25, 26], Asian-Indian [27-29], Middle-Eastern [30], and Chinese [31] subjects. The findings from these studies may yield useful insights for developing targeted exercise regimens to combat the growing type 2 diabetes epidemic in ethnic cohorts. Therefore, the purpose of this chapter is two-fold:

1) To review current exercise research in ethnic groups with type 2 diabetes with particular emphasis on diabetes outcome measures including HbA_{1c} and associated metabolic, anthropometric, and haemodynamic outcomes; and

2) To discuss the strengths and limitations of this body of research and provide a rationale for the current Ph.D project in Māori and Pacific Islands people, as well as future exercise research studies in other ethnic populations with elevated risk of type 2 diabetes.

2.3 Method

A systematic review of exercise trials in ethnic cohorts with type 2 diabetes was performed, but did not include a meta-analysis of results due to the small number of trials and the heterogeneity of prescribed exercise interventions and outcome measure assessments. Meta-analysis is not advised unless there is sufficient similarity in experimental protocols and population [32].

2.3.1 Study inclusion criteria

The following section highlights specific inclusion criteria for the systematic review relative to study design, diabetes status, ethnicity, exercise interventions, and outcome measures assessed.

2.3.1.1 Study designs

Randomised controlled trials (RCT), controlled trials, and uncontrolled trials were included. Abstracts and case reports were not considered.

2.3.1.2 Subjects

Subjects were adult men and women (≥ 18years) with diagnosed type 2 diabetes. Subjects with pre-diabetic conditions such as impaired fasting glucose or insulin resistance but without a diagnosis of type 2 diabetes were excluded.

2.3.1.3 Ethnicity

Studies were included for review if:

1) authors defined their study population as having higher rates of type 2 diabetes relative to Caucasians; or

2) if not explicitly mentioned, subjects were members of racial or ethnic groups with a known high prevalence of the disease versus European counterparts.

2.3.1.4 Interventions

PRT and/or AER trials of eight weeks or longer in duration were included for review. While 12 weeks of intervention is generally required to document appreciable changes in HbA_{1c} due to the lifespan of the red blood cell [33], eight week interventions were included because they still offer the opportunity to see shifts in other clinically relevant outcomes, including body mass and composition [34, 35].

2.3.1.5 Outcome measures

The outcome measure of primary interest was glycaemic control as determined by HbA_{1c}. Additional outcome measures of interest included body mass, body mass index, fat and lean mass, fat and lean mass percentage, waist circumference measurements, insulin resistance, insulin sensitivity, pancreatic β-cell function, blood lipids, and blood pressure. Fasting blood glucose or other indices of glucose metabolism were considered in instances where HbA_{1c} was not reported.

2.3.2 Search methodology

A literature review was conducted to include studies from 1966 to 2010, limited to the English language, using computerised databases, including Medline, CINAHL, SportDiscus, Embase, and Web of Science. The search combined key words related to type 2 diabetes (i.e. type 2 diabetes, glycaemic control, glucose, insulin, insulin sensitivity, insulin resistance), exercise (i.e. exercise, physical activity, resistance

training, weight training, strength training, aerobic training, muscle, endurance, oxygen uptake [VO_2]), and ethnicity (i.e. ethnicity, race, African, Hispanic, Latino, Pacific, Māori, Polynesian, Asian, Indian). Reference lists of retrieved articles were then screened for other additional relevant exercise intervention trials.

2.4 Results

2.4.1 Study designs and research quality

The search resulted in nine articles presenting the findings of eight trials, including five randomised controlled trials (RCT) [24, 26, 27, 29, 31] (exercise versus non-exercise control group) and three uncontrolled trials (one exercise group only [28] or comparison between two exercise groups [25, 30]) (Table 2.1). The control groups in four studies were instructed to refrain from exercise and maintain their usual diabetes care [24, 27, 29, 31], whereas another study provided sham relaxation exercises in order to motivate subjects and minimise dropout [26]. The two comparison trials stratified participants by ethnicity [30] or ethnicity by exercise training modality [25].

2.4.2 Overview of the participants

2.4.2.1 Sample size

Five hundred and eleven (n = 511) subjects were enrolled in the eight trials reviewed. Sample size ranged from 30 [27, 28] to 157 [26] subjects (Table 2.1).

2.4.2.2 Ethnicity

Studies were carried out in Asian-Indian [27-29], African-American [25], Sub-Saharan African [26], Hong Kong Chinese [31], Hispanic [24, 36], and Middle-Eastern subjects with type 2 diabetes mellitus [30]. A Caucasian-European comparison group

was included in two trials [25, 30].

2.4.2.3 Gender

Of seven trials reporting a gender breakdown, 314 women and 128 men were enrolled [24, 26-31]. Winnick *et al.* [25] did not specify gender. One study with the largest number of participants (n=157) [26] was comprised of exclusively women due to the small number of men visiting the recruitment site. All remaining trials included men and women.

2.4.2.4 Age

Age of the subjects was expressed as mean ± SD in seven trials [24, 25, 27-31] and ranged from 40.8 ± 8.1 [28] to 66.0 ± 2.0 [24]. One trial provided mean age but no standard deviation [26]. In studies that mentioned an age range [25-28], the youngest and oldest subjects enrolled were 24 [28] and 70 years [27], respectively.

2.4.2.5 Duration of type 2 diabetes

Five studies [24, 27, 29-31] reported the duration of diagnosis with type 2 diabetes, which ranged from 4.7 ± 1.7 [27] to 11 ± 1 [24] years. Three studies [24, 26, 27] provided a minimum duration with diabetes as an entry criterion ($\geq$ 6 months to > 3 years) [24, 27].

2.4.2.6 Use of diabetes medications

Five studies [24, 26, 27, 29, 30] provided information on diabetes treatment regimens. Across these trials, approximately 61% of subjects were prescribed oral hypoglycaemic agents and 22% were receiving insulin injections. In studies which

Table 2.1: Significant changes in clinical outcomes in exercise studies with high-risk ethnic groups with type 2 diabetes

Authors (year) Country	N	Study Groups (n)	Ethnicity	Exercise Intervention			Outcomes*		
				Modality	Prescription	Duration	Variable	Change	P value
Castaneda *et al.*[20] (2002) United States Brooks *et al.* [30] (2007) United States * Presented outcome results for Castaneda *et al*. and Brooks *et al* are drawn from the same study.	62	Exercise (n=31) Control (n=31)	Hispanic	PRT	5 machine-based exercises, 3 sets x 8 reps, 80% of 1RM, 3x/week	16 weeks	HbA_{1c} (%)	−1.1	≤0.01#
							HOMA-IR	−1.8	≤0.05#
							Muscle Glycogen Stores (mmol glucose/kg muscle)	+18.8	≤0.04#
							Free Fatty Acids (µmol/L)	−84.0	≤0.02#
							C-Reactive Protein (mg/L)	−0.7	≤0.05#
							Adiponectin (µg/mL)	+1.5	≤0.001#
							Trunk Fat Mass (kg)	−0.7	≤0.01#
							Whole Body Lean Mass (kg)	+1.2	≤0.04#
							Upper Body Strength (kg)	+24.0	≤0.001#
							Lower Body Strength (kg)	+230.0	≤0.001#
							Muscle Quality(1RM/lean leg mass)	+39.0	≤0.001#
							Type 1 Muscle Fiber Area (μm^2)	+861.0	≤0.04#
							Type 2 Muscle Fiber Area (μm^2)	+720.0	≤0.04#
							Systolic Blood Pressure (mmHg)	−9.7	≤0.05#
							Leisure Physical Activity Score	+19.9	≤0.001#
							Household Physical Activity Score	+19.4	≤0.001#
							<u>No significant difference from control</u>		
							Fasting Plasma Glucose (mmol/L)	−0.9	0.34
							Fasting Insulin (pmol/L)	−11.0	0.27
							Serum Triglycerides (mmol/L)	−0.2	0.08
							Total Cholesterol (mmol/L)	−0.2	0.59
							HDL Cholesterol	+1.0	0.46
							LDL Cholesterol	−0.2	0.13
							Body Weight (kg)	+0.2	0.89
							Arm Lean Mass (kg)	+0.4	0.08
							Leg Lean Mass (kg)	+0.2	0.07
							Whole Body Fat Mass (kg)	−1.0	0.26
							Arm Fat Mass (kg)	+0.1	0.69

Castaneda, Brooks (Continued)							Leg Fat Mass (kg) Waist Circumference (cm) Diastolic Blood Pressure (mmHg) Heart rate (bpm)	0.0 −2.2 −3.4 +1.0	0.41 0.07 0.52 0.74
Glans *et al.* [26] (2009) Sweden	32	Arabian (n=18) Swedish (n=14)	Middle-Eastern	COMBO	<u>Weeks 1-12</u> PRT + AER, 6 weight stations plus 6min cycling, 3x/week, <u>Weeks 13-24</u> Cycling, Walking, 60-70% VO_{2max}, 45 min, 3x/week	24 weeks	<u>Middle-Eastern</u> Glucose Oxidation (mg/kg/min) Non-Glucose Oxidation (mg/kg/min) <u>No significant difference from baseline</u> HbA_{1c} (%) Body Mass Index (kg/m^2) Fat Free Mass (kg) Insulin Sensitivity (M value) Lipid Oxidation (mg/kg/min) VO_{2max} (ml/kg/min) Workload (watts) Ventilatory Threshold (ml) <u>Swedish</u> HbA_{1c} Insulin Sensitivity (M value) Glucose Oxidation (mg/kg/min) Non-Glucose Oxidation (mg/kg/min) Ventilatory Threshold%VO_{2max} <u>No significant difference from baseline</u> Body Mass Index (kg/m^2) Fat Free Mass (kg) Lipid Oxidation (mg/kg/min) VO_{2max} (ml/kg/min) Workload (watts) Ventilatory Threshold (ml)	 −0.7 +1.7 −0.1 −0.3 0.0 +0.9 +0.3 −1.2 +5.3 +16 −0.6 +0.9 −0.2 +1.1 +11 0.0 −0.5 +0.1 +0.6 +8.0 +177	 ≤0.05‡ ≤0.05‡ NS‡ ≥0.05 ≥0.05 ≥0.05 ≥0.05 ≥0.05 ≥0.05 ≥0.05 ≤0.05‡ ≤0.005‡ ≤0.05‡ ≤0.005‡ ≤0.05 ≥0.05 ≥0.05 ≥0.05 ≥0.05 ≥0.05 ≥0.05

Misra *et al.*[24] (2008) India	30	Exercise (n=30)	Asian-Indian	PRT	6 machine-based exercises, 2 sets x 10 reps, Intensity not clearly described, 3x/week	12 weeks	HbA_{1c} (%)	−0.5	≤0.001‡
							Fasting Blood Glucose (mmol/L)	−2.7	≤0.001‡
							Total Cholesterol (mmol/L)	−0.4	≤0.003‡
							Triglycerides (mmol/L)	−0.4	≤0.001‡
							VLDL Cholesterol (mmol/L)	−0.4	≤0.003‡
							Waist Circumference (cm)	−1.6	≤0.001‡
							Hip Circumference (cm)	−1.8	≤0.001‡
							Mid-Thigh Circumference (cm)	−1.6	≤0.001‡
							Mid-Arm Circumference (cm)	−1.2	≤0.001‡
							Biceps Skinfold (mm)	−0.9	≤0.001‡
							Triceps Skinfold (mm)	−1.3	≤0.001‡
							Supscapular Skinfold (mm)	−1.6	≤0.001‡
							Anterior Axillary Skinfold (mm)	−1.0	≤0.001‡
							Suprailiac Skinfold (mm)	−1.4	≤0.001‡
							Thigh Skinfold (mm)	−1.4	≤0.001‡
							Calf Skinfold (mm)	−0.8	≤0.001‡
							Lateral Thoracic Skinfold (mm)	−1.0	≤0.001‡
							Central Skinfolds (mm)	−5.2	≤0.001‡
							Peripheral Skinfolds (mm)	−4.6	≤0.001‡
							<u>No significant difference from baseline</u>		
							HDL Cholesterol (mmol/L)	+0.02	0.33
							LDL Cholesterol (mmol/L)	−0.1	0.21
							Body Mass Index (kg/m^2)	0.0	0.61
							Waist-to-Hip Ratio	0.0	0.09
							Subscapular-to-Triceps Skinfold ratio	+0.1	0.08
							Body Fat (%)	−0.4	0.24
							Truncal-to-Total Body Fat ratio	0.0	0.96
							Lean Body Mass (kg)	+0.3	0.38
							Right Arm Fat (%)	−1.2	0.31
							Right Arm Regional Fat (%)	−1.1	0.33
							Right Arm Lean Mass (kg)	+0.1	0.17
							Right Midarm Muscle Area (cm^2)	−0.5	0.49
							Right Leg Fat (%)	−0.3	0.22
							Right Leg regional Fat (%)	−0.2	0.39

Misra (continued)							Right Leg Lean Mass (kg) Right Mid-Thigh Muscle Area (cm^2)	+0.1 +0.2	0.29 0.09
Shenoy *et al.*[23] (2009) India	30	Exercise 1 (n=10) Exercise 2 (n=10) Control (n=10)	Asian-Indian	PRT AER	PRT 7 machine-based exercises, 3 sets x 10 reps, 60-100% 1RM, 2x/week AER Walking Intensity not stated, 3x/wk	16 weeks	PRT HbA_{1c} (%) Systolic Blood Pressure (mmHg) Diastolic Blood Pressure (mmHg) Heart Rate (beats/min) Peak Flexion Force (N) Berg Balance Scale Score No significant difference from baseline Fasting Blood Glucose (mg/dl) Peak Extension Force (N) Mean Extension Force (N) Mean Flexion Force (N) AER HbA_{1c} (%) Peak Flexion Force (N) Berg Balance Scale Score No significant difference from baseline Fasting Blood Glucose (mg/dl) Systolic Blood Pressure (mmHg) Diastolic Blood Pressure (mmHg) Heart Rate (bpm) Peak Extension Force (N) Mean Extension Force (N) Mean Flexion Force (N)	 −1.9 −9.0 −8.0 −16.0 +33.7 +3.0 −69.0 −52.0 −36.2 −24.1 −1.3 +31.0 +3.0 −26.0 −3.0 −1.0 −2.0 +60.0 +35.8 +20.3	 ≤0.01# ≤0.01# ≤0.01# ≤0.01# ≤0.01# ≤0.001# >0.05 >0.05 >0.05 >0.05 ≤0.01# ≤0.01# ≤0.001# >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05

Sridhar *et al.*[25] (2010) India	105	Exercise (n=55) Control (n=50)	Asian-Indian	AER	Cycle Ergometer or Treadmill, ≤45 min, 60% HR_{max}, 5x/wk	52 weeks	HbA_{1c} (%) Systolic Blood Pressure (mmHg) Diastolic Blood Pressure (mmHg) Heart Rate Variability (beats/min)	−2.2 −8.7 −5.8 −4.5	≤0.001‡ ≤0.01‡ ≤0.01‡ ≤0.05‡
Sykes *et al.*[27] (2004) Hong Kong	36	Exercise (n=24) Control (n=12)	Chinese	AER	Treadmill, cycle, step, arm ergometer, 50-70% HRR, 45 min, 1x/wk	12 weeks	Exercise HbA_{1c} (%) Body Mass (kg) Body Mass Index (kg/m^2) HDL Cholesterol (mmol/L) 6-Minute Walk Test (m) METS No significant difference from baseline Fasting Blood Glucose (mmol/L) Fasting Insulin (mU/L) HOMA-IR Index Insulin Sensitivity (S_I) Triglycerides (mmol/L) Total Cholesterol (mmol/L) LDL Cholesterol (mmol/L) Waist Circumference (cm) Hip Circumference (cm) Waist-to-Hip Ratio Body Fat (%)	 −0.4 −0.4 −0.2 +0.1 +187.0 +2.0 0.0 −2.1 −0.1 −0.3 −0.2 +0.1 0.0 +0.2 −0.9 0.0 −0.8	 NS ≤0.045‡ ≤0.043‡ ≤0.002‡ ≤0.000‡ ≤0.000‡ >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05
Van Rooijen *et al.*[22] (2004) South Africa	157	Exercise (n=75) Control (n=74)	African	AER	Walking, Borg RPE scale=12-14, 45 min, 5-7x/week	12 weeks	Exercise HbA_{1c} (%) 6-Minute Walk Test (m) No significant difference from baseline Body Mass Index (kg/m^2) Systolic Blood Pressure (mmHg) Diastolic Blood Pressure (mmHg) Rating of Perceived Exertion	 −0.4 +48.6 +0.1 −3.7 −1.1 −0.2	 ≤0.05‡ ≤0.01‡ 0.28 0.64 0.90 0.69

Winnick *et al.*[21] (2008) USA	59	<u>African-American</u> Exercise 1 (n=12) Exercise 2 (n=24) <u>Caucasian</u> Exercise 1 (n=8) Exercise 2 (n=15)	African-American	PRT AER	<u>PRT</u> 10 reps, sets and intensity not defined <u>AER</u> Treadmill 30-40 min ~1000kcal/wk 3x/week	8 weeks	<u>PRT—African-American</u> Body Mass Index (% change) HOMA-IR (% change) Waist-to-Hip Ratio (% change) Body Fat Percent (% change) HOMA-β <u>AER—African-American</u> Body Mass Index (% change) Waist-to-Hip Ratio (% change) Body Fat (% change) HOMA-IR (% change) HOMA-β (% change) <u>PRT—Caucasian</u> Body Mass Index (% change) Waist-to-Hip Ratio (% change) Body Fat (% change) HOMA-IR (% change) HOMA-β (% change) <u>AER—Caucasian</u> Body Mass Index (kg/m^2) Waist-to-Hip Ratio (% change) Body Fat (% change) HOMA-IR (% change) HOMA-β (% change)	−2.6 −19.2 +0.1 −0.9 +84.7 +0.7 −1.0 −0.4 +3.8 +47.8 +2.6 +0.7 +1.4 +13.2 −10.7 −1.2 +0.4 −0.2 −3.7 19.0	≤0.05* ≤0.05* >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 >0.05 ≤0.05* >0.05 >0.05 <0.05 >0.05 ≤0.05* >0.05 >0.05 >0.05 >0.05

AER=Aerobic Training; COMBO=Aerobic Training plus Progressive Resistance Training; HbA_{1c}= Hemoglobin A_{1c}; HDL=High Density Lipoprotein; HOMA- β=Homeostasis Model Assessment-beta cell; HOMA-IR=Homeostasis Model Assessment-Insulin Resistance; HRR= Heart Rate Reserve; LDL=Low Density Lipoprotein; METS=Metabolic Equivalent (1 MET=3.5 mlO_2/kg body weight/min); PRT=Progressive Resistance Training; RPE=Rating of Perceived Exertion; VLDL=Very Low Density Lipoprotein.

*Significant change over time versus comparison group(s); ‡Significant versus baseline values within group; #Significant versus control group only.

reported number of subjects treated non-pharmacologically [24, 26, 27, 30], 5% were managing their diabetes by diet only. Only one study [26] listed how many subjects were receiving combined oral hypoglycaemic agents and insulin therapy (n = 12 of 157 subjects).

2.4.2.7 Comorbidities and diabetic complications

Four studies provided data on comorbidities such as hypertension [24, 26, 29, 30] and cardiovascular disease [24, 30]. The prevalence of hypertension and ischaemic heart disease ranged from 23.8 to 62.4% [24, 26, 29, 30] and 6 to 59.7% [24, 30], respectively, among enrolled participants. For reports that did not provide this information, the mean baseline clinical data gave an indication of underlying hypertension [25, 27] and hyperlipidaemia [28, 31]. Only one study [30] provided a breakdown of active diabetic complications (i.e., neuropathy, retinopathy, micro- and macroalbuminuria) likely because most investigations [25-28, 31] excluded such participants. Subjects were generally considered for inclusion in most studies if their comorbidities or complications were well-managed and medically stable. Smoking prevalence among participants was reported in three trials conducted by Castaneda *et al.* [24] (2/62 subjects, 3%), Sridhar *et al.* [29] (11/105, 10%), and Glans *et al.* [30] (11/32 subjects, 34%).

2.4.2.8 Participation

Four of eight studies reported the number of subjects who were unavailable for testing after the intervention period [24, 26, 27, 30]. Of 281 subjects enrolled in these trials, 17 (6%) did not undergo post-study testing. Three studies provided reasons for dropout [24, 26, 27] including: discontinuation with no reason given, time constraints, a

fractured leg, medical reasons unrelated to the study, and death.

2.4.3 Overview of exercise interventions

The following section presents details regarding the exercise interventions, including: prescription (i.e. frequency, intensity, duration, and modalities), supervision, compliance, and adverse events.

2.4.3.1 Intervention duration

Duration of the exercise interventions ranged from eight weeks [25] to 12 months [29], with most studies lasting from 12 to 16 weeks [24, 26-28, 31] (Table 2.1).

2.4.3.2 Modality

Machine-based resistance training was used in three studies [24, 27, 28]. Aerobic training alone was employed in three trials [26, 29, 31] and consisted of walking, leg and arm cycle ergometry, and stepping exercise. Two investigations compared the efficacy of aerobic versus resistance training [25, 27] and one trial prescribed a combination of aerobic and resistance exercise [30].

2.4.3.3 Frequency

Frequency of exercise sessions ranged from one [31] to seven days per week [26], with most trials [24, 25, 27-30] prescribing exercise three to five days per week.

2.4.3.4 Intensity and volume

In general, exercise intensity for both aerobic and resistance training modalities

was not adequately described. Based on contextual descriptions, most studies appeared to be of moderate intensity.

Three studies employing aerobic training protocols described intensity as a percentage of maximal oxygen consumption (VO_{2max}) [30], heart rate reserve [31], or maximal heart rate [26]. All ranged from 50 to 70% of maximum intensity.

Resistance training was prescribed at moderate [25, 27, 28, 30] and high-intensity [24] and generally provided a range of two to three sets of eight to 10 repetitions. Four studies reported the number of resistance exercises performed, which ranged from four to seven [24, 27, 28, 30]. Winnick and colleagues [25] did not fully describe the training intensity, but stated that participants performed multiple sets of 10 repetitions. Glans *et al.* [30] did not detail the number of repetitions performed, but instead mentioned a duration of three minutes per resistance training station, suggesting that the exercises were likely performed at a lower intensity.

2.4.3.5 Duration of exercise sessions

Aerobic exercise sessions ranged from 30 to 45 minutes [25-27, 29-31] with three trials explicitly mentioning warm-up and cool-down components included within [30] or in addition to [29, 31] the total exercise time. Exercise duration was generally not a consideration in resistance training studies [24, 25, 27, 28] due to the intermittent nature of the protocol, but Castaneda *et al.* [24] mentioned a total session time of 45 minutes including warm-up and cool-down.

2.4.3.6 Supervision

Direct supervision of exercise sessions by research staff was mentioned in five studies [24, 28-31] and ranged from one to five days per week. Two studies were

unclear as to the level of supervision provided [25, 27]. Van Rooijen *et al.* [26] recommended daily unsupervised walking exercise plus supervised fortnightly sessions to educate and reinforce home exercise guidelines to participants. Two studies mentioned the use of self-report exercise logbooks which were periodically evaluated for compliance to protocols [25, 26].

2.4.3.7 Compliance

Four reports [24, 26, 30, 31] provided details regarding compliance to exercise training (i.e., sessions attended) and ranged from 88 to 91%. While Van Rooijen *et al.* [26] did not provide the percent of exercise session attended, the authors did mention "high attendance" to supervised fortnightly sessions and "very low compliance" to non-supervised exercise sessions. Winnick *et al.* [25] stated that the investigators reviewed exercise logs on a weekly basis; however, these results were not reported.

2.4.3.8 Adverse events

Three trials [24, 26, 27] provided information on adverse events related to exercise participation. Castaneda and colleagues [24] reported five hypoglycaemic events and three episodes of chest pain. All events were managed and resolved without complication and none resulted in subject drop-out. No adverse events were reported by Van Rooijen *et al.* [26] or Shenoy *et al.* [27].

2.4.4 Metabolic adaptations to exercise

2.4.4.1 Glycaemic control

Statistically significant ($P < 0.05$) reductions in HbA_{1c} (−0.37 to −2.21%) were reported in six trials [24, 27-30] secondary to PRT [24, 27, 28], AER [26, 27, 29] and

combined training modalities [30] (Table 2.1). The greatest improvements were noted in Latino [24] and Asian-Indian [27, 29] subjects prescribed ≥16 weeks of PRT [24] or AER [27, 29]. Another trial in African-American subjects [25] reported pre- but not post-intervention HbA_{1c} values so a direct assessment of the change in glycaemic control could not be ascertained.

HbA_{1c} remained unchanged after AER in trials including Chinese [31] and Sub-Saharan African [26] subjects. In the latter trial [26], there was also an unexpected statistically significant reduction in HbA_{1c} in women randomised to a control group performing sham relaxation movements.

Glans *et al.* [30] demonstrated that 12 weeks of combined PRT and AER followed by 12 weeks of AER significantly reduced HbA_{1c} in Swedish-European (−0.6%; $P < 0.05$) but not in Middle-Eastern subjects (−0.1%).

2.4.4.2 Insulin action

Indices of insulin action were reported in five studies [25, 28, 30, 31, 36] and were quantified by various methods. Winnick *et al.* [25] demonstrated that 8-weeks of PRT resulted in a significant percent reduction in insulin resistance as measured by homeostasis model assessment (HOMA-IR) in African-American (−19.2 ± 9%) versus an increase in Caucasian subjects performing the same exercise modality (+13.1 ± 11.9%) ($P < 0.05$). Pancreatic β-cell function in African-American subjects as measured by HOMA-β tended to improve (+84.7% ± 32.4) as compared to Caucasian subjects (−10.7% ± 42.9) but was not statistically significant. Similarly, Brooks *et al.* [36] reported a reduction in HOMA-IR from 7.1 ± 5.7 to 5.3 ± 5.5 in Latino subjects after 16 weeks of PRT as compared to control ($P < 0.05$). Misra *et al.* [28] measured insulin sensitivity by the short insulin tolerance test and reported an increase in K value

from 1.22 ± 0.73 to 2.13 ± 0.75 ($P < 0.0001$) after 12 weeks of PRT in Asian-Indian subjects. Glans *et al.* [30] determined insulin sensitivity from glucose infusion rates during the last 60 minutes of the euglycaemic insulin clamp (M-value) expressed as glucose uptake per kilogram of body weight and observed a 26% increase in insulin sensitivity across the entire cohort after six months of exercise training ($P < 0.05$). However, the authors did not evaluate these results within or between ethnic groups.

2.4.4.3 Anthropometry and body composition

Body mass index (BMI) ranged from 24.1 to 33.6 kg/m^2 across all studies [24-31]. Two studies reported significant reductions in BMI following PRT in African-American participants (−2.6 ± 0.89%; $P < 0.05$) [25] and after AER in Hong Kong Chinese subjects (−0.02 ± 4.6 kg/m^2; $P = 0.04$) with a concomitant reduction in body mass (−0.4 kg; $P = 0.045$), but no significant change in body fat percent [31]. Other authors reported no statistically significant differences [28, 30] or did not report follow-up BMI data [24, 27, 29]. Another study reported a statistically significant decrease in BMI (−0.25 ± 0.08 kg/m^2; $P < 0.01$) in the control group prescribed sham relaxation exercise [26].

Castaneda *et al.* [24] reported a significant decrease in visceral fat (18.8 ± 1.1 to 18.1 ± 1.2 kg; $P = 0.01$), an increase in whole body lean tissue mass (44.3 ± 1.7 to 45.5 ± 1.9 kg; $P = 0.04$), and a trend toward increased trunk lean mass (21.9 ± 0.8 to 22.4 ± 0.8 kg; $P = 0.08$) after PRT as determined *via* dual energy x-ray absorptiometry (DEXA) scan in older (aged ≥ 55 years) Latinos with type 2 diabetes. The authors also noted a 2.2 cm reduction in waist circumference in the exercising participants, though this finding did not achieve statistical significance ($P = 0.07$).

Misra *et al.* [28], employing both DEXA and computed tomography, reported no statistically significant change in whole body or regional fat and lean mass in an Asian-Indian cohort but reported a significant 1.6 cm reduction in waist circumference ($P < 0.001$). A 5.2 mm reduction in central (i.e., subscapular, anterior axillary, lateral thoracic, and suprailiac sites) skinfold thickness was also evaluated in this trial ($P \leq 0.001$).

Glans *et al.* [30] reported no significant difference in lean mass after 24 weeks of exercise training as determined *via* bioelectrical impedance analysis.

2.4.4.4 Blood lipids

Three studies evaluated blood lipid profiles [24, 28, 31, 36]. In an uncontrolled trial involving Asian-Indian participants, Misra *et al.* [28] determined that 12-weeks of PRT induced statistically significant reductions in total cholesterol ($P = 0.003$) and triglycerides ($P < 0.001$) (Table 2.1), while low- (LDL) and high-density lipoprotein (HDL) cholesterol remained unchanged after the exercise intervention. Sykes *et al.* [31] determined that Chinese participants performing one AER exercise session per week for 12-weeks was associated with a significant increase in HDL cholesterol ($P = 0.002$) (Table 2.1), while Castaneda *et al.* [24] reported a trend toward reduced triglycerides ($P = 0.08$) secondary to 16 weeks of PRT in their Latino participants, but no change in total cholesterol, LDL, or HDL cholesterol. In another report based on the same study, Brooks *et al.* [36] observed a reduction in free fatty acids from 656 ± 41.9 to 572.4 ± 45.3 μmol/l ($P = 0.02$).

2.4.4.5 Haemodynamic changes

Statistically significant reductions in systolic (SBP) [24, 27, 29] and diastolic

(DBP) [27, 29] blood pressure were demonstrated after exercise training in Latino and Asian-Indian cohorts, while other studies have reported no change in these parameters [26, 28]. Resistance training reduced SBP [24, 27] and DBP [27] secondary to PRT, whereas Sridhar *et al.* [29] reported a reduction in both parameters following one year of AER training (Table 2.1). Sridhar *et al.* [29] also noted a significant increase in heart rate variability index after their training program, indicating enhanced parasympathetic (vagal) tone.

2.5 Discussion

The main finding of this review is that structured exercise has been shown to improve glycaemic control and associated metabolic outcome measures in several ethnic populations disproportionately afflicted with type 2 diabetes [24-31] (Table 2.1). Longer intervention durations appear to be associated with the largest magnitudes of change in HbA_{1c}, suggesting a potential dose-response relationship. For example, the largest reductions (−1.1 to 2.2%) were observed in studies of at least 16 weeks [24, 27, 29]. The overall reduction in HbA_{1c} ranged from 0.37 to 2.2% in the trials reviewed [24-31] and is a particularly important finding given the elevated risk for cardiovascular morbidity and mortality in high-risk ethnic groups [37]. The United Kingdom Prospective Diabetes Study [38] demonstrated that, after adjustment for ethnicity, each 1% reduction in HbA_{1c} was associated with a 14% reduction in myocardial infarction, 37% reduction in microvascular complications, and a 21% reduction in diabetes-related deaths. Thus, any therapy which may improve cardiovascular and microvascular end points in high-risk ethnic groups warrants further investigation.

The statistically significant reductions in SBP [24, 27] and DBP [27] in Latino [24] and Asian-Indian [27] subjects after PRT and in SBP and DBP in Asian-Indian

subjects after AER training [29] are clinically important findings for high-risk populations with diabetes. Subjects with type 2 diabetes have a two- to four-fold increased risk of adverse cardiovascular events [39], so any regimen that can reduce hypertension in diabetic subjects is desirable. Subjects with high normal blood pressure (SBP 130 to 139 and/or DBP 85 to 90 mmHg) experience higher rates of adverse cardiovascular events compared to those with normal blood pressure (120/80 mmHg) [40]. According to the American College of Sports Medicine position stand on exercise and hypertension [41], endurance exercise, resistance training, or a combination of both prevent hypertension and lower blood pressure in those with hypertension. Moreover, the blood pressure-lowering effect of exercise is more pronounced in subjects with the highest baseline blood pressures undertaking endurance type exercise [41]. As little as a 2 mmHg decrease in SBP and DBP translates to a reduction in risk of coronary artery disease by 9% and 6%, and a reduction in risk of stroke by 14 and 17%, respectively, in the general population [41].

Sridhar *et al.* [29] reported a significant increase in heart rate variability index after 12 months of aerobic training in Asian-Indian subjects with type 2 diabetes only and in subjects with type 2 diabetes plus underlying hypertension compared to non-exercising control groups. Heart rate variability provides an index of cardiac function by autonomic and other physiological systems in subjects with existing coronary artery disease, particularly in post-myocardial infarction subjects [42]. Abnormally low heart rate variability has been associated with elevated risk for cardiovascular events [43]. Taken as a whole, PRT and AER training in high-risk ethnic populations with type 2 diabetes may reduce blood pressure and heart rate variability and minimise morbidity and mortality secondary to myocardial infarction and stroke.

Only two studies evaluated the metabolic response to exercise between different

ethnic groups [25, 30]. Glans *et al.* [30] reported a statistically significant 0.6% reduction in HbA_{1c} and a 41% increase in insulin sensitivity in Swedish but not Middle-Eastern participants performing the same exercise protocols. The lack of change in these outcomes in the Middle-Eastern group compared to the Swedish group might be explained by: 1) lower exercising workloads (105.3 ± 22.0 vs. 123.0 ± 22.0 W) and achieved training heart rates (63% vs. 73% maximum heart rate), respectively; 2) fewer subjects available for follow-up hyperinsulinaemic-euglycaemic clamp assessments, thus potentially diluting the statistical power of this outcome measure in both groups; and 3) baseline HbA_{1c} levels in both groups were already below 7%, so the physiological ceiling for improvement in the Middle-Eastern group may have been diminished [30]. In another study comparing exercise modality by race, Winnick *et al.* [25] reported a significant reduction in BMI and HOMA-IR scores and a trend toward improved β-cell function in African-American subjects receiving eight weeks of PRT compared to Caucasian subjects receiving identical training volumes. Insofar as African-Americans and continental Africans exhibit higher levels of insulin resistance than European-Americans [44], the preferential reduction in insulin resistance and improved insulin secretory capacity (i.e., β-cell function) in African-Americans compared to Caucasians after PRT are important findings [25] which, under similar experimental conditions, suggest that different exercise modalities may exert differential effects in different racial groups. Moreover, Caucasian subjects experienced a larger reduction in BMI in response to AER training compared to African-Americans, further supporting the possibility that the efficacy of exercise management of type 2 diabetes may be relative to modality and race. Additional studies comparing ethnic groups are necessary to confirm these preliminary findings.

The lack of significant change in glycaemic control and associated health

outcomes in two studies [26, 31] may be due to heterogeneity in exercise prescription variables and identified methodological and reporting inadequacies. For example, while most trials [24, 25, 27-30] prescribed exercise three to five days per week, the lack of change in HbA_{1c} in Chinese subjects reported by Sykes *et al.* [31] was likely due to an insufficient exercise stimulus associated with one supervised training session per week for 12 weeks. In another study by Van Rooijen *et al.* [26], there was no change in HbA_{1c} in Sub-Saharan African women randomised to perform 45 minutes of daily unsupervised walking for 12 weeks. Exercise log books completed by subjects revealed poor compliance (no percentage provided) to exercise recommendations [26] and may therefore have resulted in a less than optimal training stimulus insufficient to effect significant improvements in glycaemic control. Future investigations should prescribe at least three exercise sessions per week, provide adequate supervision, and report detailed compliance data in order to identify contributing factors which may explain enhanced or decreased efficacy of specific exercise interventions.

The disparities in type 2 diabetes prevalence and prognosis in high-risk ethnic groups are multi-factorial and are likely the result of the complex interaction between environmental, genetic, and physiological factors. Documented interethnic differences in insulin secretion and sensitivity [11, 12, 14, 44-46] and, more recently, in response to a structured exercise prescription, [25, 30] raise questions about whether the impact of a quantified dose of exercise would be the same across all ethnic groups. Although this systematic review is limited by the small number of published exercise trials in high-risk ethnic groups with type 2 diabetes, it provides the necessary starting point to facilitate discussions and prompt additional research in this area. Future investigations should provide thorough descriptions of all experimental protocols consistent with the latest Consolidated Reporting of Standard Trials statement [47], with detailed

information regarding exercise modality, frequency, intensity, duration, attendance, and compliance. A greater understanding of the physiological impact of exercise on glycaemic control and associated clinical outcomes may be useful in establishing targeted evidence-based exercise prescription guidelines which may lead to enhanced diabetes management strategies and reduced morbidity and mortality in high risk ethnic groups with type 2 diabetes.

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CHAPTER 3

Cultural Considerations, Methodology, and Implementation of a Randomised Trial of Exercise Training in New Zealand Māori and Pacific Islands People

3.1 Introduction

Exercise, in conjunction with diet and medication, plays an important role in the management of type 2 diabetes. Chapters 1 and 2 presented the findings of lifestyle interventions for reducing diabetes risk factors [1-4] and obesity [5] in Māori [1, 2] and Pacific Islands people [3-5], and clinical trials of exercise training in other high-risk ethnic groups [6-13]. However, a number of methodological and reporting limitations such as insufficient training stimulus (i.e., low exercise frequency and intensity), inadequate supervision of exercise sessions, or incomplete descriptions of methods and results limit the extent to which inferences can be made regarding the efficacy of exercise in high risk ethnic cohorts. A review of studies published prior to beginning the **S**outh **P**acific **I**slands **R**esist diabetes with **I**ntense **T**raining (SPIRIT) study were taken into consideration in the development of the research design and study for this Ph.D project.

In the present trial, there are three overarching outcome measure categories which address metabolic control, cardiovascular risk, and quality of life. First, it is hypothesised that improvements in glycaemic control and insulin sensitivity will be mediated by favourable changes in blood and muscle markers and anthropometric measurements. Glycosylated haemoglobin is the primary outcome and is widely used for determining glycaemic control over a 90 to 120 day time frame [14]. Both aerobic [15-17] and resistance exercise [6, 15, 18, 19] have been previously shown to reduce glycosylated haemoglobin, which may translate to a significant reduction in risk for the development of long-term diabetes complications [20]. Fasting plasma glucose and insulin provide an overall indication of glycaemia and insulinaemia and are required for the determination of insulin resistance via the homeostatic model assessment calculator [21]. The McAuley Index is a novel measure of insulin sensitivity previously validated

in the New Zealand population and provides a higher sensitivity and specificity for predicting insulin sensitivity compared to only fasting insulin [22]. Plasma free fatty acids are frequently elevated in patients with hepatic and peripheral insulin resistance [23], with exercise shown to result in a favourable reduction in this parameter [24]. C-peptide is a by-product of the post-translational processing of insulin and provides an indication of whether pancreatic β-cells are still able to synthesise and secrete insulin [25]. Enhanced insulin sensitivity in individuals with type 2 diabetes may result in decreased insulin demand and therefore and associated reduction in stress on pancreatic β-cells [26]. Markers of systemic low-grade inflammation such as C-reactive protein are associated with insulin resistance [27-29] and may predict the onset of type 2 diabetes [30]. Adiponectin is an adipocytokine which is inversely associated with adiposity, with lean individuals exhibiting higher levels of adiponectin compared to more obese individuals with comparably lower concentrations [31]. Exercise has been shown to improve both C-reactive protein [32, 33] and adiponectin profiles [34] which may further help explain improvements in insulin sensitivity.

Skeletal muscle is the primary site for glucose uptake [35] and is known to be mediated by stimulation and translocation of both contraction- and insulin-dependent GLUT4 transport proteins [36]. Both aerobic and resistance exercise have been shown to increase GLUT4 content in skeletal muscle [37, 38], which may explain improvements in insulin action and, consequently, enhanced glycaemic control. Aerobic exercise-induced increases in capillary density are positively associated with greater myocellular oxidative capacity, particularly in type I muscle fibres, and is associated with enhanced insulin sensitivity [24].

Height and weight are standard anthropometric measures necessary for calculating body mass index, a general indicator of body size relative to health risk [39].

However, body mass index does not provide a direct indication of changes in body composition. Bioelectrical impedance analysis is a readily available and previously validated field measure [40] useful for determining lean body mass, fat mass, and percent body fat. This particular method is practical in a research setting due to its ease of use, non-invasive nature, subject comfort, and low cost. Identified exercise-induced increases in muscle mass and reductions in fat mass [6] may explain potential improvements in glycaemic control, secondary to enhanced insulin sensitivity and glucose uptake. Waist circumference has been shown to correlate with more sensitive measures for determining visceral adiposity (i.e., CT scans, MRI) [41] and is linearly associated with cardiometabolic risk factors [42]. In conjunction with body composition data, reductions in abdominal fat depots may also explain composition-mediated improvements in insulin sensitivity.

Individuals with type 2 diabetes are at two to four times greater risk for the development of cardiovascular disease, chiefly due to a combination of impaired blood lipid profiles and hypertension [43, 44]. Structured exercise has been shown to favourably alter blood lipids [45], as well as lower blood pressure [46]. Thus, an improvement in these parameters may significantly improve long-term prognosis in this high-risk Polynesian population.

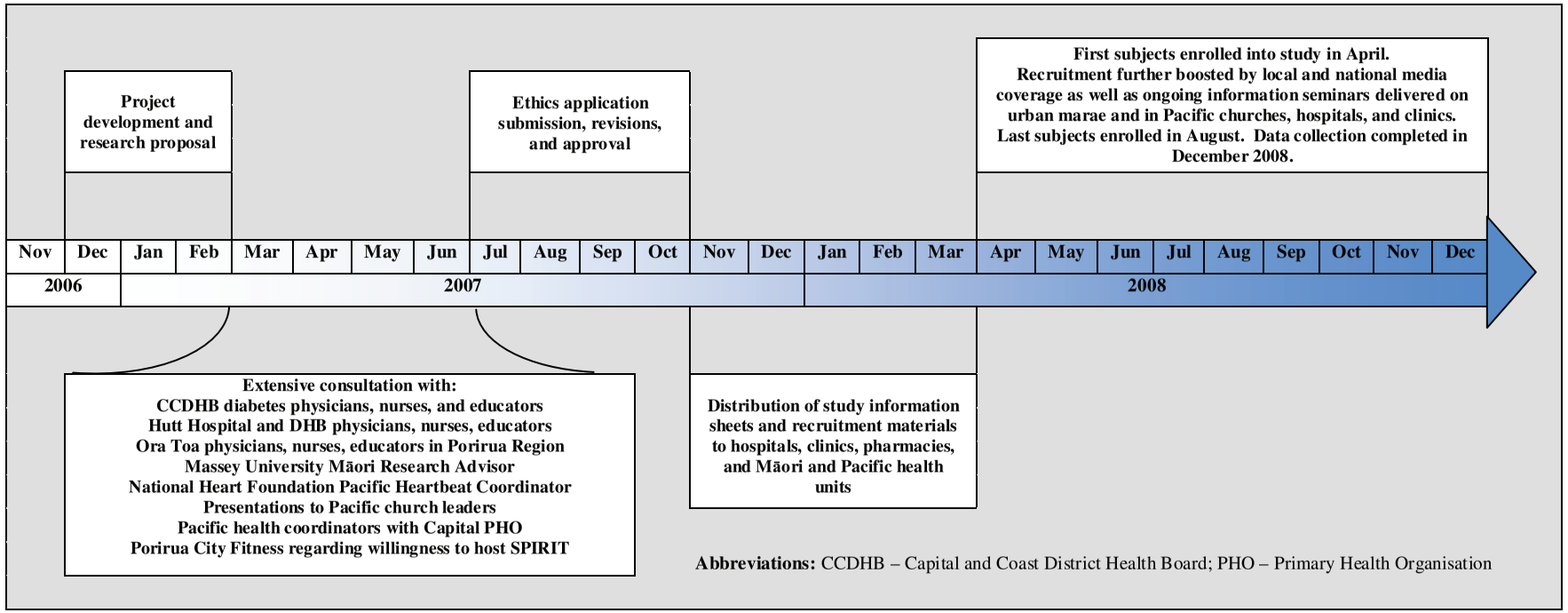
Quality of life is reduced in people with type 2 diabetes, secondary to the adverse effects of comorbid conditions and diabetic complications [47-50]. Preliminary evidence suggests a role for exercise training [51] or exercise consultation [52] for improving quality of life outcomes. The Medical Outcomes Trust Short Form-36 Health Survey (SF36) has been validated in a New Zealand population [53], but to date no studies have been conducted on the impact of exercise in a Polynesian cohort with type 2 diabetes.

The purpose of this chapter is to comprehensively describe the experimental design and methodology of the SPIRIT study. Research within New Zealand must also be carried out in a culturally-sensitive manner with respect to Māori and Pacific Islands people. Accordingly, this chapter will also describe the extensive consultation that took place with Māori and Pacific cultural and community leaders, medical and allied health professionals working in hospitals, and health clinics in the greater Wellington region to enable undertaking of the SPIRIT study.

3.2 Cultural, medical, and organisational consultation

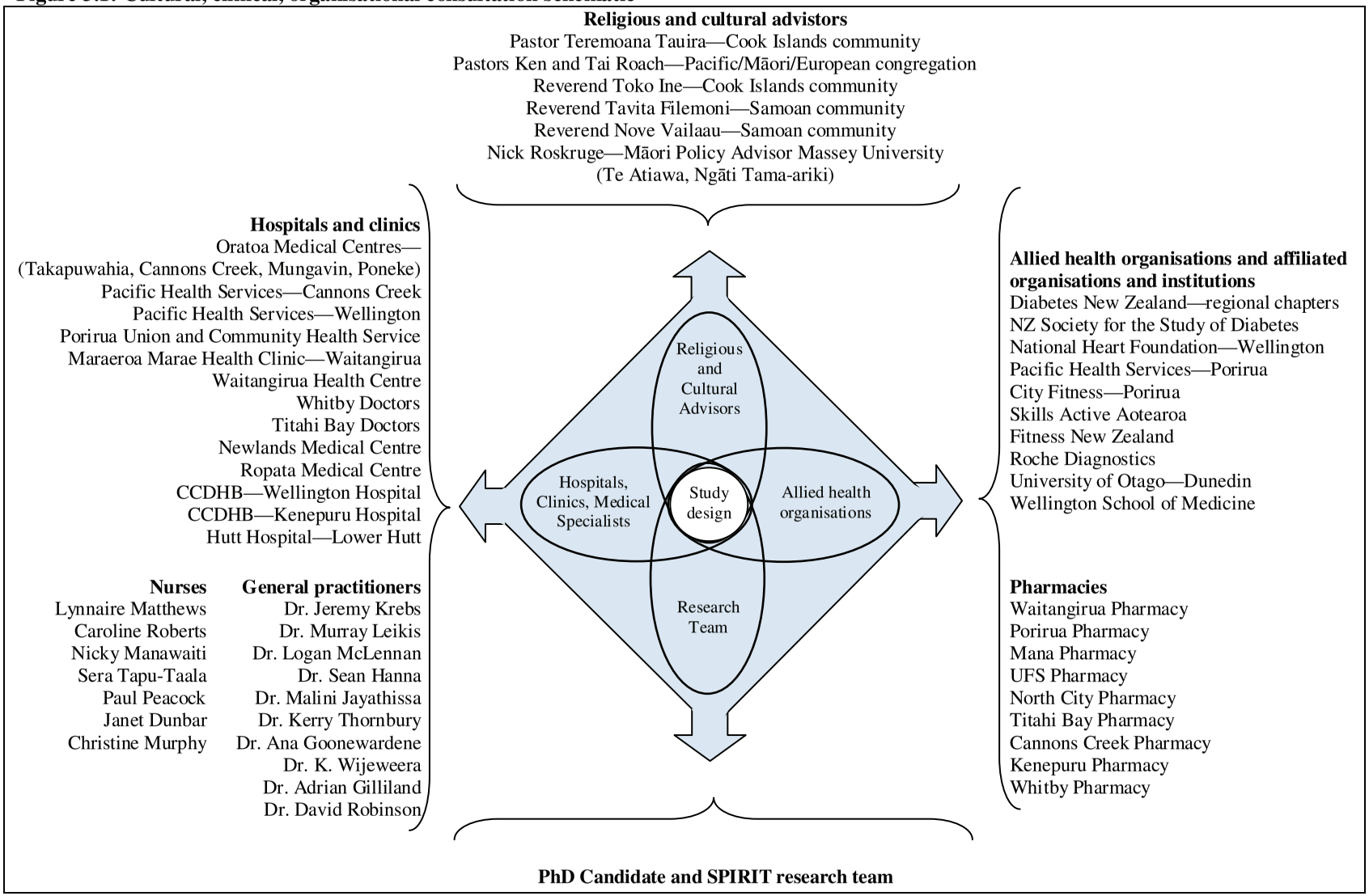
In conceptualising the present study, extensive consultation was undertaken with cultural, religious, community and health care leaders (Figure 3.1) throughout the Porirua and Wellington regions for a period of 18 months (Figure 3.2) prior to enrolling the first subjects in April 2008. Consultation consisted of numerous meetings and presentations to Māori and Pacific cultural leaders and health care liaisons to discuss participant safety and the potential benefit to the Polynesian community. Proposed research protocols and participant literature (information sheets, consent forms, questionnaires, etc) were developed in partnership with cultural consultants and were given approval before submission to the ethics review board. Endocrinologist Dr. Jeremy Krebs joined the study as a medical specialist collaborator and provided initial and ongoing technical and medical advice regarding the study design and safety protocols. Organisational support and guidance were received from the National Heart Foundation's Pacific Heartbeat liaison, Capital and Coast District Health Board, Ora Toa Health Services, Pacific Health Services Wellington, University of Otago, and Roche Diagnostics. This feedback was integrated into the research proposal which, once approved by cultural liaisons, was submitted to and approved by the Central

Figure 3.2 – SPIRIT study timeline



Abbreviations: CCDHB – Capital and Coast District Health Board; PHO – Primary Health Organisation

Figure 3.1: Cultural, clinical, organisational consultation schematic



Regional Ethics Committee in Wellington.

Religion is a prominent focal point in the lives of many New Zealand Māori and Pacific Islands people, with the church (and Marae, a Māori meeting place where cultural and spiritual identity is reaffirmed) being a central meeting place to affirm spiritual and cultural identities. The SPIRIT study title reflected this and was well received by study participants and cultural and religious leaders.

3.3 Participants

3.3.1 Sample size

The SPIRIT study was initially intended to be a randomised controlled trial comparing a resistance training group to a non-exercise control group. A sample size of 12 per group was determined *a priori* based on a previous study of similar design by Castaneda *et al.* [6] and is illustrated below.

Table 3.1: Sample size calculation

T-tests: Means: Difference between two independent means (two groups)
Analysis: A priori: Compute required sample size

Input	Tail(s)	=	Two
	Effect size d	=	1.2162423
	α err prob	=	0.05
	Power (1- β err prob)	=	0.80
	Allocation ratio N2/N1	=	1
Output	Noncentrality parameter δ	=	2.979173
	Critical t	=	2.073873
	Df	=	22
	Sample size group 1	=	12
	Sample size group 2	=	12
	Total sample size = 24		

However, upon initiation of subject recruitment, many subjects stated they would drop out if randomised to a non-exercise control group because they knew exercise could potentially improve their diabetes and facilitate weight loss. After further consultation with cultural liaisons, the substitution of an aerobic exercise group in place of the control group was deemed a feasible and acceptable option to participants.

3.3.2 Subject screening

Individuals were selected for participation in the trial if they met the following inclusion criteria: 1) self-identified Māori or Pacific Islands descent; 2) diagnosis of type 2 diabetes by physician [54]; 3) waist circumference of ≥ 88 cm for women and ≥ 102 cm for men; 4) physically inactive for ≥ six months; 5) no change in diabetes medications for previous two months; and 6) no acute or chronic medical conditions for which exercise would be contraindicated as outlined by the American College of Sports Medicine (ACSM) [55]. All protocols and safety procedures were developed in partnership with consulting diabetes specialists and were in accordance with established international safety guidelines for exercise set forth by the American Diabetes Association [56] and ACSM [55].

After initial telephone pre-screening, potential participants were invited along with family and friends for a private consultation to learn more about the SPIRIT study and ask questions. Home and office visits were made by the principal investigator (WRS) to accommodate busy work and family schedules. Written informed consent (Appendix A) was obtained from all subjects and their respective general practitioners, with the latter responsible for conducting a thorough medical history review of each participant. This review entailed physicians reviewing their patients' records and completing a detailed checklist (Appendix B) before giving signed authorisation for

participation in the study. All procedures and protocols were approved by the Central Regional Ethics Committee (CEN/07/08/054), and the trial was registered with the Australian New Zealand Clinical Trials Registry (number: ANZCTR12609001085268) (Appendix C)

3.3.3 Recruitment

The SPIRIT recruitment process differed markedly from the usual procedure of placing a newspaper advert or strict reliance upon referrals from medical management teams. Health care professionals affiliated with clinics in the Porirua region initially provided the SPIRIT study contact details to potentially eligible diabetic patients but this resulted in few referrals. This was addressed by instead having general practitioners and practice nurses forward the names and phone numbers of interested and eligible candidates (with permission) to WRS, at which time first contact was initiated. The first wave of enrolled subjects referred friends, family, co-workers, and fellow church congregants to the study similar to the "snowballing" effect previously described by Murphy and colleagues [2]. Some subjects contacted WRS after viewing several media stories on the study (Appendix D).

3.3.4 Randomisation

Following baseline testing, participants were randomly assigned *via* computer-generated randomisation list [57] stratified by gender in blocks of four to receive 16 weeks of either PRT or AER. Randomisation assignments were generated by an investigator who was not involved in testing or training and delivered to patients in opaque sealed envelopes on the completion of all baseline testing.

3.4 Exercise venue

Exercise sessions were initially planned to take place at the fitness centre on Massey University's Wellington campus, but several issues including traffic, distance, lack of parking, and scheduling arrangements in relation to existing programs would have adversely impacted upon recruitment and implementation. Instead, the trial was conducted at Porirua City Fitness gym. The club is located in the largely Polynesian suburb of Porirua (21 km north of Wellington) and has a high Māori and Pacific membership base. Participants were welcomed by members and employees, many of whom were already close personal contacts from the community. Porirua City Fitness management allocated staff time and resources (offices, equipment) at no cost to the SPIRIT study to help ensure the smooth execution of the study protocols. Participants received free memberships for the duration of the study intervention period (16 weeks) and were encouraged by investigators to bring family and friends free of charge to support their efforts. During initial consultation with cultural leaders and allied health professionals, there was concern that a commercial fitness centre would be a potential barrier to Māori and Pacific Islands people. However, participants anecdotally stated their satisfaction with Porirua City Fitness, and that the large Polynesian membership and cultural influence within the venue created a comfortable environment which enhanced the experience and facilitated the study's execution. For example, some participants spoke their native language and engaged in prayer with fellow study participants and club members before or after training sessions.

3.5 Intervention

Group exercise training sessions were held three times per week (Monday, Wednesday, and Friday) in the morning and afternoon and lasted no longer than 50

minutes, including warm-up and cool-down procedures. Pre- and post-exercise pulse rate, blood pressure, and capillary blood glucose (via Accu-Chek Performa glucometer, Roche Diagnostics, Auckland, New Zealand) were monitored and recorded at each session (Appendix B). WRS maintained ongoing communication with each participant's diabetes management team (e.g., endocrinologist, general practitioner, diabetes nurse specialist) and reported any untoward signs or symptoms. Subjects continued to receive their usual medical care and were instructed to maintain their current dietary and physical activity habits. Weekly status checks (Appendix B) were conducted and any adverse signs or symptoms were reported to participants' general practitioner.

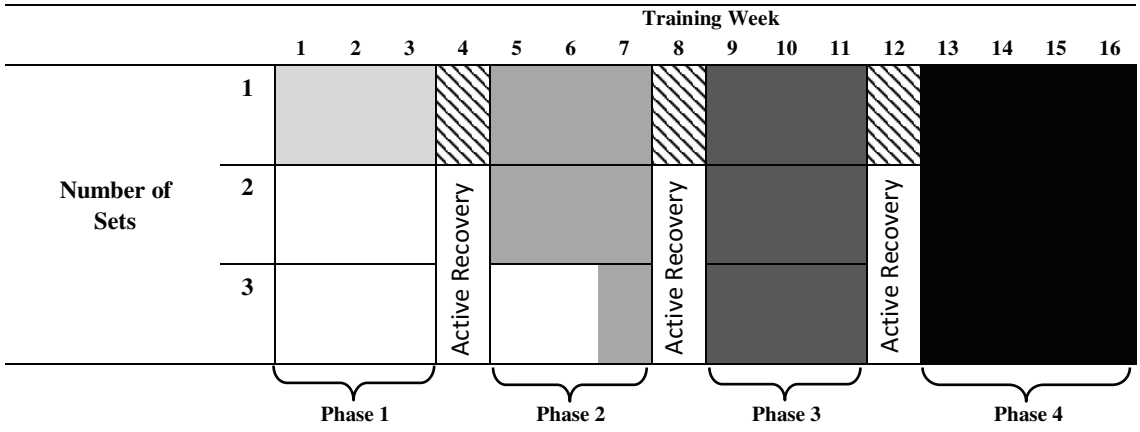
3.5.1 Exercise leaders

All exercise sessions were personally supervised by WRS, a qualified clinical exercise physiologist with extensive experience working with obese, diabetic, and cardiac patients. Four advanced (year 3) exercise science students from Massey University and three New Zealand Registry of Exercise Professionals-certified personal trainers from Porirua City Fitness were familiarised with the intervention protocols and assisted in providing one-on-one attention to participants before, during, and after exercise in order to ensure both safety and compliance to study protocols. Four of the seven exercise leaders were of Māori and Pacific Islands heritage and regularly reaffirmed cultural and ethnic identities. Furthermore, a number of Māori and Pacific religious and community leaders involved in establishing the study were also Porirua City Fitness members and periodically provided on-site encouragement to participants.

3.5.2 Progressive resistance exercise

After a five minute warm-up, subjects performed eight machine-based resistance exercises in a circuit format targeting all major muscle groups: seated leg press, knee extension, knee flexion, chest press, lat pulldowns, overhead press, biceps curls, triceps extension (Cybex International, Medway, MA). Due to the level of physical deconditioning and class III morbid obesity (Body Mass Index [BMI] = 43.8 ± 9.5 kg/m^2; n = 18) observed in this cohort, a one-repetition maximum (1RM) lift at baseline was deemed inappropriate for safety reasons. Initial weights were therefore determined as a percentage of the extrapolated 1RM as previously described by Brzycki [58]. A graduated periodised regimen was employed as illustrated in Figure 3.3 and 3.4. Subjects progressed from 65% to 85% of their extrapolated 1RM over the course of phase 1, two sets at 85% during phase 2, three sets at 85% during phase 3, and a continuation of three sets at 85% until conclusion of the intervention. This regimen was chosen because it is known to promote muscular hypertrophy and therefore enhance insulin sensitivity and glucose uptake [59]. Subjects performed six to eight repetitions with a one minute rest between sets. Workloads were increased by five percent when subjects could

Figure 3.3: Progressive resistance training schematic



Weeks 4, 8, and 12 were designated active recovery weeks where resistance was reduced by 10%.

Figure 3.4: Progressive resistance training subjects

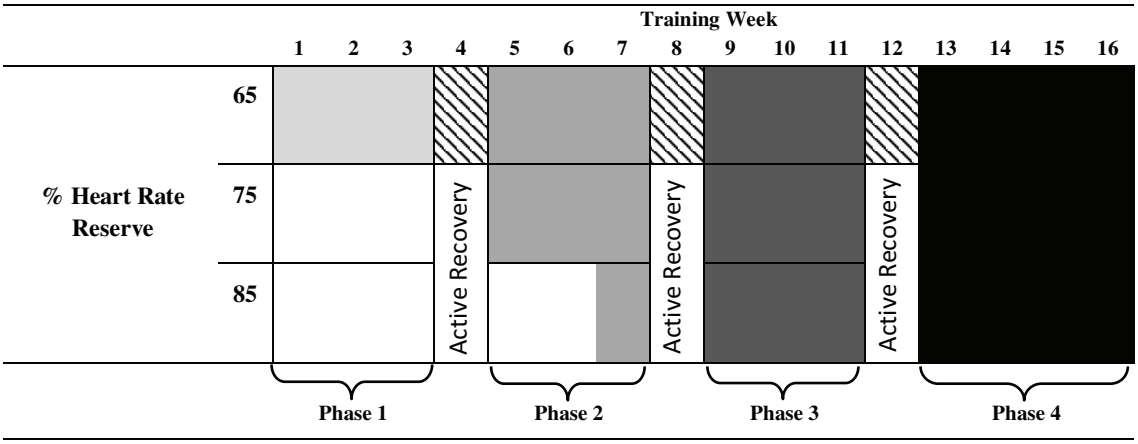
perform 10 repetitions. Exercise leaders encouraged subjects to exercise at a perceived exertion of "hard," or 15, on the Borg scale (6 – 20 scale) [60]. In order to minimise the risk of overtraining, weeks four, eight, and 12 were designated active recovery weeks in which subjects performed one set on each exercise at a weight 10% less than the previous week's peak workload.

3.5.3 Aerobic exercise

Subjects randomised to the AER group performed a graduated cycle ergometry (Life Fitness, Schiller Park, IL, USA) protocol (Figure 3.5 and 3.6) in parallel with the PRT group. An equivalent training frequency, duration, and intensity were prescribed to evaluate the training response between modalities. AER not only improves cardiovascular fitness, but is also known to enhance insulin sensitivity and consequently glycaemic control [59]. After familiarisation with the equipment at week 0, subjects

gradually progressed from 65 to 85% of their heart rate reserve during subsequent sessions. They were encouraged to sustain a rating of perceived exertion of "hard," or '15' on the Borg scale [60]. Heart rate and blood pressure were monitored and recorded at peak steady state workloads (Appendix B). Watts and duration at peak intensity were increased to accommodate improved fitness levels over time. Similar to the resistance training group, weeks four, eight, and 12 were designated active recovery weeks in which subjects exercised at an intensity 10% less than the previous week's peak workload achieved during the previous week.

Figure 3.5: Aerobic training schematic



Weeks 4, 8, and 12 were designated active recovery weeks where intensity was reduced by 10%.

Figure 3.6: Aerobic exercise subjects

3.6 Outcome measure assessments

Outcome measure assessments were performed at baseline and after 16 weeks of exercise training. Health history assessment forms (Appendix B) and the Medical Outcomes Study Short-Form General Health Survey version 1 (SF36) quality of life (QOL) questionnaire [61] (Appendix B) were completed in a quiet room at Porirua City Fitness gym. Blood draws, anthropometric, haemodynamic, and muscle biopsy procedures were performed at Kenepuru Hospital in Porirua after an overnight fast. Many subjects were familiar with the hospital because they (or family) had previously been admitted as a patient or attended health education classes. Moreover, it is also a trusted local healthcare institution with multilingual signage and culturally-diverse staff. SPIRIT study investigators or hospital staff greeted participants upon arrival and guided them to the exam rooms.

3.6.1 Biochemical measurements

Fasting blood draws were performed by hospital phlebotomists and sent to the medical laboratories at the Capital and Coast District Health Board and Canterbury District Health Board for analysis. Glycosylated haemoglobin was the primary outcome measure and was determined by ion exchange high pressure liquid chromatography using the Bio-Rad D-10 analyser (Bio-Rad Laboratories, Hercules, CA, USA) with a coefficient of variation (CV) of 3%. Plasma glucose was determined by the hexokinase enzymatic method on the Roche Modular Analyser (Roche Diagnostics, Indianapolis, IN, USA) with a CV of 3%. Serum free insulin concentration was determined by electrochemiluminescence immunoassay using an Elecsys 2010 immunoanalyser (Roche Diagnostics, Indianapolis, IN, USA) with a CV of 3.8%. Insulin resistance was estimated by two methods: 1) from fasting glucose and insulin *via* homeostasis model assessment (HOMA2-IR software, version 2.2.2, Oxford University) [21], a method previously validated against the euglycaemic clamp [62]; and 2) the McAuley Index (MI) (calculated as MI = EXP [2.63 – 0.28LN(fasting insulin) – 0.31LN(fasting triglycerides)]), which has also been validated against the euglycaemic insulin clamp [22]. Serum free fatty acids were determined enzymatically by the ACS-ACOD method (Wako Chemicals, Neuss, Germany). Serum C-peptide concentrations were determined by electrochemiluminescence immunoassay using an Elecsys 2010 immunoanalyser (Roche Diagnostics, Indianapolis, IN, USA) with a CV of 4.5%. Serum total cholesterol, high density lipoprotein (HDL) cholesterol, and triglyceride concentrations were measured using standard enzymatic methods (Roche/Hitachi lipid assay kits) with a Roche Modular Analyser with a CV of 3% on each assay. Low density lipoprotein cholesterol was mathematically determined as total cholesterol – HDL – (0.45 × TG). C-reactive protein was determined by latex agglutination method on the Roche Modular

Analyser with a CV of 4%. Adiponectin was measured by radioimmunoassay (Linco Research, St. Charles, MO, USA) with a CV of 8.8%. Data sheets are presented in Appendix B.

3.6.2 Anthropometric and haemodynamic measurements

Height and weight were measured to the nearest 0.1 cm and 0.1 kg on a calibrated hospital stadiometer and scale, respectively. BMI (in kg/m^2) was calculated from these measures. Lean body mass, fat mass, and percent body fat were estimated *via* bioelectrical impedance analysis (Tanita TBF-310 analyser, Tanita Corporation, Arlington Heights, Illinois, USA). Waist circumference was measured to the nearest 0.1cm at the end of normal expiration and the midpoint between the lower costal margin and the iliac crest using a retractable steel tape measure (model F10-02. KDS Corporation, Japan). Resting blood pressure was measured in duplicate from the left arm after 5 minutes of seated rest on a standard hospital sphygmomanometer, with the lowest blood pressure being recorded. Large adult cuffs were used if the subject's arm was too large for the standard cuff size. Data sheets are presented in Appendix B.

3.6.3 Muscle biopsy procedure

3.6.3.1 Specimen harvest

Muscle biopsy samples (~200 mg) were harvested from the right vastus lateralis under local anaesthesia (1% Xylocaine, Astra Zeneca Ltd, Auckland, New Zealand) using a 5 mm Bergstrom needle with applied suction [63] at baseline and 16 weeks. Consistent with previous research [64], follow-up testing was standardised to 72 hours after completion of the final exercise session to minimise the potential confounding

effect of the acute exercise response from the last training session. Participants were given the opportunity to speak with the physician performing the biopsy, ask questions, and reserved the right to refuse the procedure. All subjects gave separate written informed consent for the biopsy procedure (Appendix A). Muscle samples were oriented longitudinally in Tissue-Tek optimal cutting temperature (OCT) embedding medium (Sakura Finetek Ltd, Tokyo, Japan) and snap frozen in liquid nitrogen-cooled isopentane and stored in Eppendorf cryotubes at −80 °C until analysed. Following the biopsy, the incision site was cleaned, closed with sterile adhesive strips, dressed in gauze, and covered by a waterproof Tegaderm dressing (3M, St. Paul, MN, USA).

3.6.3.2 Muscle sectioning and immunohistochemistry

Serial 10 μm transverse muscle biopsy sections were cut using a CM1850 Cryostat (Leica Microsystem, Nussloch, Germany) and mounted on standard laboratory microscope slides treated with Vectabond Reagent (Vector Laboratories, Burlingame, CA, USA). Glucose transporter 4 (GLUT4) and capillary density were determined by immunohistochemical labelling. Sections were dried at room temperature for 30 minutes followed by a 15 minute rinse in phosphate buffered saline (PBS) to remove OCT residue. Slides were treated with 100 μl of 1% bovine serum albumin (BSA), incubated for 30 minutes, then rinsed with PBS before application of primary antibodies. For each subject, two slides were incubated for four hours with 100 μl Abcam rabbit anti-GLUT4 antibody (1:1000) (AB654, Sapphire Bioscience Pty Ltd, NSW, Australia) and two slides with 100 μl rabbit anti-von Willebrand Factor antibody (1:2000) (AB7356, Chemicon). Primary antibodies were not applied to negative control slides and were treated with 100 μl of 1% BSA only. After rinsing with PBS, all slides were treated for four hours with 100 μl of AlexaFluor 594-conjugated anti-rabbit (1:250

each) secondary antibodies (Invitrogen, Auckland, NZ). Slides were rinsed and cover-slipped with Vecta-Shield anti-fade mounting medium (Vector Laboratories, Burlingame, CA, USA).

3.6.3.3 Muscle outcomes quantification

Muscle sections were examined using an Olympus BX-50 upright compound fluorescent microscope (Olympus Ltd, Tokyo, Japan) and images were captured with a SPOT-RT Slider cooled CCD camera (Diagnostic Instruments, Sterling Heights, MI, USA) (Figures 3.7 and 3.8). Image quantification was performed by an independent assessor unaware of subject group assignment. Uncompressed eight-bit TIFF images were opened in Adobe Photoshop CS4. The image capture protocol was defined so images contained data only in the red channel. The background colour range (red channel) was determined by examination of histograms for negative control specimens and indicated the maximum grey level for any background pixel in the red channel was 50. Therefore, in reacted specimens, any pixels with grey levels above 55 in the red channel were deemed immunolabelled. An unfeathered colour range selection of 55−255 in the red channel was created and saved. Each imaged was opened, the colour range selection tool activated, and the previously saved 55−255 selection was loaded. The number of pixels enclosed by the selection was recorded from the histogram palette. GLUT4 and capillary density were quantified as number of reactive pixels per muscle fibre. The values for labelled pixels were recorded for serial images within subjects and exported to a Microsoft Excel spread sheet. Values were averaged and exported to the statistics package for further analysis.

Figure 3.7: Capillary density

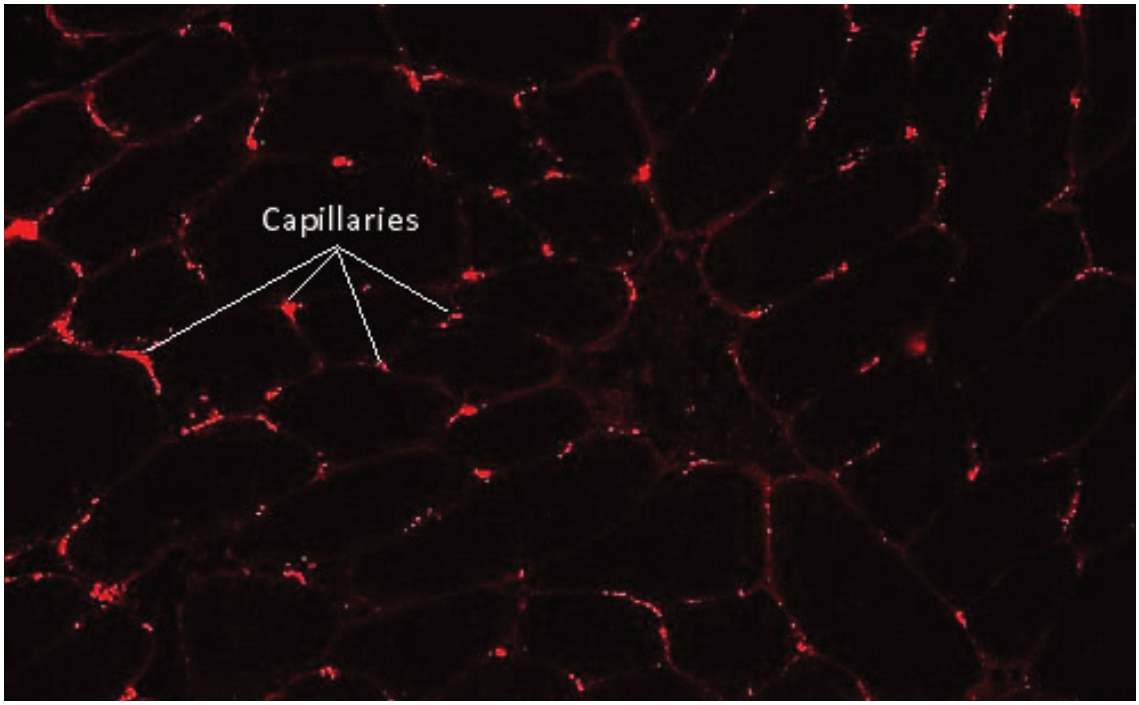
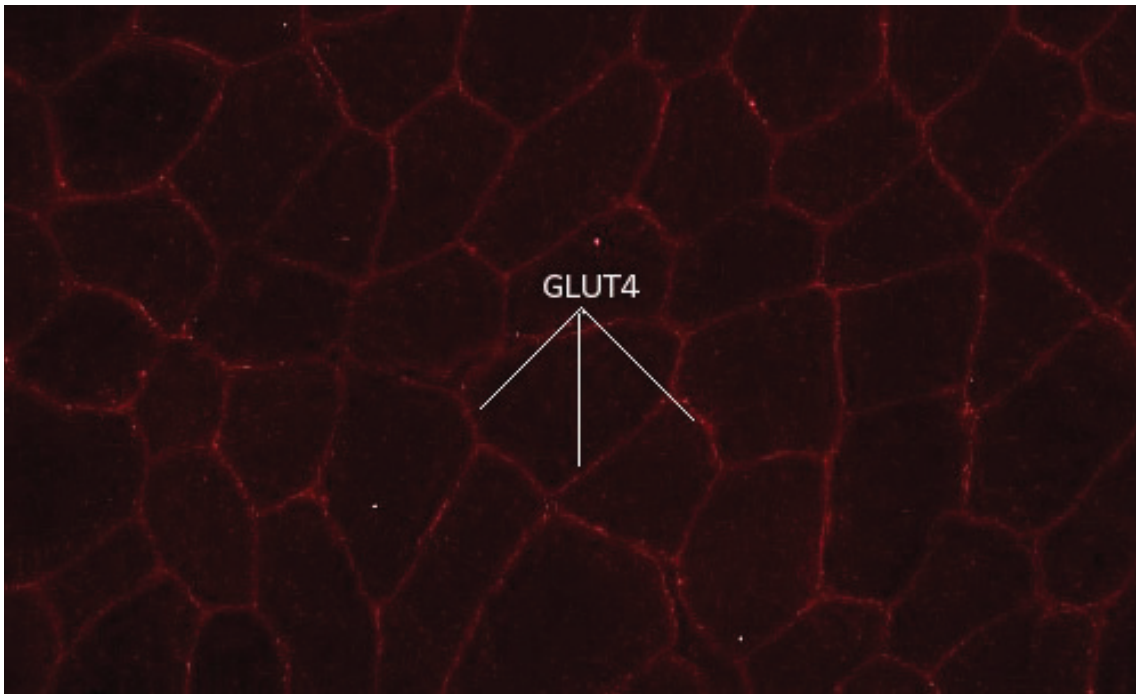


Figure 3.8: GLUT4 density



3.6.4 Quality of life assessment

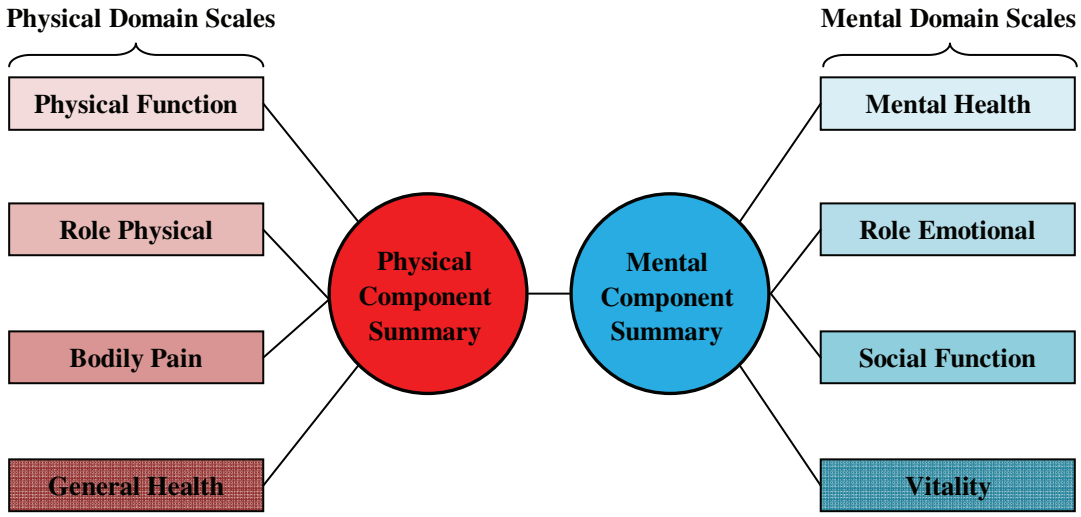
The SF36 (version 1) questionnaire was used to evaluate health-related QOL [61] (Appendix C). This survey has been validated in patients with type 2 diabetes [53] and in the general New Zealand population, including Māori and Pacific Islands people [65]. The questionnaire is comprised of 36 questions represented by eight scales measuring physical (Physical Functioning, Role-Physical, Bodily Pain, and General Health) and mental domains (Mental Health, Role-Emotional, Social Functioning, and Vitality). Higher scores (range 0–100) indicate better perceived QOL. Physical and Mental Component Summary scores are also derived from four physical and four mental domain scales, respectively, and provide an overall score for the physical and mental well-being of the respondent (Figure 3.9).

The practical meaning of changes in SF36 domain scores have been previously described by Ware and Gandek [61]. Improvements in Physical Functioning suggest an enhanced ability to perform all types of physical activities, including those classified as vigorous, without health-related limitations. Improvements in the Role-Physical domain indicate subjects were able to carry out their activities of daily living without difficulty. Improved Bodily Pain scores indicate no pain or limitations due to pain. Higher General Health scores reflect improved subjective perception of personal health. Enhanced Vitality scores indicate improved feelings of vigour and energy. Social Functioning improvements indicate subjects were able to perform their usual social activities without interference due to physical or emotional problems. Role-Emotional improvements indicate no limitation in the ability to perform work or other activities of daily living due to emotional difficulties. Improved Mental Health scores reflect feelings of mental peace, calm, and happiness. The Physical Component Summary

score is drawn from the four main physical domains (Physical Functioning, Role-Physical, Bodily Pain, and General Health) and higher scores reflect an overall subjective improvement in physical status, well-being, and energy levels. The Mental Component Summary is drawn from the four mental health domains (Vitality, Social Functioning, Role-Emotional, and Mental Health) with higher scores reflecting improved psychological well-being and a reduction in limitations in work duties and activities of daily living secondary to emotional distress.

The SF36 was administered to subjects in a quiet office before randomisation and after the 16 week intervention period.

Figure 3.9: SF-36 physical and mental component summary scales. Adapted from Ware and Gandek (1998) [21]



3.7 Statistical analyses

Statistical analyses were performed on metabolic, anthropometric, haemodynamic, and muscle biopsy data using StatView™ statistical software package (Version 5.0 SAS Institute, Cary, NC). Data from patients who were unavailable for

post-16 week assessments were excluded, as per protocol analysis. All data were visually inspected and statistically evaluated for normality (skewness and kurtosis between –1 and +1). Normally distributed data were described as mean ± SD. Non-normally distributed continuous variables were log-transformed before analysis via parametric models. Data are presented as back transformed means ×/÷ factor standard deviation. Change scores are presented as back transformed mean difference (95% confidence limits). Baseline differences between groups were compared using an independent t-test for continuous variables. Within and between group changes from weeks 0 to 16 were analysed by repeated measures ANOVA. Linear univariate regression analyses were performed using pooled data from the whole cohort to evaluate relationships between: 1) changes in HbA_{1c} and biochemical, anthropometric, and muscle biopsy outcome measures; 2) the number of sessions attended and changes in all outcome measures, including QOL domain scores. A p-value of < 0.05 was accepted as statistically significant.

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CHAPTER 4

Metabolic, Anthropometric, and Haemodynamic Adaptations in New Zealand Māori and Pacific Islands People After 16 Weeks of High Intensity Progressive Resistance Training and Aerobic Exercise

4.1 Introduction

Numerous reviews underscore the efficacy of progressive resistance training (PRT), aerobic exercise (AER), or a combination of both as potent therapeutic modalities for improving glycaemic control and insulin sensitivity in individuals with type 2 diabetes [1-12]. Three recent meta-analyses [13-15] determined that exercise reduces glycosylated haemoglobin (HbA_{1c}) by 0.6% to 0.8%. The clinical and practical significance of tight glycaemic control has been well-documented in the United Kingdom Prospective Diabetes Study [16] in which each 1% reduction in HbA_{1c} was associated with a reduced risk of myocardial infarction (14%), microvascular complications (37%), and diabetes-related mortalities (21%).

These results clearly strengthen the argument for the clinical application of exercise for enhanced type 2 diabetes management, however, the majority of studies included in the reviews and meta-analyses were conducted with primarily Caucasian-European subjects and did not account for the potential variation which might be introduced by ethnicity. Globally, ethnic groups are disproportionately afflicted with type 2 diabetes and associated comorbidities compared to those of European-Caucasian heritage, including when sharing a common environment [17, 18]. Physiological evidence that insulin sensitivity and pancreatic β-cell function vary among high-risk ethnic groups [17, 19-23] has given rise to speculation that the exercise response might also be influenced by ethnicity. As discussed in the systematic review in chapter 2, an increasing number of exercise trials have been conducted in African [24, 25], Middle-Eastern [26], Asian Indians [27-29], Hispanic [30], and Chinese [31] subjects with type 2 diabetes, but none in a Polynesian cohort.

Four multidisciplinary lifestyle interventions for diabetes prevention [32-35] and weight reduction [36] have been conducted in obese Polynesian cohorts but the multi-

modal nature of the experimental protocols were not designed to isolate the specific impact of the exercise component (chapter 1). This doctoral research project was the first investigation to employ structured high-intensity exercise in a cohort of Māori and Pacific Islands people (n = 18) with type 2 diabetes and class III morbid obesity. Therefore, the purpose of this chapter is two-fold: 1) to evaluate whether 16 weeks of high-intensity PRT or AER improves glycaemic control and associated cardiometabolic, anthropometric, haemodynamic, and intramyocellular aberrations in sedentary Polynesian people with diagnosed type 2 diabetes and morbid obesity; and 2) to determine which modality is more effective for improving HbA_{1c} given a similar training intensity and duration.

4.2 Methods

Specific details regarding methodology for subject recruitment and collection and analysis of biochemical, anthropometric, haemodynamic, and muscle biopsy samples are presented in chapter 3.

4.3 Results

4.3.1 Subject recruitment

The recruitment algorithm is illustrated in Figure 4.1. Fifty potential subjects expressed interest in the study. Thirteen (26%) were excluded because they did not meet entry criteria (i.e., not Māori or Pacific Islands person, currently exercising, or did not have type 2 diabetes), lived too far away from the study venue (i.e., in Auckland, Christchurch, or lived in the Wellington region but it was too far to commute to Porirua), or exhibited medical contraindications for which high-intensity exercise was inappropriate (i.e., diabetic neuropathy, unstable angina, or diabetes not well-managed,

or non-compliant with recommended medical treatment). Of 37 eligible subjects, 11 (30%) declined to participate (i.e., scheduling conflicts with work, family, extracurricular activities, or no reason given). Twenty-six participants comprised of 13 Māori and 13 Pacific Islands people (Samoan (6), Cook Islander (3), Fijian (2), Tokelauan (1), Tongan (1)) were randomised to receive PRT or AER for 16 weeks (Table 4.1).

Eighteen (10 New Zealand Māori and eight Pacific Islands people) of 26 (69%) randomised participants completed the study for a drop out rate of 31% (Figure 4.1). Reasons for drop out were: work-related obligations (n = 4), no reason given (n = 2), lived too far from the study venue (n = 1), and a new pregnancy (n = 1). Nine subjects per group completed the protocol and were included in final statistical analyses.

4.3.2 Subject characteristics

Subject baseline characteristics are presented in Table 4.1. Respective baseline values for PRT and AER subjects were: age (48 ± 6 and 51 ± 4 years); years with type 2 diabetes (2.6 ± 1.8 and 3.9 ± 4.3 years); body mass index (BMI) (42.7 ± 15.5 and 45 ± 6.5 kg/m^2); waist circumference (125.4 ± 39.8 and 131.9 ± 13.5 cm); and glycosylated haemoglobin (10.7 ± 3.2 and 8.9 ± 1.9%). Systolic blood pressure (SBP) in the AER group (147.3 ± 16.1 mmHg) was significantly higher than the PRT group (123.2 ± 19.4 mmHg) at baseline (P = 0.01). PRT subjects were prescribed more blood pressure and lipid-lowering medications as compared to the AER group.

Figure 4.1: Recruitment flowchart

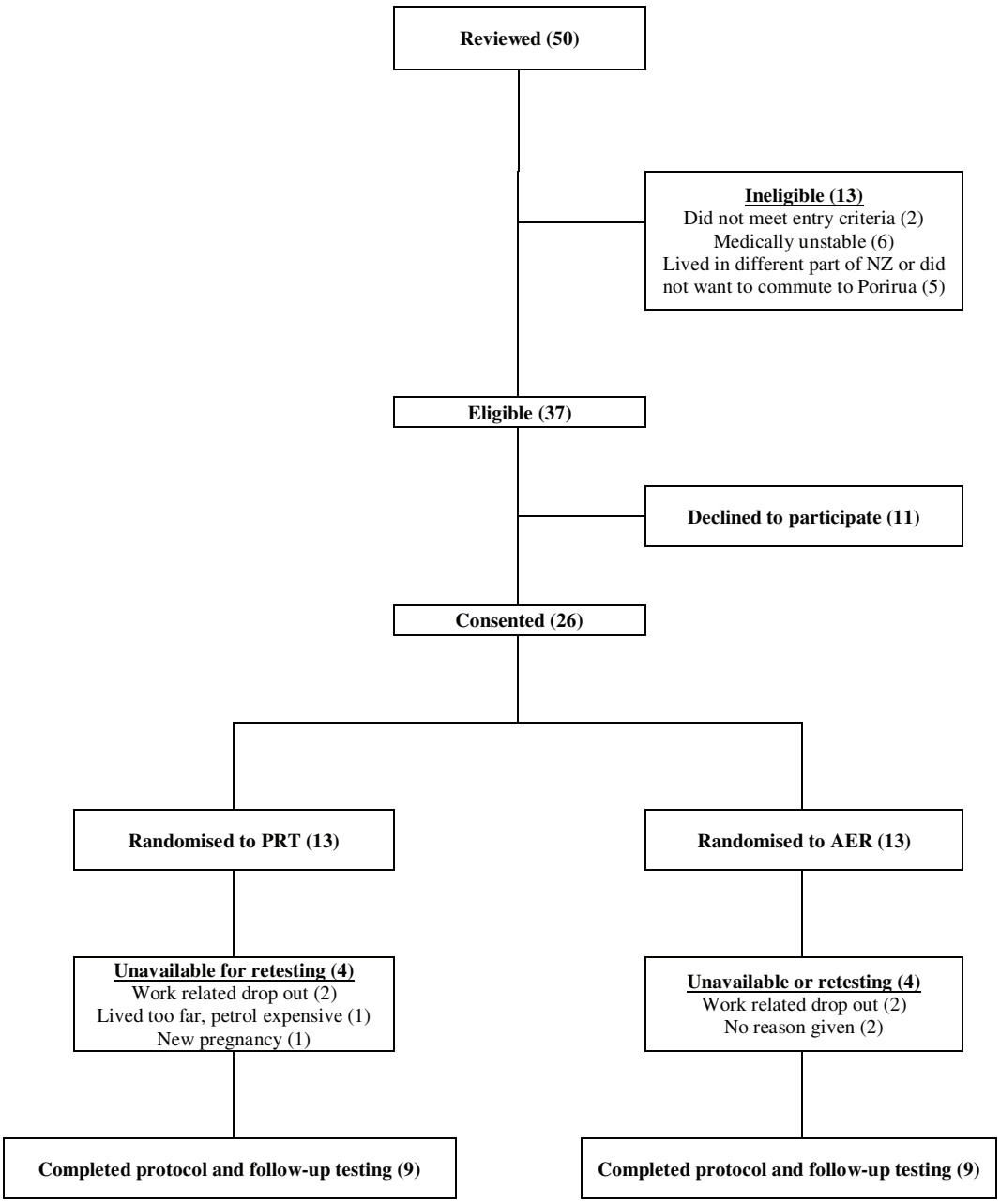


Table 4.1: Baseline subject characteristics for subjects completing the protocol (n = 18)

Characteristic	PRT Group	AER Group	Total Cohort
n	9	9	18
Age (years)	48 ± 6	51 ± 4	49 ± 5
Sex (female/male)	6/3	7/2	13/5
Height (cm)	166.2 ± 8.2	167.9 ± 5.0	167.1 ± 6.7
Weight (kg)	118.6 ± 46.0	126.8 ± 18.6	122.7 ± 29.6
Body Mass Index (kg/m^2)	42.7 ± 15.5	45.0 ± 6.5	43.8 ± 9.5
Waist Circumference (cm)	125.4 ± 39.8	131.9 ± 13.5	128.7 ± 18.7
Systolic Blood Pressure (mmHg)	123.2 ± 19.4	147.3 ± 16.1†	135.3 ± 21.3
Diastolic Blood Pressure (mmHg)	85.7 ± 13.8	90.4 ± 5.7	88.1 ± 10.6
Self-identified ethnicity			
New Zealand Māori	6	4	10
Cook Islands Māori	1	2	3
Samoan	1	1	2
Fijian	-	1	1
Tokelauan	1	-	1
Tongan	-	1	1
Diabetes duration (years) [range]	2.6 ± 1.8 [0.5 – 5]	3.9 ± 4.3 [0.5 – 13]	3.3 ± 3.3 [0.5 – 13]
Glycosylated hemoglobin (HbA_{1c}) (%)	10.7 ± 3.2	8.9 ± 1.9	9.8 ± 2.1
Diabetes management regimen			
Diet only (*n*)	1	2	3
Oral hypoglycemics (*n*)	7	6	13
Oral hypoglycemics and insulin (*n*)	1	1	2
Blood pressure lowering medications (*n*)			
ACE inhibitors (*n*)	7	4	11
Diuretics (*n*)	4	0	4
β – blockers (*n*)	2	1	3
Angiotensin II receptor antagonist (*n*)	1	0	1
Lipid lowering medication medications (*n*)	5	3	8
Current smoker (*n*)	3	2	5

Data expressed as mean ± SD. Baseline comparisons determined by independent sample t test.
†Statistically significant difference observed between groups at baseline ($P \leq 0.05$). ACE—Angiotensin converting enzyme.

4.3.3 Compliance

Eight of 18 subjects attended at least 36 of 48 (75%) available sessions. Common reasons for missed sessions were work, family, flu, funerals, and pre-existing obligations planned prior to volunteering for the study. However, compliance with PRT and AER protocols was 100% when subjects were present for exercise sessions and was ensured through direct supervision by the high ratio of qualified exercise leaders to subjects (chapter 3.5.1).

4.3.4 Adverse events

No hypoglycaemic episodes were reported during or after exercise, or at home on non-training days as determined *via* weekly status checks. No exercise-related musculoskeletal injuries were reported. Some subjects experienced mild muscle soreness after the initial exercise session, but this was managed conservatively and did not require treatment. One PRT subject experienced a syncopal episode during exercise which spontaneously resolved upon placing him in the supine position. Further evaluation at a nearby hospital ruled out myocardial infarction. This subject resumed exercise after receiving written clearance from his general practitioner. No other adverse events were reported during the intervention period.

4.3.5 Primary outcome measures

There was a trend towards higher HbA_{1c} at baseline in the PRT group as compared to the AER group (10.7 ± 2.1 vs. 8.9 ± 1.9%, respectively; $P = 0.07$) (Table 4.1). A summary of primary outcome measure results for within and between group comparisons after 16 weeks of exercise training are presented in Table 4.2. There were no statistically significant within or between group differences in HbA_{1c} after PRT or

AER (10.6 ± 2.4 vs. 8.8 ± 2.1%, respectively; $P = 0.92$).

4.3.6 Secondary outcome measures

Secondary outcome measure results are presented in Table 4.2. No statistically significant differences were observed within or between groups for fasting plasma glucose, HOMA2-IR, McAuley Index, or C-peptide.

For blood lipid outcomes, no significant within or between group changes were observed in total cholesterol, HDL cholesterol, total cholesterol to HDL cholesterol ratio, or LDL cholesterol (Table 4.2). Serum triglycerides significantly increased after AER ($P = 0.004$) and this change was significant between groups ($P = 0.03$). No within or between group differences were observed in adiponectin, C-reactive protein (CRP), or plasma free fatty acids.

For anthropometric outcomes, there was a statistically significant reduction in hip circumference after AER ($P = 0.02$) and PRT ($P \leq 0.05$), but was not statistically significantly different between groups (Table 4.2). Body weight, BMI, waist circumference, waist to hip ratio, lean body mass, fat mass, and body fat percent were not significantly different within or between groups after 16 weeks of exercise.

Systolic and diastolic (DBP) blood pressures were significantly reduced after 16 weeks of AER ($P = 0.006$ and $P = 0.02$, respectively), but were not significantly different after PRT. Between groups, only SBP was significantly reduced after AER as compared to PRT ($P = 0.02$) (Table 4.2).

For muscle immunohistochemistry, within group analyses revealed a significant increase in GLUT4 ($P = 0.02$) and capillary density ($P \leq 0.05$) after 16 weeks of AER, with no significant differences observed after PRT (Table 4.2).

Table 4.2: Summary of within and between group differences at 16 weeks for primary and secondary outcome measures

Outcome Measures	PRT				AER				*P* (between groups)
	Week 0	Week 16	Change	*P*	Week 0	Week 16	Change	*P*	
Primary outcome									
HbA1c (%)	10.7 ± 2.1	10.6 ± 2.4	−0.1 ± 1.1	0.86	8.9 ± 1.9	8.8 ± 2.1	−0.1 ± 0.6	0.60	0.92
Secondary outcomes									
Body weight (kg)	118.6 ± 38.5	118.9 ± 37.5	+0.2 ± 3.4	0.85	126.8 ± 18.6	125.5 ± 19.7	−1.3 ± 3.6	0.30	0.35
BMI (kg/m^2)	42.7 ± 12.1	42.7 ± 11.7	0.0 ± 1.1	0.91	45 ± 6.5	44.5 ± 6.9	−0.5 ± 1.3	0.32	0.37
Waist circumference (cm)	125.4 ± 23.2	124.3 ± 23.2	−1.1 ± 2.8	0.30	131.9 ± 13.5	131.1 ± 14.7	−0.8 ± 5.1	0.64	0.91
Hip circumference (cm)	130.8 ± 16.4	129.2 ± 16.3	−1.7 ± 2.2	0.05	139.3 ± 16.6	136.8 ± 16.2	−2.5 ± 2.5	0.02	0.46
Waist to hip ratio	0.96 ± 0.1	0.96 ± 0.1	0.0 ± 0.0	0.65	0.95 ± 0.1	0.96 ± 0.1	0.01 ± 0.04	0.43	0.58
Body fat (%)	50.2 ± 7.6	49.8 ± 6.1	−0.4 ± 2.5	0.68	49.6 ± 5.2	48.8 ± 6	−0.7 ± 2.6	0.43	0.76
Lean body mass (kg)	56.7 ± 8.2	57.8 ± 11.2	+1.2 ± 3.9	0.40	63.4 ± 8.6	63.6 ± 9.6	+0.1 ± 3.0	0.92	0.53
Fat mass (kg)	61.9 ± 31.3	61.0 ± 27	−0.9 ± 5.7	0.63	63.4 ± 13.3	61.9 ± 14.5	−1.5 ± 4.3	0.33	0.82
SBP (mmHg)	123.2 ± 19.4	125.6 ± 17	+2.3 ± 16.9	0.69	147.3 ± 16.1	131.1 ± 9.1	−16.2 ± 13.0	0.006	0.02
DBP (mmHg)	85.7 ± 13.8	83.1 ± 8	−2.6 ± 11.2	0.51	90.4 ± 5.7	85.8 ± 4.6	−4.7 ± 4.9	0.02	0.61
Fasting glucose (mmol/L)	9.5 ± 3.5	11.4 ± 4*	+1.9 ± 3.2	0.17	10.2 ± 3.3	10.4 ± 2.9	+0.2 ± 1.6	0.72	0.19
Fasting insulin (pmol/L)	140.7 ± 100.1	134.1 ± 103.1*	−6.6 ± 24	0.50	177.4 ± 82.5	134.8 ± 64.1	−42.7 ± 65.8	0.09	0.19
HOMA2-IR Index	2.9 ± 2.0	2.9 ± 1.9*	0.0 ± 0.5	1.00	3.9 ± 1.9	2.9 ± 1.3	−0.9 ± 1.6	0.13	0.17
McAuley Index	5.2 ± 1.5	5.2 ± 1.3	0.0 ± 0.5	0.85	5.2 ± 0.8	5.3 ± 0.8	+0.1 ± 0.7	0.59	0.95
C-peptide (nmol/L)	1.6 ± 1.1	1.6 ± 1.0	+0.1 ± 0.5	0.69	1.4 ± 0.3	1.5 ± 0.7*	+0.1 ± 0.5	0.52	0.85
Free Fatty Acids (mEq/L)	0.5 ± 0.3	0.6 ± 0.3	+0.1 ± 0.2	0.40	0.7 ± 0.2	0.7 ± 0.2*	0.0 ± 0.2	0.86	0.69
Total cholesterol (mmol/L)	4.9 ± 1.5	4.5 ± 1.0	−0.4 ± 0.9	0.21	4.5 ± 0.4	4.7 ± 0.4	+0.3 ± 0.6	0.22	0.08
HDL cholesterol (mmol/L)	1.3 ± 0.4	1.3 ± 0.5	0.0 ± 0.1	0.37	1.1 ± 0.2	1.1 ± 0.2	0.0 ± 0.1	0.80	0.64
Total cholesterol/HDL ratio	4.2 ± 1.9	3.9 ± 1.1	−0.3 ± 1.0	0.40	4.1 ± 1.0	4.2 ± 0.8	+0.2 ± 0.6	0.35	0.22
LDL cholesterol (mmol/L)	2.7 ± 1.4	2.4 ± 0.7	−0.3 ± 0.8	0.27	2.6 ± 0.6	2.7 ± 0.4	+0.1 ± 0.5	0.71	0.23
Triglycerides (mmol/L)	2.2 ± 1.2	2.0 ± 1.0	−0.2 ± 0.6	0.35	1.6 ± 0.5	1.9 ± 0.6	+0.3 ± 0.2	0.004	0.03
Adiponectin (µg/ml)	5.6 ± 1.9	5.6 ± 2.2	0.0 ± 1.4	0.96	6.7 ± 3.3	6.7 ± 3.2	+0.1 ± 2.2	0.94	0.93
Capillary Density (px/fibre)	748.9 ± 605.4	689.2 ± 411.2	−59.7 ± 674.8	0.80	386.9 ± 238.6	648.9 ± 241.0**	+262.1 ± 319.0	0.05	0.24
C-reactive protein (mg/L)†	4 (×/÷ 3.1)	2.8 (×/÷ 3.4)	−1.2 (± 3)	0.41	6.4 (×/÷ 2.5)	4.2 (×/÷ 2.4)	−2.2 (± 3.7)	0.22	0.90
GLUT4 (px/fibre)†	496.1 (×/÷ 3.1)	495.4 (×/÷ 5.1)	−0.8 (± 385.2)	1.00	190.3 (×/÷ 2.5)	348.7 (×/÷ 2.3)**	+158.5 (±133.6)	0.02	0.17

Data expressed as mean ± SD unless otherwise noted. *N = 7. **N= 8. †= C-reactive protein and GLUT4 were non-normally distributed and were log transformed. Data at weeks 0 and 16 are expressed as back-transformed means ×/÷ factor standard deviation. Change scores are presented as the difference in back transformed means (95% confidence limit). Abbreviations: PRT—Progressive Resistance Training; AER—Aerobic Exercise; HbA_{1c}—Hemoglobin A_{1c}; BMI—Body Mass Index; SBP—Systolic Blood Pressure; DBP—Diastolic Blood Pressure; HOMA2-IR—Homeostasis Modeling Assessment for Insulin Resistance; LDL—Low Density Lipoprotein; HDL—High Density Lipoprotein; GLUT4—Glucose Transporter (fourth isoform).

Functional performance data for each group are presented in Table 4.3. Lower and upper body 1-repetition maximum (1-RM) significantly increased in the PRT group ($P \leq 0.001$). Power output (W) was significantly increased after 16 weeks of AER training, with a concomitant increase in peak heart rate attained during exercise.

Table 4.3: Functional performance measures at baseline and after 16 weeks

Outcome measure	Week 0	Week 16	Change	*P*
PRT group				
Lower body strength*	125.9 ± 49.9	229 ± 54.1	+103.1 ± 20.4	< 0.001
Upper body strength*	46.4 ± 23.5	65.4 ± 29.9	+19 ± 11.3	0.001
AER group				
Power output (watts)**	46.3 ± 5	110 ± 36.2	+63.7 ± 34	< 0.001

Data expressed as mean ± SD. *1-repetition maximum extrapolated from 10-repetition maximum based on Brzycki formula [37]. Lower body strength determined on Cybex Leg Press machine. Upper body strength determined by Cybex Chest Press machine. **Power output (watts) derived from stationary bike display panel when subjects were exercising at peak rating of perceived exertion of 15 and/or 85% of heart rate reserve, but were not determined from a maximal aerobic test. Abbreviation: PRT—Progressive Resistance Training; AER—Aerobic Exercise.

A comparison between subjects who attended at least 36 of 48 (75%) exercise sessions versus those who attended less than 75% (Table 4.4) revealed that high attendance subjects (independent of exercise modality) exhibited statistically significant reductions in waist circumference ($P < 0.001$) and hip circumference ($P = 0.001$), a significant increase in GLUT4 ($P = 0.02$), and tendency towards a reduction in body weight ($P = 0.11$) and plasma insulin ($P = 0.11$). There was a trend towards an increase in triglycerides ($P = 0.08$) in subjects attending greater than 75% of exercise sessions. Glycaemic control (HbA_{1c}) was not significantly different between high and low attendance groups ($P \geq 0.50$).

Table 4.4: Comparison of subjects who attended greater than 75% of available sessions to those with less than 75% attendance[#]

Outcome measure	Attendance ≥ 75%	*P*	Attendance ≤ 75%	*P*
n	8		10	
HbA_{1c} (%)				
Week 0	9.8 ± 2.3		9.8 ± 2.1	
Week 16	9.9 ± 2.7	0.75	9.6 ± 2.3	0.50
Body weight (kg)				
Week 0	131.1 ± 38		116 ± 20.5	
Week 16	129.8 ± 36.6	0.11	116.1 ± 21.9	0.97
Waist circumference (cm)				
Week 0	134.4 ± 23.4		124.1 ± 13.6	
Week 16	130.7 ± 22.9†	< 0.001	125.4 ± 16.5	0.34
Hip circumference (cm)				
Week 0	135.4 ± 15.7		134.9 ± 18.1	
Week 16	132.3 ± 15.3	0.001	133.6 ± 17.8	0.14
Insulin (pmol/L)				
Week 0	197.9 ± 108.3		124.9 ± 48.4*	
Week 16	154.8 ± 99.1	0.11	114.3 ± 55.3*	0.40
Triglycerides (mmol/L)				
Week 0	1.7 ± 0.5		2 ± 1.2	
Week 16	1.9 ± 0.7	0.08	2 ± 0.9	0.19
GLUT4 (px/fibre)[†]				
Week 0	215.7 ×/÷ 2.6		443.7 ×/÷ 3.4	
Week 16	339.2 ×/÷ 2.3	0.02	507.7 ×/÷ 5	0.74

Data expressed as mean ± SD. [#]Only results which indicated a trend or statistically significant change from baseline are presented. HbA_{1c} results are shown because this is the primary outcome measure.
[†]= GLUT4 was non-normally distributed and was log transformed. Data at weeks 0 and 16 are expressed as back-transformed means ×/÷ coefficient of variation between subjects. **n* = 8 (two outliers excluded from analysis). Abbreviations: HbA_{1c}—Haemoglobin $A_{1c;}$ GLUT4—Glucose Transporter (fourth isoform).

Using pooled data of both groups, regression analysis across the entire cohort revealed that higher subject attendance was associated with the largest reductions in waist circumference (r = –0.664; *P* = 0.003), waist to hip ratio (r = –0.520; *P* = 0.03), and CRP (r = –0.492; *P* = 0.04) (Table 4.5).

Table 4.5: Correlation between number of exercise sessions attended and change scores (week 16 – week 0) for metabolic, anthropometric, haemodynamic, and muscle outcomes (n = 18)

	r	*P*
Outcome Measure		
HbA_{1c}	−0.09	0.72
Body weight	−0.12	0.64
Body Mass Index	−0.09	0.71
Waist Circumference	−0.66	0.003
Hip Circumference	−0.24	0.33
Waist to Hip Ratio	−0.52	0.03
Lean Body Mass	+0.18	0.46
Fat Mass	−0.21	0.39
Body Fat Percentage	−0.15	0.55
Systolic Blood Pressure	−0.14	0.59
Diastolic Blood Pressure	+0.32	0.19
Plasma Glucose	−0.32	0.24
Plasma Insulin**	−0.16	0.57
HOMA2-IR**	−0.22	0.42
C-peptide*	−0.37	0.16
Free Fatty Acids*	+0.15	0.57
Total Cholesterol	+0.29	0.25
HDL Cholesterol	+0.08	0.74
Total Cholesterol to HDL Ratio	+0.27	0.27
LDL Cholesterol	+0.23	0.36
Triglycerides	+0.32	0.20
C-Reactive Protein	−0.49	0.04
Adiponectin	−0.27	0.28
GLUT4**	+0.31	0.22
Capillary density**	+0.05	0.86

r = correlation coefficient. *P* = 0.05. *n=16. **n=17. Abbreviations: HbA_{1c}—Haemoglobin A_{1c}; HDL—High Density Lipoprotein; LDL—Low Density Lipoprotein; GLUT4—Glucose Transporter 4^{th} Isoform.

The change in HbA_{1c} was positively associated with changes in glucose (r = +0.655; *P* = 0.01), CRP (r = +0.474; *P* = 0.05), and body fat percent (r = 0.430; P = trend 0.08), and inversely associated with lean body mass (r = −0.444; *P* = trend 0.06) (Table 4.6). One unexpected finding was that change in HbA_{1c} was positively correlated with the change in capillary density (r = +0.545; *P* = 0.02).

Table 4.6: Correlation between change in HbA_{1c} and change scores (week 16 – week 0) for metabolic, anthropometric, haemodynamic, and muscle outcomes (n = 18)

	r	*P*
Outcome Measure		
Body weight	+0.01	0.97
Body Mass Index	+0.03	0.91
Waist Circumference	−0.18	0.48
Hip Circumference	+0.02	0.95
Waist to Hip Ratio	−0.23	0.36
Lean Body Mass	−0.44	0.06
Fat Mass	+0.31	0.20
Body Fat Percentage	+0.43	0.08
Systolic Blood Pressure	+0.10	0.70
Diastolic Blood Pressure	−0.08	0.74
Plasma Glucose*	+0.66	0.01
Plasma Insulin*	−0.12	0.67
HOMA2-IR*	−0.03	0.90
C-peptide*	−0.28	0.30
Free Fatty Acids*	−0.33	0.21
Total Cholesterol	+0.01	0.96
HDL Cholesterol	−0.03	0.92
Total Cholesterol to HDL Ratio	+0.13	0.62
LDL Cholesterol	−0.02	0.93
Triglycerides	+0.12	0.64
C-Reactive Protein	+0.47	0.05
Adiponectin	+0.01	0.96
GLUT4**	+0.03	0.91
Capillary density**	+0.55	0.02

r = correlation coefficient. *P* = 0.05. *n=16. **n=17. Abbreviations: HOMA2-IR—Homeostasis Model Assessment for Insulin Resistance; HDL—High Density Lipoprotein; LDL—Low Density Lipoprotein; GLUT4—Glucose Transporter 4^{th} Isoform.

4.3.7 Individual subject results

Due to the small number of subjects recruited in the present study, individual subject results for key outcome measures were visually inspected to determine if group changes were driven by large intra- and/or inter-individual variability at baseline or 16 weeks. Normal reference ranges for select outcome measures are presented in Table 4.7. Individual results for HbA_{1c} (Figure 4.2), insulin (Figure 4.3), indices of insulin resistance (Figure 4.4 and 4.5), blood pressure (Figure 4.6 and 4.7), blood lipids (Figures 4.8 – 4.12), and body composition (Figure 4.13 and 4.14) are presented below

and will be further expanded upon in the discussion. Individual results for all outcome measures are presented in Appendix E.

Table 4.7: Normal values for select metabolic, haemodynamic, and anthropometric outcomes

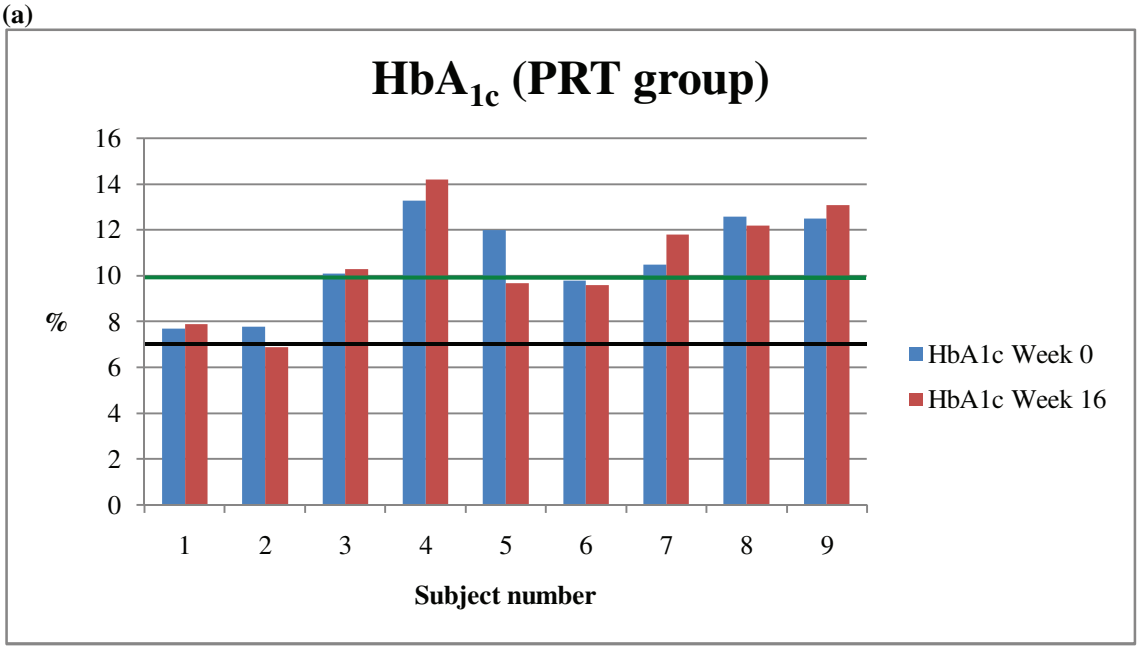
Outcome	Reference Range	Reference
HbA_{1c}	≤ 7%*	New Zealand Guidelines Group [38]
Plasma fasting insulin	10 to 80 pmol/L	CCDHB laboratory reference range
HOMA2-IR Index	≤ 1.8	Geloneze et al (2009) [39]
McAuley Index	≥ 6.3	McAuley et al (2001) [40]
Systolic/Diastolic Blood	≤ 130/80 mmHg*	New Zealand Guidelines Group [38]
Total cholesterol	≤ 4 mmol/L*	New Zealand Guidelines Group [38]
HDL cholesterol	≥ 1 mmol/L*	New Zealand Guidelines Group [38]
Total cholesterol:HDL ratio	≤ 4*	New Zealand Guidelines Group [38]
LDL Cholesterol	≤ 2 mmol/L*	New Zealand Guidelines Group [38]
Triglycerides	≤ 1.7 mmol/L*	New Zealand Guidelines Group [38]
Lean body mass	N/A	Relative to individual subject Δ
Fat mass	N/A	Relative to individual subject Δ

* New Zealand Guidelines Group recommended ranges for individuals with diagnosed type 2 diabetes. Abbreviations: HbA_{1c}—Haemoglobin A1c; HOMA2-IR—Homeostasis Model Assessment for Insulin Resistance; HDL—High Density Lipoprotein; LDL—Low Density Lipoprotein.

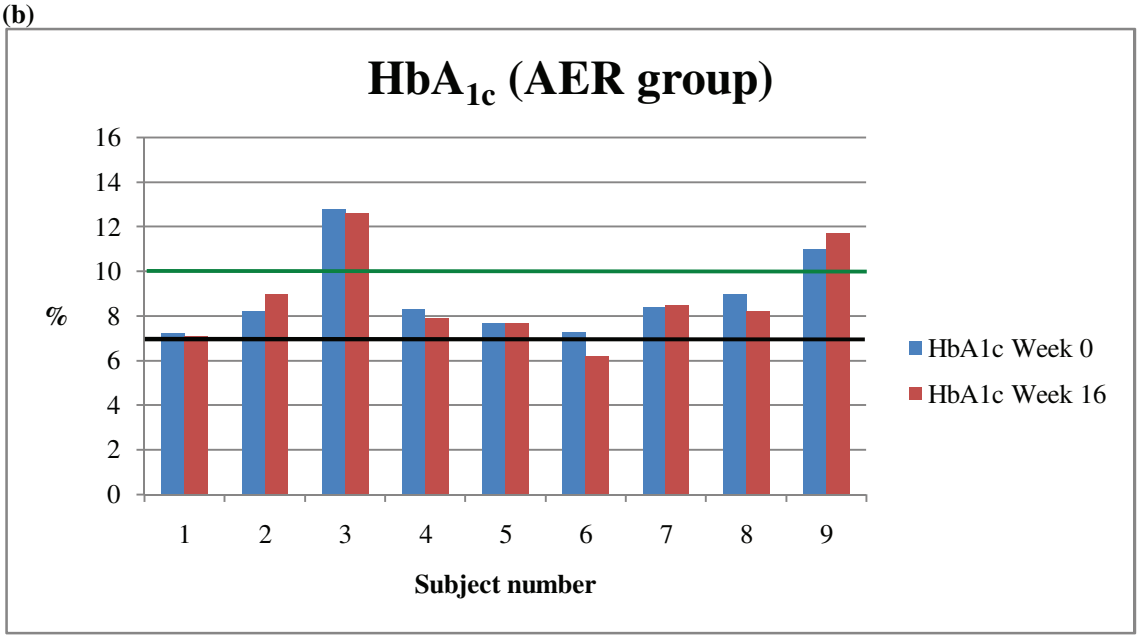
HbA_{1c} was elevated in all subjects at baseline (≥ 7%) with eight subjects (6 PRT, 2 AER) presenting with values greater than 10% (Figure 4.2a and b).

Figure 4.2: Individual baseline and 16 week HbA_{1c} results for the PRT (a) and AER (b) group. Optimal HbA_{1c} is ≤ 7% [38] as indicated by black line. Poor glycaemic control (≥ 10%) is indicated by dark green line.

(a)



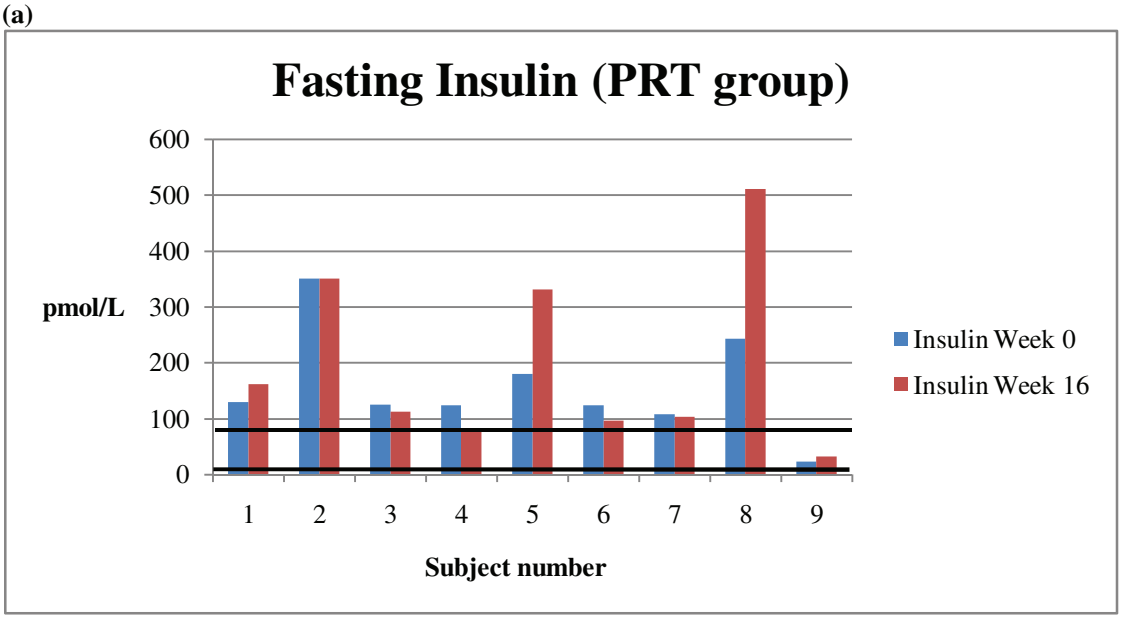
(b)



Sixteen subjects (eight PRT, eight AER) were hyperinsulinaemic (≥ 80 pmol/L) (Figure 4.3a and b) and nearly all were insulin resistant as determined by HOMA2-IR (Figure 4.4a and b) and the McAuley Index (Figure 4.5a and b).

Figure 4.3: Individual baseline and 16 week fasting insulin results for the PRT (a) and AER (b) group. Normal range for fasting insulin is 10 to 80 pmol/L as indicated by black lines.

(a)



(b)

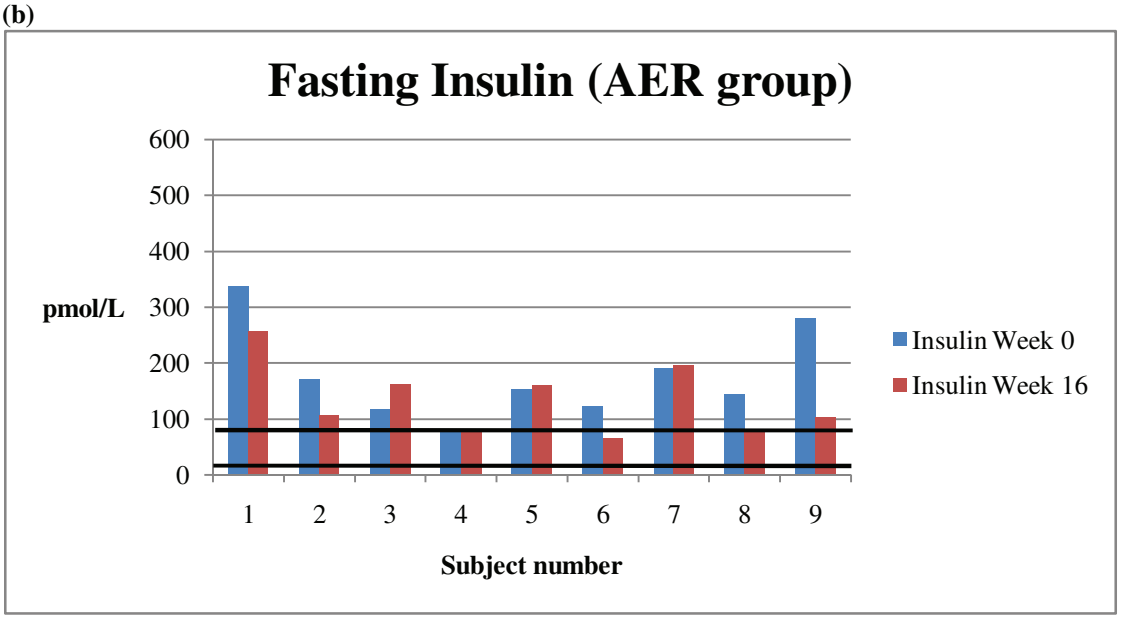
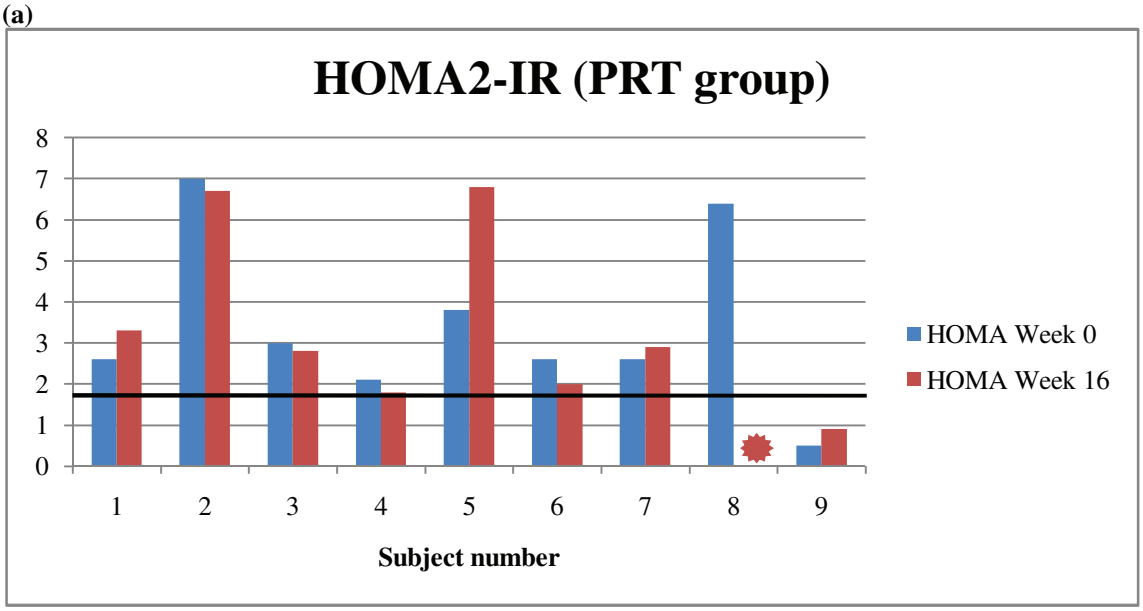
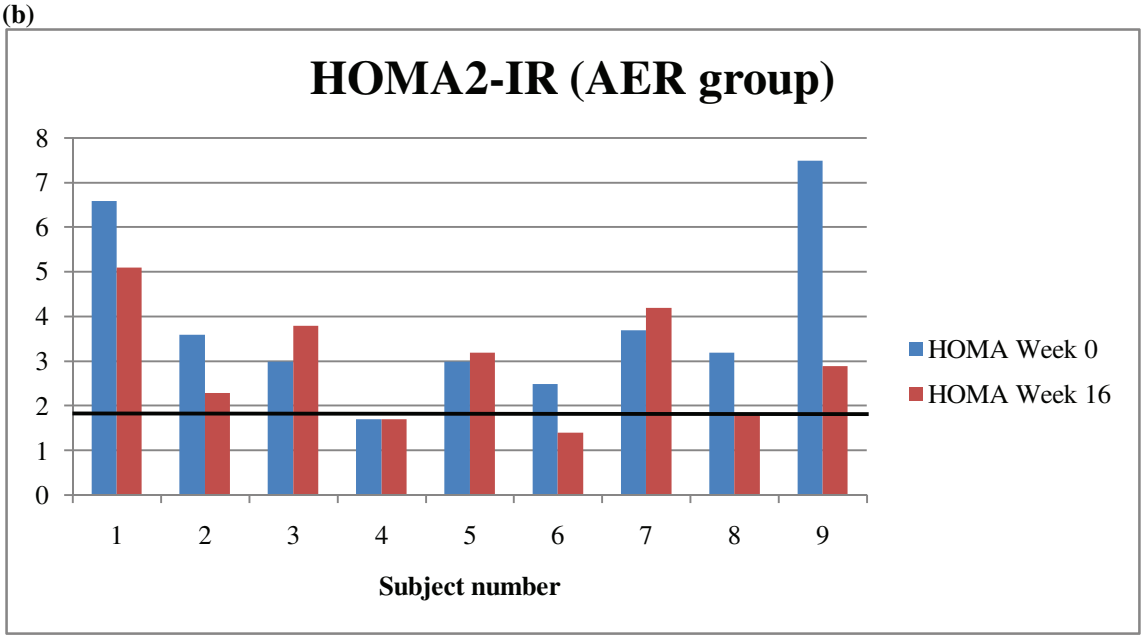


Figure 4.4: Individual baseline and 16 week HOMA2-IR results for the PRT (a) and AER (b) group. Normal value for HOMA2-IR is ≤ 1.8 [39] and is indicated by black line.

(a)



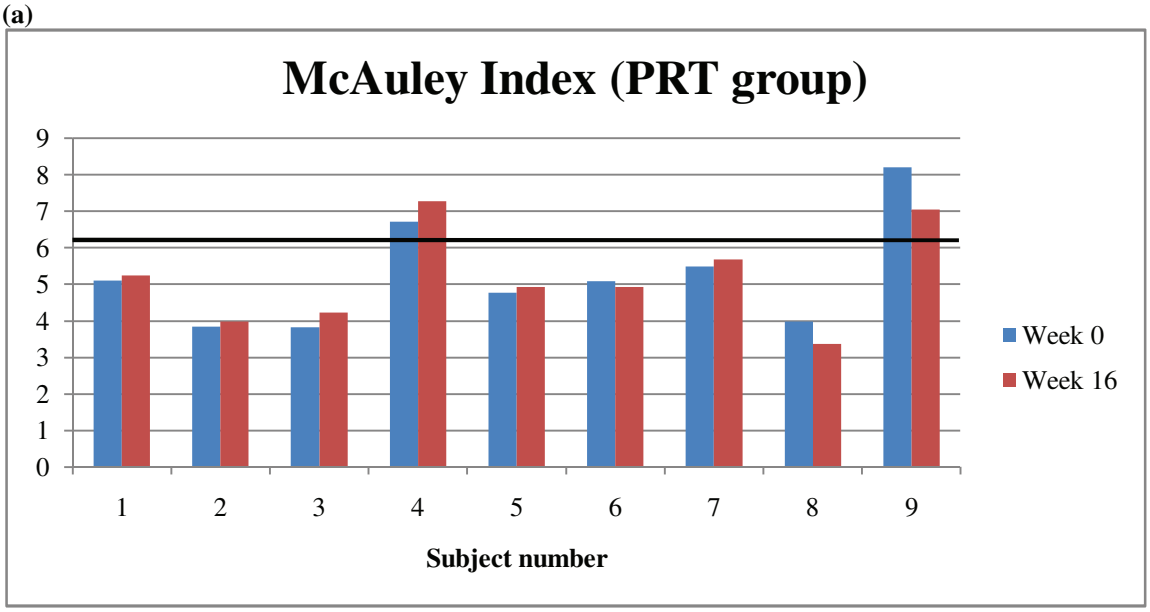
(b)



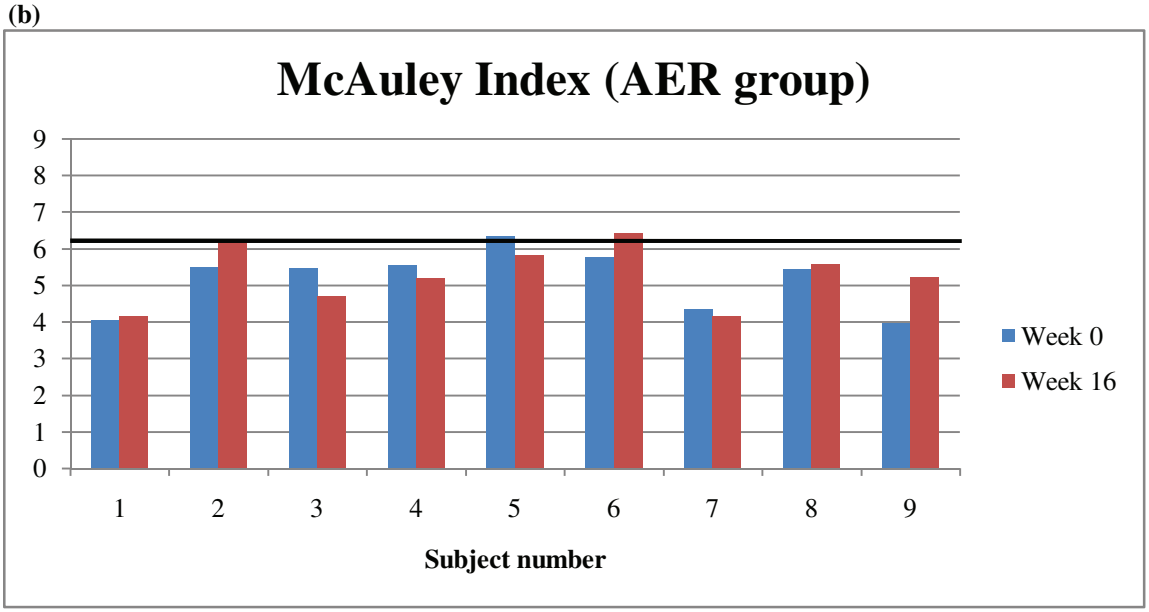
***HOMA for PRT subject 8 exhibited anomalously high plasma insulin which was beyond the limits of the HOMA calculator. Therefore, a value could not be determined.**

Figure 4.5: Individual baseline and 16 week McAuley Index results for the PRT (a) and AER (b) group. Insulin resistance is defined as ≤ 6.3 [40] and is indicated by black line.

(a)



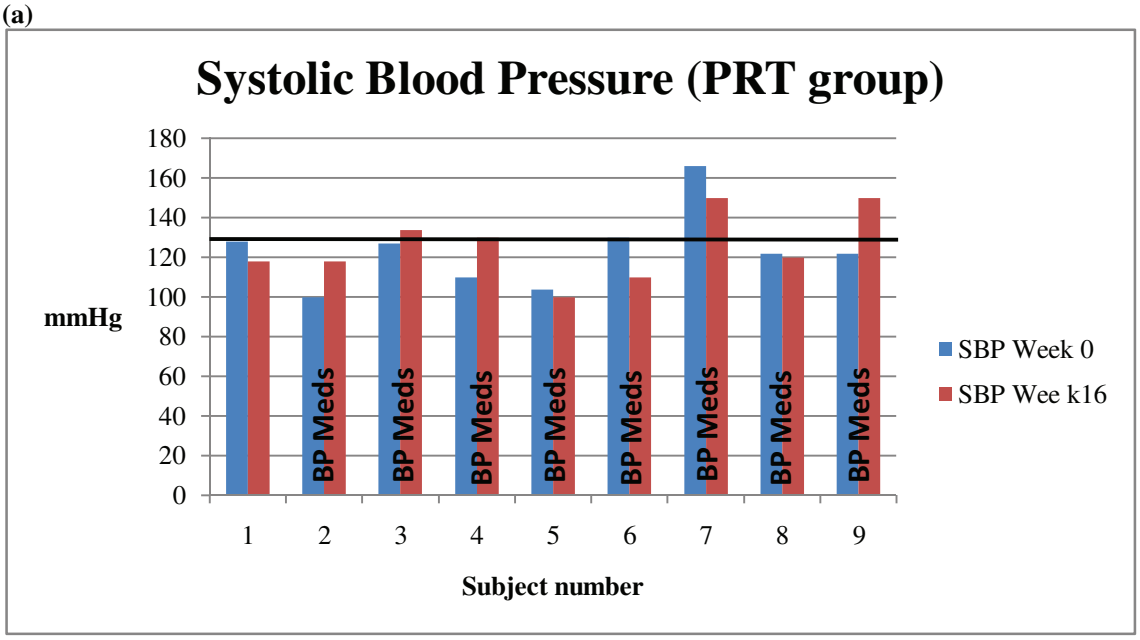
(b)



Baseline SBP (Figure 4.6) and DBP (Figure 4.7) were elevated in 10 (two PRT, eight AER) and 15 (six PRT, nine AER) subjects, respectively.

Figure 4.6: Individual baseline and 16 week systolic blood pressure results for the PRT (a) and AER (b) group. Desirable systolic blood pressure is ≤ 130 mmHg [38] and is indicated by black line. "BP Meds" indicates subjects treated with antihypertensive medications.

(a)



(b)

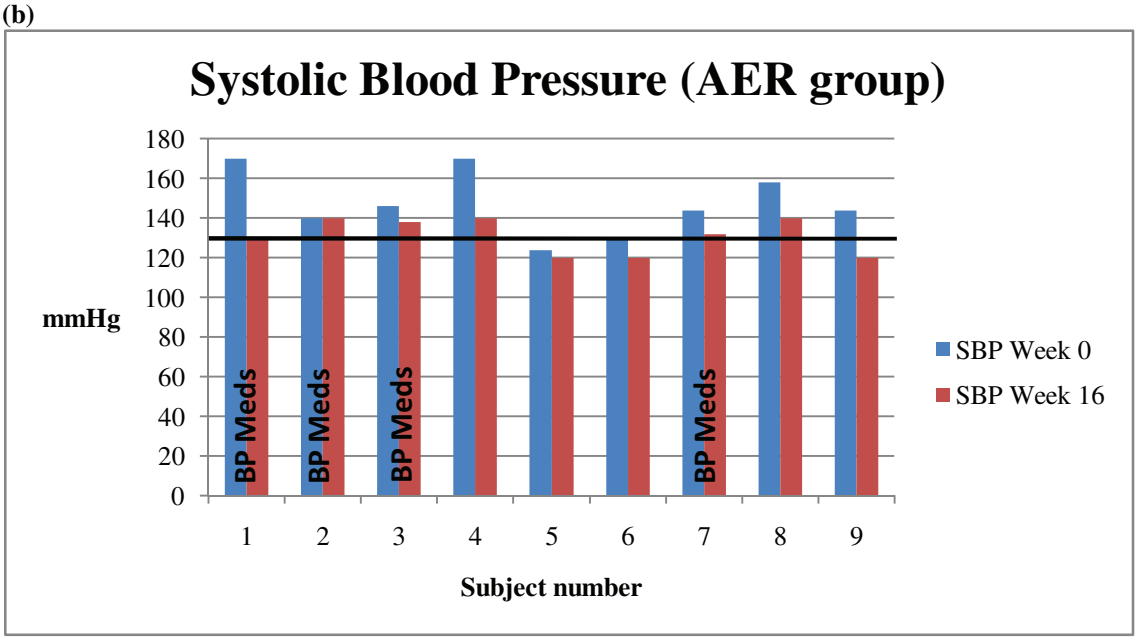
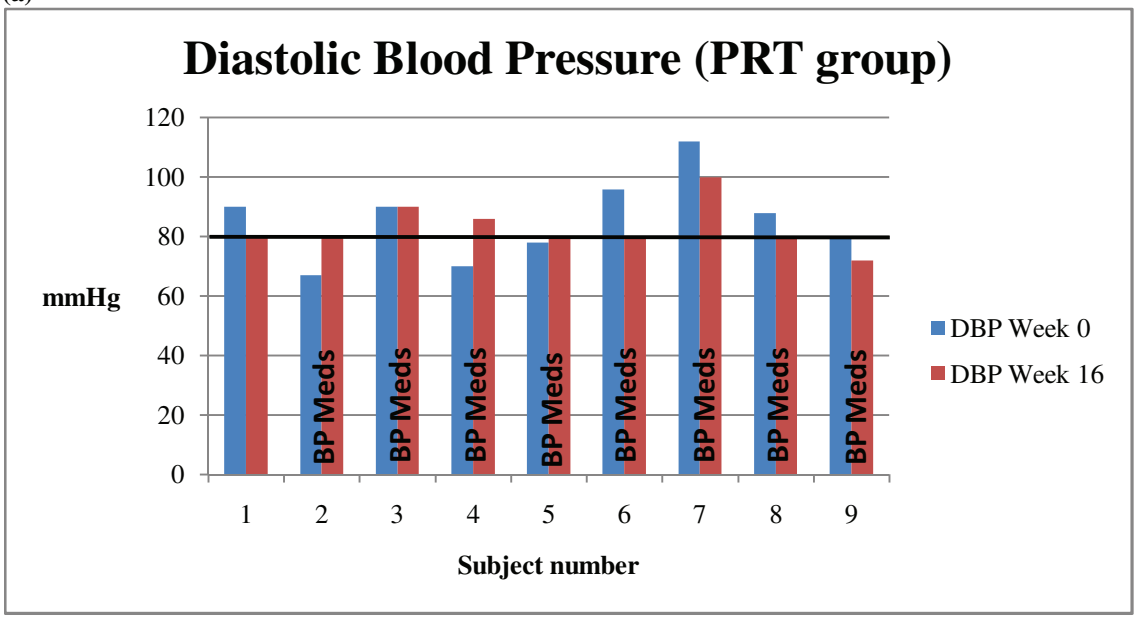
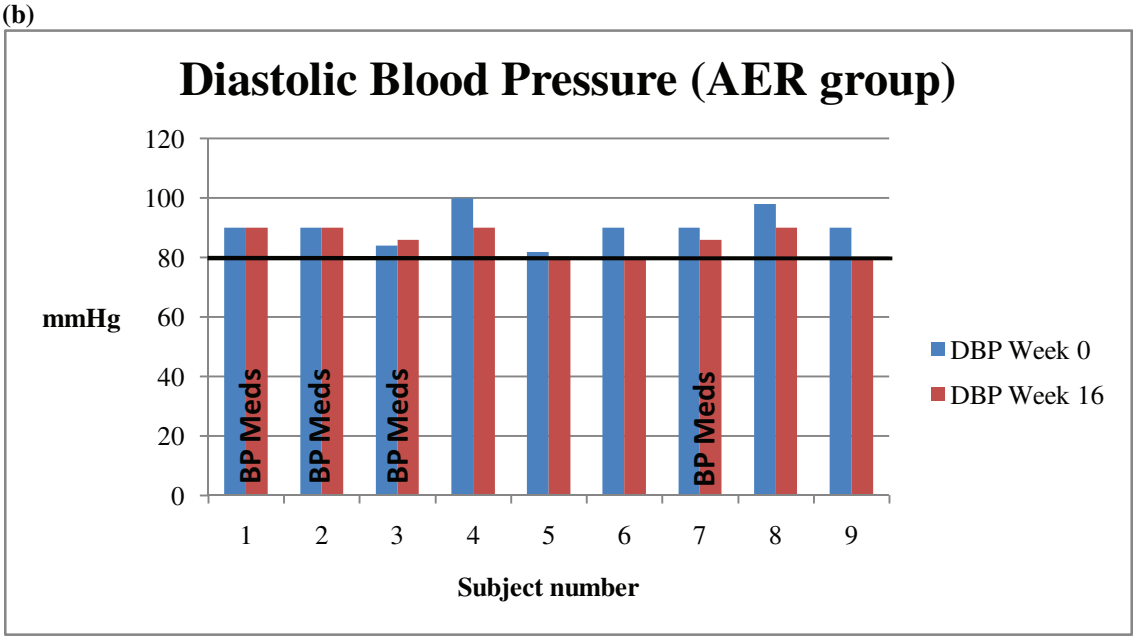


Figure 4.7: Individual baseline and 16 week diastoli blood pressure results for the PRT (a) and AER (b) group. Desirable diastolic blood pressure is ≤ 80 mmHg [38] as indicated by black line. "BP Meds" indicates subjects treated with antihypertensive medications.

(a)



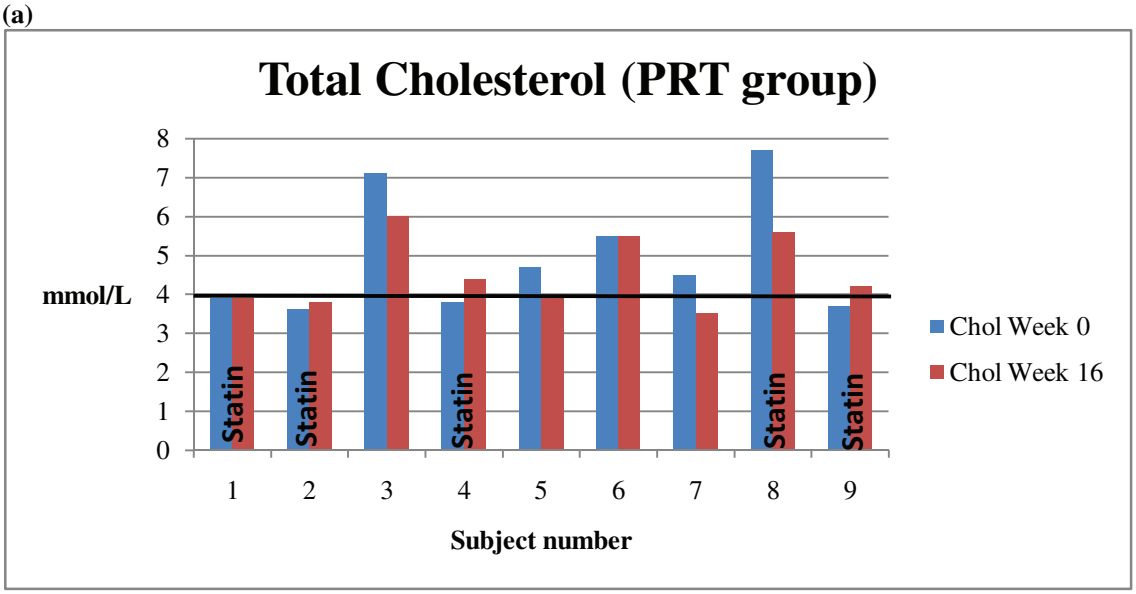
(b)



Baseline total cholesterol (Figure 4.8) was above 4 mmol/L in 13 (five PRT, eight AER) subjects and two subjects (one PRT, one AER) had HDL cholesterol below 1 mmol/L (Figure 4.9). 12 subjects (six PRT, six AER) displayed a total cholesterol to HDL ratio below 4.5 (Figure 4.10).

Figure 4.8: Individual baseline and 16 week total cholesterol results for the PRT (a) and AER (b) group. Desirable total cholesterol level is ≤ 4.0 mmol/L [38] as indicated by black line. "Statin" indicates which subjects were taking prescribed statin (lipid-lowering) medication.

(a)



(b)

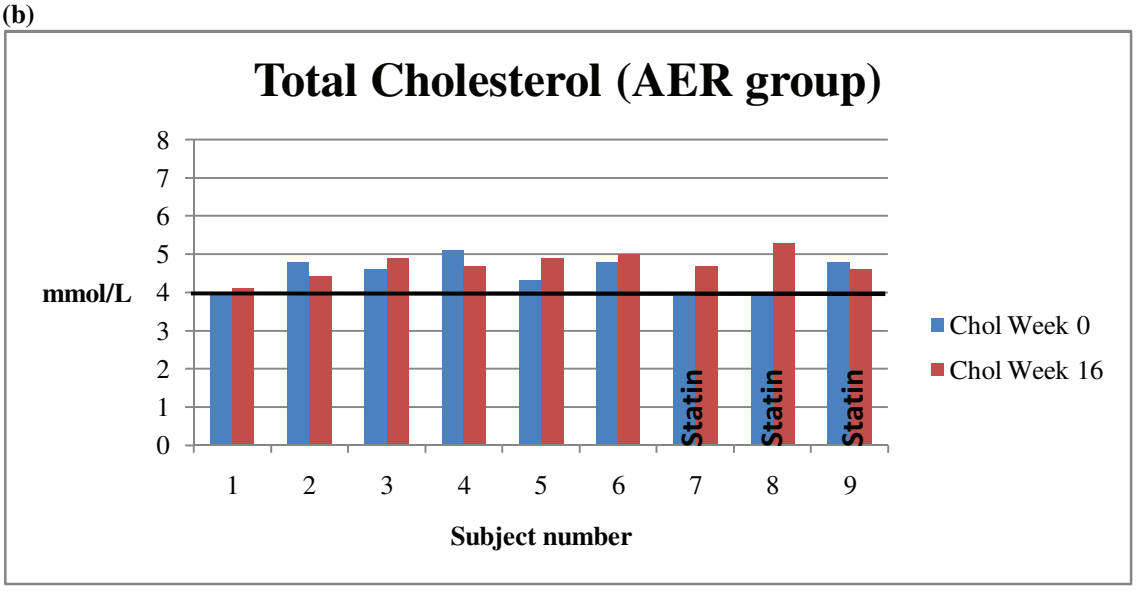
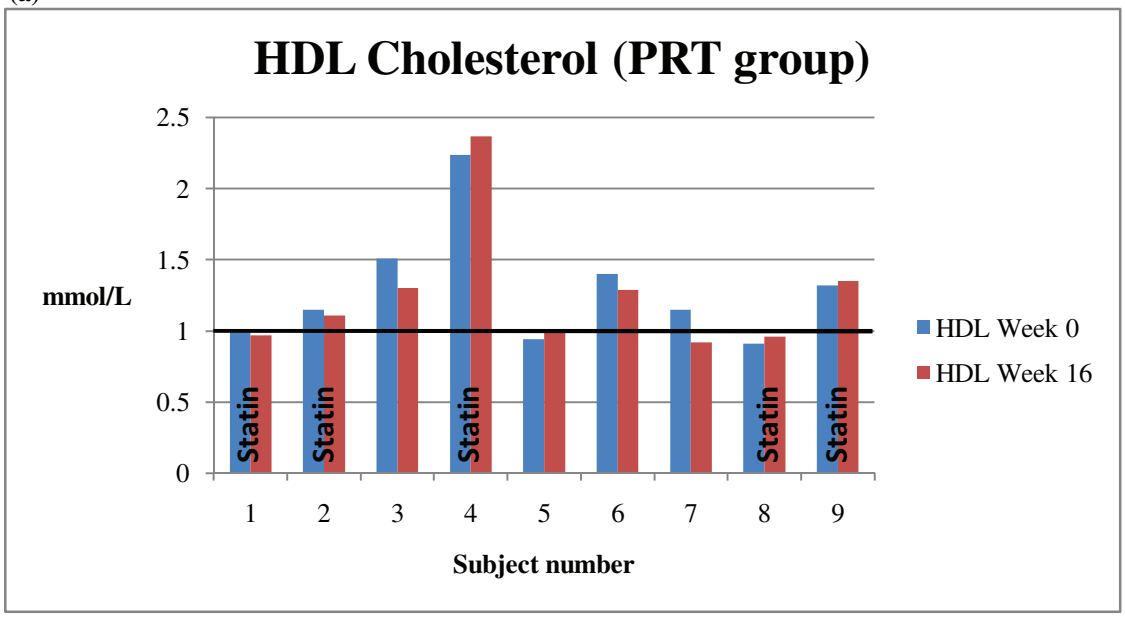


Figure 4.9: Individual baseline and 16 week HDL cholesterol results for the PRT (a) and AER (b) group. Desirable HDL cholesterol level is ≥ 1.0 mmol/L [38] as indicated by black line. "Statin" indicates which subjects were taking prescribed statin (lipid-lowering) medication.

(a)



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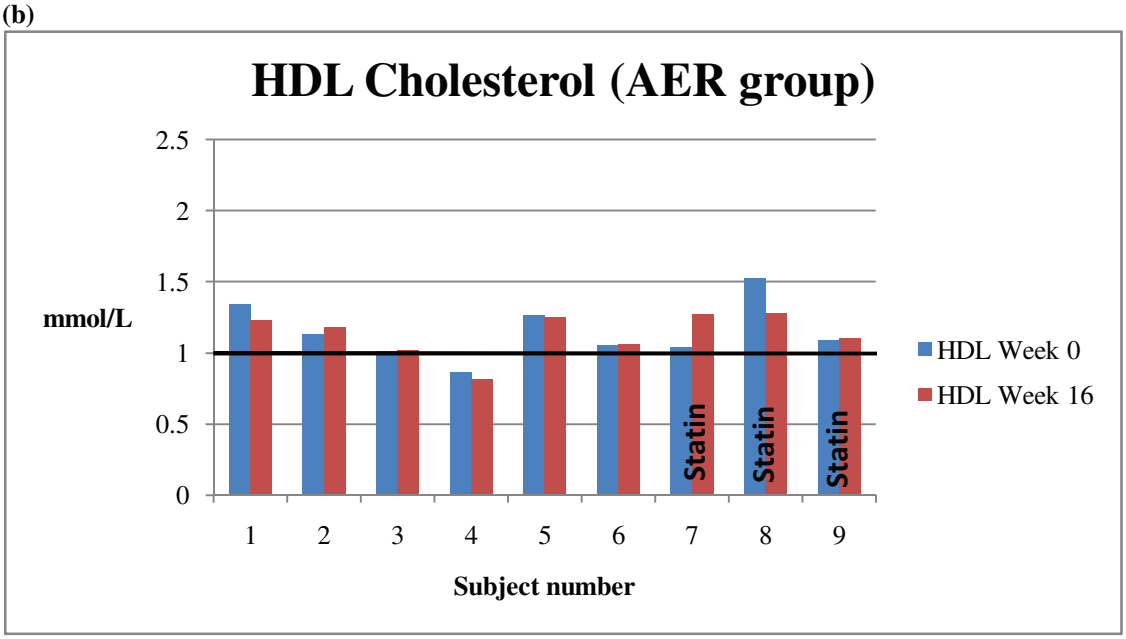
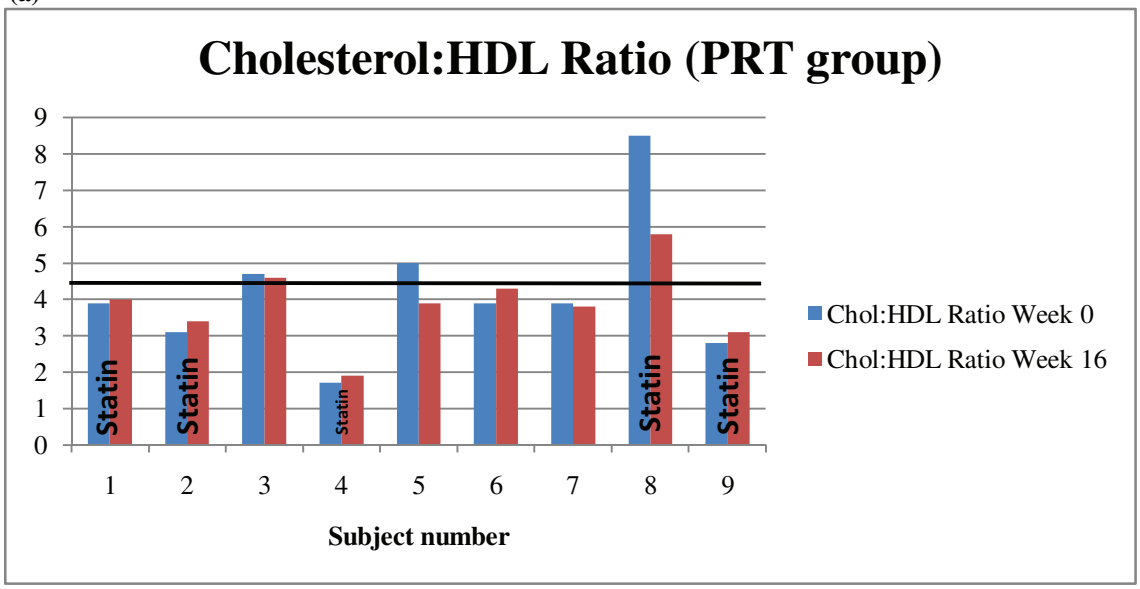
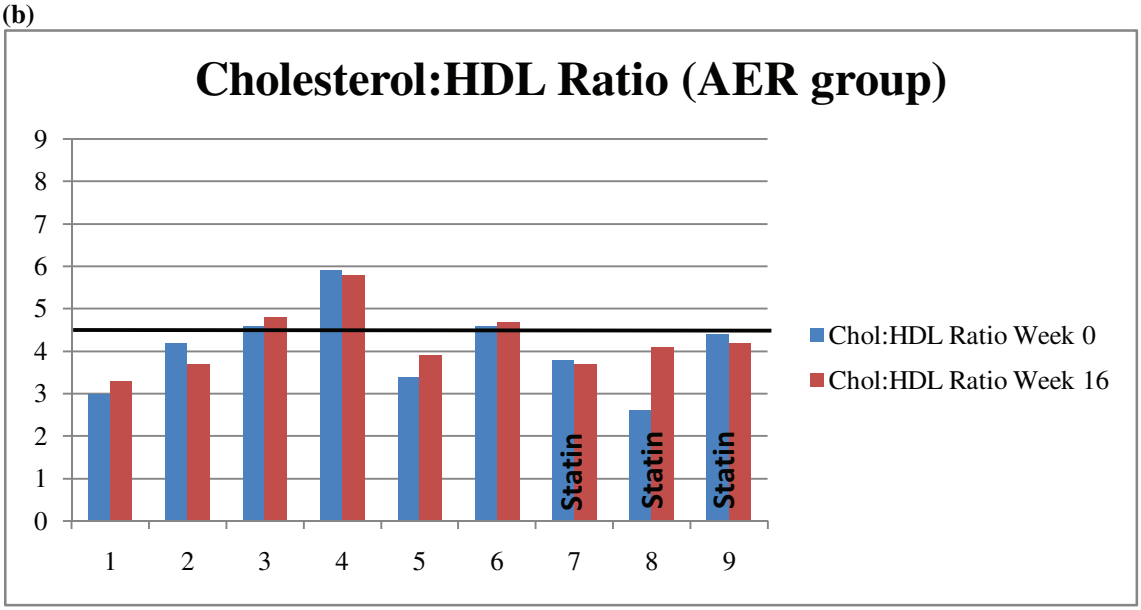


Figure 4.10: Individual baseline and 16 week total cholesterol to HDL ratio results for the PRT (a) and AER (b) group. Desirable total cholesterol to HDL ratio is ≤ 4.5 [38] as indicated by black line. "Statin" indicates which subjects were taking prescribed statin (lipid-lowering) medication.

(a)



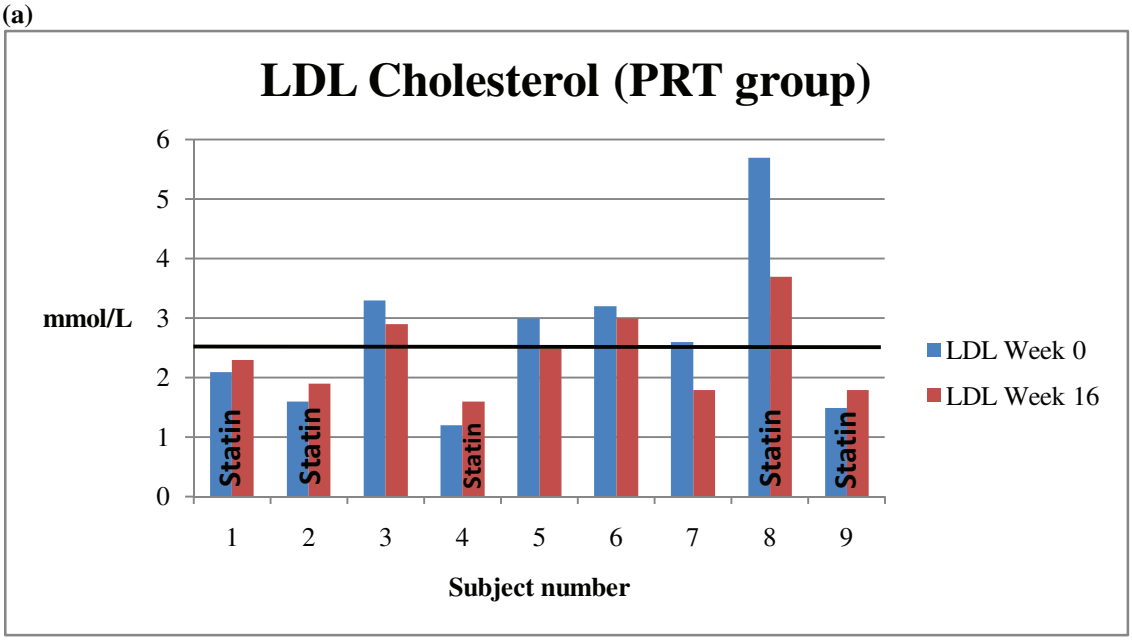
(b)



Baseline LDL cholesterol and triglycerides were elevated in 11 (five PRT, six AER) and 11 (eight PRT, three AER) subjects, respectively (Figures 4.11 and 4.12).

Figure 4.11: Individual baseline and 16 week LDL cholesterol results for the PRT (a) and AER (b) group. Desirable LDL cholesterol level is ≤ 2.5 mmol/L [38] as indicated by black line. "Statin" indicates which subjects were taking prescribed statin (lipid-lowering) medication.

(a)



(b)

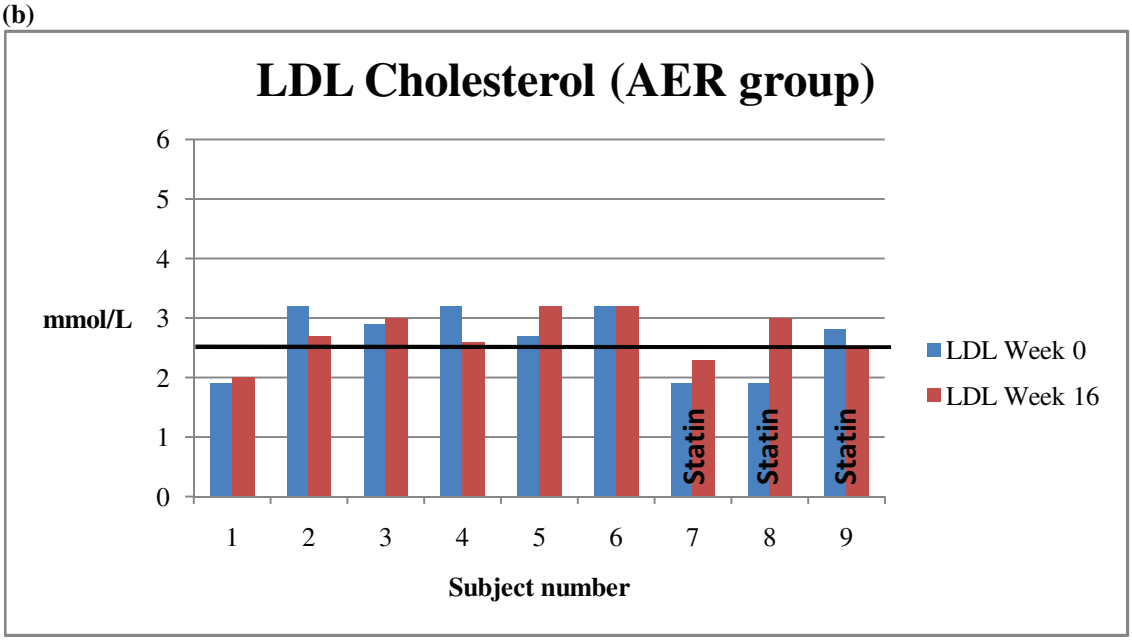
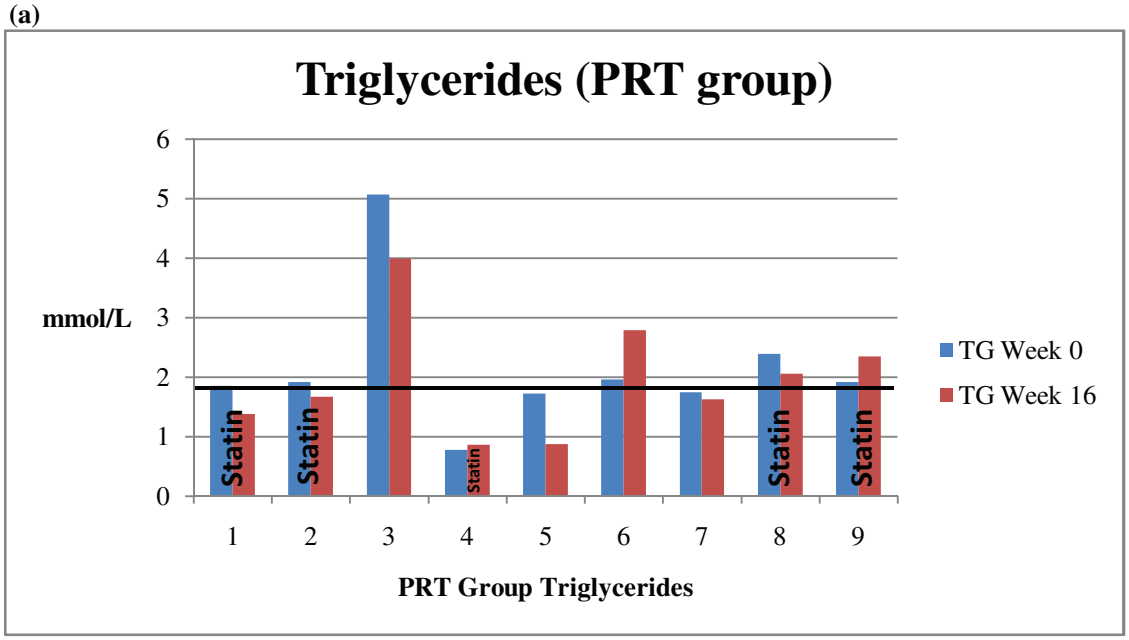
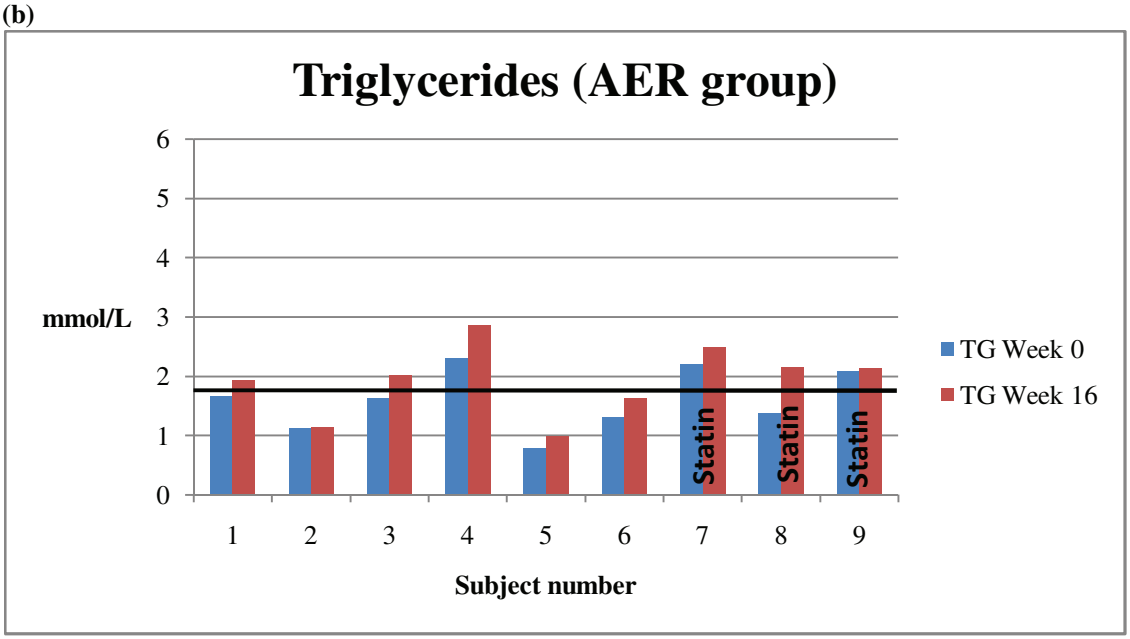


Figure 4.12: Individual baseline and 16 week triglyceride results for the PRT (a) and AER (b) group. Desirable triglyceride level is ≤ 1.7 mmol/L [38] as indicated by black line. "Statin" indicates which subjects were taking prescribed statin (lipid-lowering) medication.

(a)



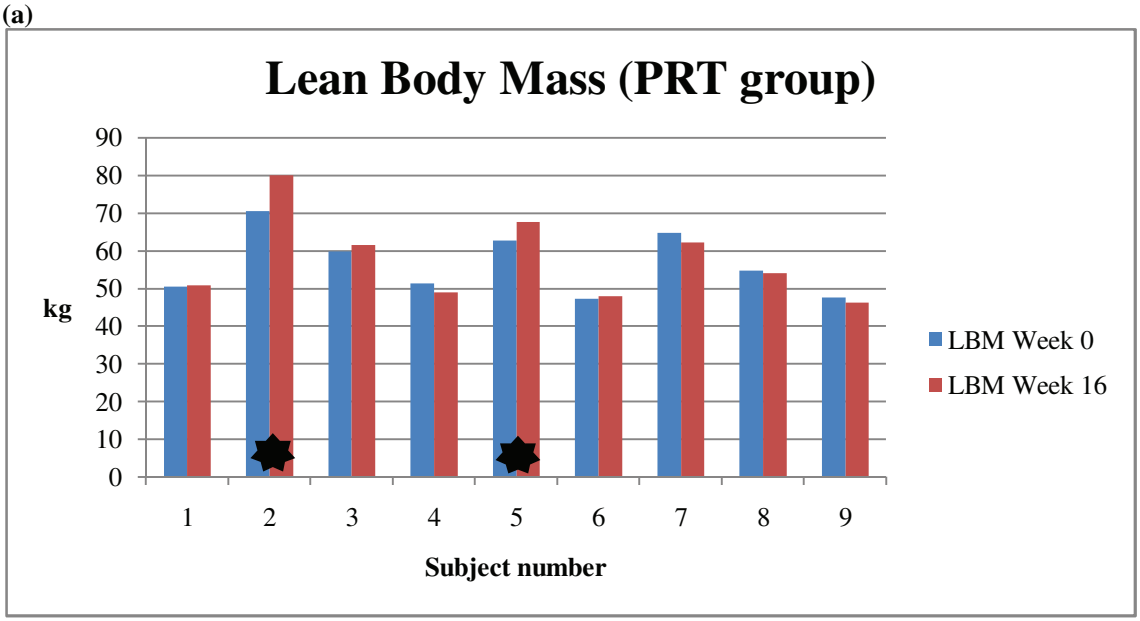
(b)



At 16 weeks, there were three subjects (two PRT, one AER) with large increases (≥ 5 kg) in lean body mass (Figure 4.13) and three subjects (one PRT, two AER) with large reductions (≥ 5 kg) in fat mass (Figure 4.14) relative to other subjects.

Figure 4.13: Individual baseline and 16 week lean body mass results for the PRT (a) and AER (b) group. *PRT subjects 2 and 5 and AER subject 9 experienced the largest (> 5kg) increase in lean mass.

(a)



(b)

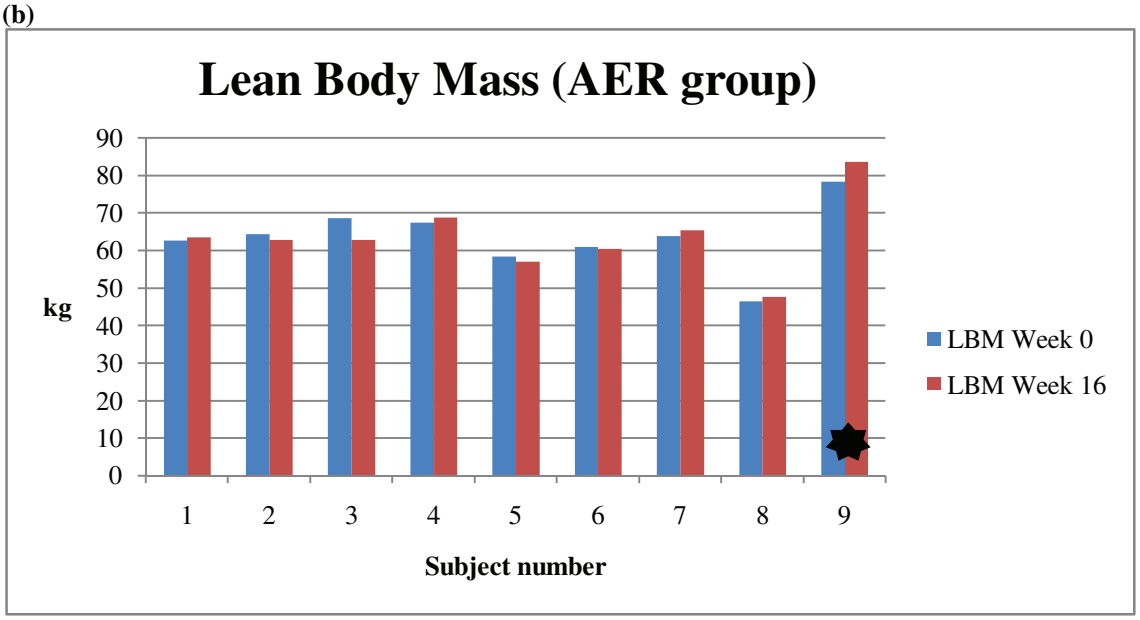
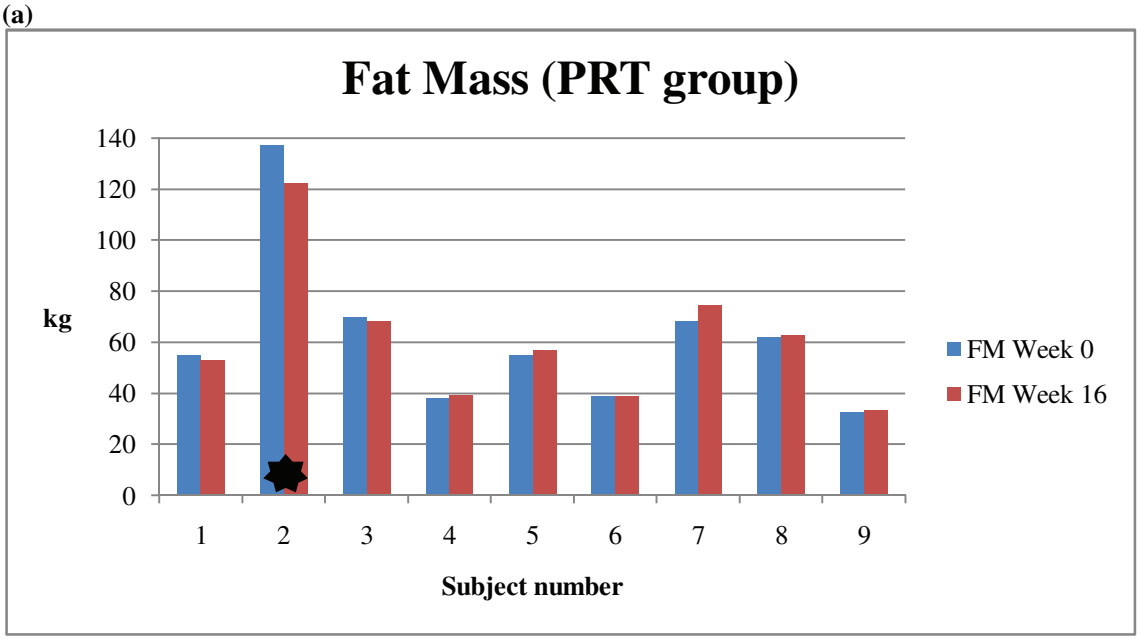
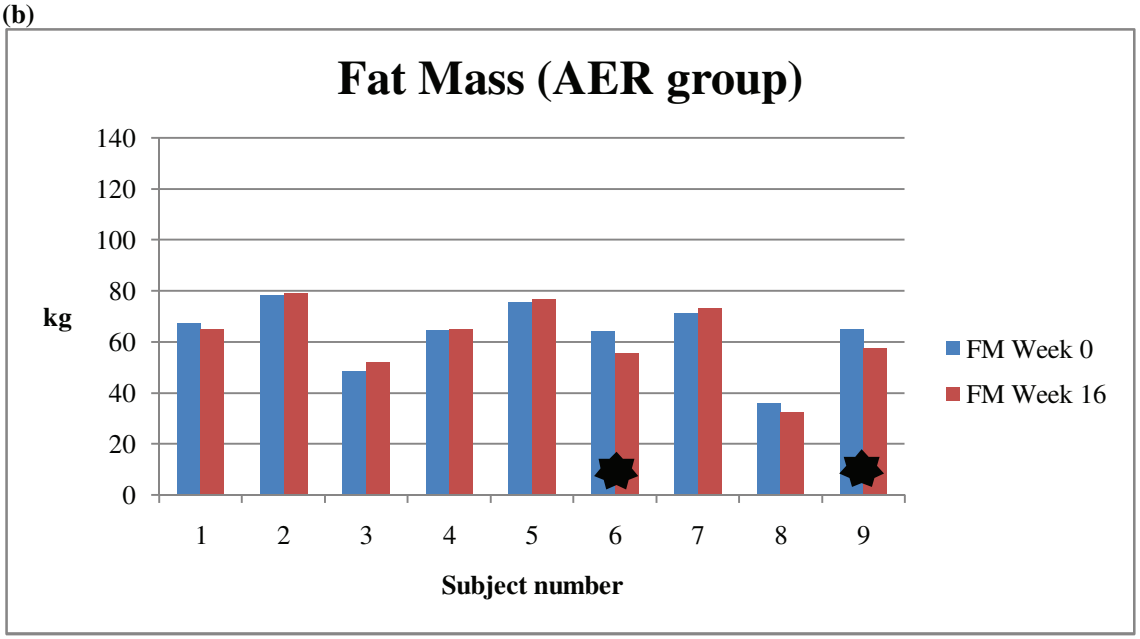


Figure 4.14: Individual baseline and 16 week fat mass results for the PRT (a) and AER (b) group. *PRT subject 2 and AER subjects 6 and 9 experienced the largest (> 5 kg) reduction in fat mass.

(a)



(b)



4.4 Discussion

The SPIRIT study is the first investigation to demonstrate that 16 weeks of high-intensity PRT or AER is safe and well-tolerated by New Zealand Māori and Pacific Islands people with type 2 diabetes and class III morbid obesity, but may be insufficient to improve glycaemic control. Aerobic exercise resulted in a statistically significant and clinically important reduction in systolic blood pressure and hip circumference, an increase in serum triglyceride concentrations, GLUT4, capillary density, and power output. Progressive resistance training resulted in a reduction in hip circumference and increased upper and lower body strength.

There were no statistically significant changes in HbA_{1c} in either group in the present investigation. This is in line with the findings of previous resistance training studies of comparable duration (≥ 16 weeks) and intensity (~8 to 10 reps and three sets) that reported nil to small reductions in HbA_{1c} ranging from 0.0 to 0.3% [41, 42], but differs from other resistance exercise studies of similar training volume which reported comparatively large reductions up to 1.2% [30, 43, 44]. The lack of change in HbA_{1c} in the AER group is consistent with other studies of similar duration and intensity which reported reductions of 0.0 to 0.4% [42, 43, 45-48]. Aerobic training studies with greater magnitudes of change [49-51] may have been due to the addition of a dietary arm [49], repeated exercise-induced acute hypoglycaemic episodes which may have unduly influenced HbA_{1c} results [50], or supplementation with branched chain amino acid supplements [51].

A number of reasons may explain the lack of improvement in glycaemic control and related outcome measures in the present study. Firstly, although subjects were 100% compliant with exercise protocols when present for training sessions, low attendance rates reduced overall training volume and may have blunted the

effectiveness of the exercise stimulus. Only eight (three PRT, five AER) of 18 subjects that completed the entire 16 week intervention attended at least 36 of 48 (75%) available exercise training sessions. However, post-hoc analysis comparing subjects who attended at least 75% of exercise sessions to those who attended less than 75% did not reveal any significant improvement in $HbA_{1c,}$ but did indicate significant reductions in waist and hip circumference and GLUT4 in those with higher attendance. There was also a tendency toward a reduction in body weight and fasting plasma insulin and an increase in triglycerides. Univariate linear regression analysis across all subjects revealed that the highest rates of attendance were associated with significant reductions in waist circumference, waist to hip ratio, and CRP, but not HbA_{1c}. Future exercise studies of longer duration employing robust behavioural techniques such as motivational interviewing [52] to enhance subject attendance may yield more appreciable changes in key metabolic outcomes.

Secondly, the level of obesity seen in this cohort (BMI = 43.8 ± 9.5 kg/m^2; n = 18) was considerably higher than in subjects in previous exercise interventions for type 2 diabetes management (BMI ≤ 36 kg/m^2) [30, 42, 53, 54] and may have delayed the effect of the exercise stimulus. Obesity-linked elevations in plasma free fatty acids are associated with hepatic and peripheral insulin resistance [55]. The accumulation of intra- and perimuscular long-chain fatty acyl CoA and associated lipid moieties such as ceramide and diacylglycerol have been shown to disrupt key enzyme chains (i.e., insulin receptor substrate-1-associated phosphatidylinositol-3-kinase) in the insulin-dependent signalling cascade responsible for glucose uptake [55-57]. Sustained perturbations in hepatic glucose production and uptake may contribute to and prolong the hyperglycaemic state, with this condition further exacerbated by the inability of the peripheral musculature to effectively extract glucose from the

blood [55, 58]. Exercise, on the other hand, has been shown to reduce insulin resistance and stimulate both insulin-independent and insulin-dependent glucose uptake and metabolism *via* increased expression and activity of important signalling proteins [12]. This effect has been shown to be mediated by exercise-induced augmentations in lean body mass [59, 60] with concomitant decreases in visceral and abdominal subcutaneous adiposity [61]. In the present study, there were no statistically significant increases in lean mass or reductions in fat mass and visceral adiposity (i.e., waist circumference), with HbA_{1c}, plasma glucose, plasma insulin, HOMA2-IR, C-peptide, and free fatty acids all remaining elevated after the intervention. Taken as a whole, it is possible the high degree of adiposity in this cohort may have been so extreme as to delay the potential benefits of 16 weeks of high-intensity PRT or AER. Thus, future exercise investigations of longer duration, more frequent and intense training sessions, and with enhanced subject attendance may provide the necessary stimulus to improve glycaemic control in Māori and Pacific Islands people with type 2 diabetes and class III (morbid) obesity.

Thirdly, previous studies with the largest reductions (−1.2%) in HbA_{1c} [30, 43, 44] might be explained by the statistically significant increase in lean body mass associated with PRT (+0.5 to 3.2 kg), compared to subjects allocated to AER exercise [43] or a non-exercise control group [30, 44]. It is well-established that skeletal muscle is a major site for glucose disposal in the body, with augmentations in lean mass shown to be associated with improvements in glycaemic control and insulin sensitivity [3]. In the PRT group in the present study, even with a seemingly comparable, albeit not statistically significant, increase in lean mass (+1.2 kg) and reduction in fat mass (−0.9 kg), this change in body composition was not associated with improved glycaemic control. Upon review of individual subject data, this

apparently large absolute change in body composition was driven by one PRT subject (subject 2) who experienced a comparably large increase in lean mass (+9.6 kg) (Figure 4.13a) and reduction in fat mass (−14.6 kg) (Figure 4.14a) relative to other PRT subjects. When subject 2 was temporarily omitted from analysis, the mean increase in lean mass for the PRT group was reduced to only 0.1 kg with fat mass increased by 0.7 kg. Interestingly, this subject had one of the highest attendance rates in the study and also demonstrated a 0.9% reduction in HbA_{1c}. Similarly, another subject (subject 5) with an attendance rate of 73% experienced an increase of 5 kg of lean body mass and a 2.3% reduction in HbA_{1c}. These findings suggest that despite such anomalously large changes in body composition relative to other subjects, these improvements in glycaemic control were likely valid findings. Moreover, this lends additional support to the hypothesis that improved attendance across the cohort might have resulted in favourable improvements in body composition and glycaemic control.

Fourthly, SPIRIT study participants were comparatively younger (~49 years) than subjects in other studies (range ~56 to 67 years) with the largest magnitudes of change in glycaemic control [30, 43, 44]. The older subjects in these earlier trials may have exhibited some degree of age-related sarcopenia as evidenced by lower lean body mass (range ~44 to 52 kg) as compared to that of SPIRIT study participants (range ~57 to 63 kg), thus conferring a higher physiological ceiling for composition-mediated improvements in glycaemic control not seen in the SPIRIT study's relatively younger, more muscular Polynesian cohort. However, more sensitive measures for assessing body composition in obese subjects such as dual energy x-ray absorptiometry (DEXA) [62] might have provided a more accurate estimate of changes in fat and lean mass in this morbidly obese cohort. Bioelectrical impedance analysis and circumference measures were employed in the present study mainly due

to funding limitations (i.e., price of more sensitive scans and technician hours), as well as practical aspects of transporting subjects (i.e., fuel cost, traffic, limited parking) from Porirua to Wellington Hospital where the DEXA unit was available. Additional research is warranted to investigate the impact of lean mass augmentations on glucose disposal and long-term glycaemic control in a Polynesian cohort with type 2 diabetes.

Lastly, upon review of individual subject data, there were several subjects in both groups at baseline with HbA_{1c} values only slightly higher (7.2 to 7.8%) than New Zealand Guidelines Group target of $\leq 7\%$ and was likely due to effective pharmacologic management (Figure 4.2a and b). As these subjects were closer to desirable HbA_{1c} levels prior to commencing the exercise intervention, their physiological margin for improvement would have been comparably diminished in contrast to other participants with poor glycaemic control ($HbA_{1c} \geq 10\%$). At 16 weeks, HbA_{1c} percentages in subjects that exhibited better baseline glycaemic control remained unchanged or modestly decreased. Furthermore, clinically important reductions in HbA_{1c} ranging from 0.8 to 2.3% in some subjects were negated by increases in other subjects by up to 1.3%, creating a net effect of no statistically significant difference within or between groups at 16 weeks. In order to address these limitations, future investigations with a larger number of subjects should: 1) stratify subjects by respective HbA_{1c} ranges via a minimisation approach [63] to determine if inter-individual variance in pre-intervention HbA_{1c} levels among subjects impacts the post-intervention magnitude of change; and 2) employ more sensitive methods for assessing body composition such as DEXA, computed tomography, or magnetic resonance imaging in order to determine if improvements in glycaemic control are associated with favourable changes in body composition.

Despite no statistically significant reduction in HbA_{1c}, there was a tendency

toward small reductions in fasting plasma insulin in the AER group only. Initial statistical analyses on the PRT group revealed an increase in plasma insulin (+41.6 ± 102.1 pmol/L) and HOMA2-IR (+1.4 ± 2.5) after 16 weeks. However, because the HOMA2 calculator relies on the input of accurate fasting plasma glucose and insulin values, it was necessary to visually inspect these data for large intra- and inter-subject variability. Upon further review, this finding was observed to be driven by two subjects in the PRT group (subjects 5 and 8) (Figures 4.3a and 4.4a) who presented with insulin levels at week 16 that were anomalously high. The reason for this is not known, but may reflect technical measurement error in the laboratory, subjects were not fasted at the time of the blood draw, or a potential worsening of their diabetes management. Adjusted analyses after removal of fasting glucose, insulin, and HOMA2-IR values for these subjects (as per consulting endocrinologist Dr. Jeremy Krebs) considerably reduced statistical variability and indicated a non-significant reduction in plasma insulin and no change in HOMA2-IR in the PRT group. Secondary analysis for insulin resistance assessed *via* the McAuley Index revealed that all except for two PRT subjects (subjects 4 and 9) were insulin resistant (Figures 4.5a and 4.5b). Both subjects exhibited low insulin levels relative to other study participants and, given their low C-peptide concentrations, were more likely a result of pancreatic β-cell dysfunction than the training regimen. Moreover, one of these subjects was also prescribed exogenous insulin injections. Taken together, statistical inferences regarding fasting insulin and insulin resistance must be interpreted with caution given the small number of subjects recruited and the heterogeneity of inter-individual differences. It is also important to acknowledge that even if the small reductions in plasma insulin and HOMA2-IR in the AER group are valid findings, these subjects still remained hyperinsulinaemic and insulin resistant at 16 weeks.

Additional biochemical measures investigated in this study included adiponectin and CRP, both of which have been associated with insulin sensitivity [55, 64, 65]. Adiponectin, a protein hormone secreted from white adipose tissue [66], is positively associated with enhanced insulin sensitivity [67] and inversely associated with atherogenic [67] and inflammatory markers [68, 69]. A reciprocal relationship exists between adiposity and circulating adiponectin, with lean individuals exhibiting higher levels of adiponectin in contrast to comparably lower concentrations in obese subjects [70-72]. High-intensity PRT [73, 74] and moderate intensity AER [75, 76] have been shown to increase plasma adiponectin levels and improve insulin sensitivity in overweight non-diabetic [74-76] and type 2 diabetic [73] subjects. Other exercise studies have also reported enhanced insulin action despite no change [77] or a decrease [78] in adiponectin levels after chronic (≥ 6 weeks) aerobic exercise training in overweight and obese [77] and healthy non-obese [78] subjects. However, the precise mechanisms by which exercise-induced increases adiponectin play a role in enhancing insulin sensitivity is not clear, but may stem from weight loss [77], reductions in fat mass [75, 76] and augmentations in lean body mass [73]. In the present investigation, baseline adiponectin levels in both groups (~5.6 to 6.7 µg/ml) were within the desired 5–25 µg/ml range [79] and did not significantly change in either group after 16 weeks of exercise training. Given that decreased adiposity is inversely associated with adiponectin [70-72], the small absolute reductions in fat mass and waist and hip circumference in both groups were likely insufficient to effect any appreciable increase in adiponectin and, consequently, fasting insulin or HOMA2-IR.

Empirical evidence suggests that chronic low-grade inflammation may predict the onset of type 2 diabetes [64] and that markers of systemic inflammation such as

CRP are strongly correlated with insulin resistance [80-82]. Progressive resistance training [73] and aerobic exercise [83-85] have previously been shown to reduce CRP levels in overweight [83, 84] and diabetic [73, 85] subjects, with concomitant improvements in insulin sensitivity [73, 83, 85]. In line with the small reduction in insulin and HOMA2-IR in the AER group in the present study, other investigators have reported enhancements in insulin sensitivity after 16 weeks of aerobic training without significant reductions in CRP [76]. The precise mechanism by which exercise may reduce CRP is not clear but it has been proposed that adiponectin modulates CRP levels through inhibition of the pro-inflammatory effects of tumour necrosis factor-α in vascular endothelial cells and adipose tissue [86]. It is therefore possible that the lack of a statistically significant reduction in CRP in both groups in the present study may be related to the lack of change in adiponectin secondary to negligible improvements in body composition. However, it is interesting to note that across the entire cohort, subjects with greater than 75% attendance experienced a statistically significant reduction in waist circumference with a concomitant trend towards a reduction in CRP, suggesting that a dose-dependent reduction in visceral adiposity may contribute to improved adipocytokine profiles which mediate CRP. Future exercise investigations in obese Polynesian people with type 2 diabetes should evaluate a more extensive array of adipocytokines and anti-inflammatory markers to provide a more comprehensive understanding of their role mediating improvements in glycaemic control and insulin sensitivity.

Skeletal muscle is a major site for glucose disposal which is known to be mediated by stimulation and translocation of both contraction- and insulin-dependent GLUT4 transport proteins [87]. Individuals with impaired glucose tolerance and type 2 diabetes may benefit from this variability in signaling mechanisms given their

propensity towards peripheral insulin resistance. Chronic aerobic [88-91] and resistance training [92] regimens of six to 12 weeks duration have been shown to increase GLUT4 content in subjects with impaired glucose tolerance [88, 91] and type 2 diabetes [89, 90, 92], resulting in improved insulin action [88, 92] and non-oxidative glucose metabolism *via* increased glycogen synthase activity [90]. Although other aerobic [93] and resistance training [94] studies (both 16 weeks duration) reported no increase in GLUT4 mRNA expression, improvements in other molecular markers such as human sodium-dependent glucose co-transporter 3 [94], peroxisome proliferator-activated receptor-δ and uncoupling protein 3 [93] were associated with improved insulin sensitivity [93] and glycaemic control [94]. In the present investigation, GLUT4 content significantly increased in the AER group after 16 weeks with a concomitant tendency toward reduced fasting plasma insulin, whereas no significant difference was noted in the PRT group in any of these parameters. In the absence of statistically significant reductions in both fasting plasma glucose and HbA_{1c}, this might suggest that AER is able to elicit favourable improvements at the myocellular level that were not yet reflected in blood markers of glycaemic control. Moreover, subjects with greater than 75% attendance, irrespective of exercise modality, experienced larger increases in GLUT4 as compared to those with less than 75% attendance, further suggesting that enhanced attendance may be required to elicit improvements in key outcome measures.

The statistically significant increase in capillary density in the AER group is an expected finding and is in agreement with the known effects of aerobic exercise on muscle capillarisation [95, 96]. This is an important morphological adaptation because insulin sensitivity is positively associated with muscle oxidative capacity, particularly in type I muscle fibres which are rich in oxidative mitochondrial enzymes

and exhibit greater capillary density [97, 98]. Within the microvascular endothelium, insulin stimulates production of nitric oxide which augments skeletal muscle perfusion and increases myocellular glucose uptake [99]. However, in the setting of obesity, fatty acid elevations induce cellular defects at the level of the insulin signalling cascade which disrupt the dilatory effects of insulin and promote insulin resistance and decreased peripheral glucose disposal [100]. Kim *et al.* [91] reported an increase in capillary density and fatty acid oxidation in older men with impaired glucose tolerance secondary to 12 weeks of aerobic exercise, but did not assess insulin sensitivity or glucose uptake. In the present investigation, the increase in capillary density in the AER group occurred in tandem with a tendency towards a reduction in fasting plasma insulin. Clearly this is not a conclusive finding given the small number of subjects recruited, but it may further support the hypothesis that molecular-level changes may be occurring even without significant improvements in other blood markers or anthropometric measures. Other investigators affiliated with the SPIRIT study are currently analysing key mitochondrial oxidative enzymes associated with lipid and energy metabolism with the aim of identifying molecular-level adaptations which may precede appreciable changes in blood markers.

The observed decrease in SBP (−16.2 mmHg; $P = 0.006$) and DBP (−4.7 mmHg; $P = 0.02$) in the AER group is a clinically important finding. AER subjects were taking fewer hypertension medications than the PRT group and, upon review of individual subject data, seven of nine AER subjects (subjects 1, 3, 4, 5, 6, 7, 8, 9) experienced a reduction in SBP and one subject did not change (Figure 4.6b). Six of nine AER subjects (subjects 4, 5, 6, 7, 8, 9) experienced a reduction in DBP whereas two did not change and one increased by 2 mmHg (Figure 4.7b). Therefore, these findings were likely due to the effects of AER exercise and were not driven by large

changes in one or two subjects. People with type 2 diabetes have a two to four times higher risk of developing cardiovascular disease [101], so any treatment modality that can reduce hypertension, particularly in high-risk populations, is desirable. Subjects with high normal blood pressure (SBP 130 to 139 mmHg; DBP 85 to 90 mmHg, or both) have been shown to experience higher rates of cardiovascular events compared to those with normal blood pressure (SBP 120 mmHg; DBP 80 mmHg) [102]. According to an American College of Sports Medicine position stand on exercise and high blood pressure, endurance exercise, resistance training, or both can prevent hypertension and lower blood pressure in those with elevated blood pressure [103]. Furthermore, the blood pressure-lowering effect of exercise is more pronounced in those with the highest baseline blood pressures undertaking endurance type exercise [103], as was observed in the AER group the present study. As little as a 2 mmHg decrease in SBP and DBP translates to a reduction in risk of coronary artery disease by 9% and 6%, and a reduction in risk of stroke by 14% and 17%, respectively, in the general population [103]. The comparatively large improvement in SBP and DBP in the present study underscore the importance of prescribing aerobic exercise in this population.

The lack of significant change in SBP and DBP in the PRT group was not an unexpected finding, as eight of nine subjects were taking prescription medications for hypertension and exhibited near normal blood pressure at baseline (Table 4.1 and Figures 4.6a and b). Therefore, it is likely the physiological margin for improvement in PRT subjects was already diminished before commencing the study. Future studies which match subjects for degree of hypertension and medication via a minimisation approach [63] may provide a more accurate indication of the inter-modality effect of exercise on blood pressure in this cohort.

Insulin resistance and type 2 diabetes are associated with atherogenic lipid and lipoprotein profiles [104]. In the present investigation, LDL cholesterol remained elevated in both groups after exercise (Figures 4.11a and 4.11b), however, this measure does not account for LDL particle size or number which may be better predictors of cardiovascular risk [105]. Though total cholesterol levels in each group (Figure 4.8) were above the New Zealand Guidelines Group recommendation of ≤ 4.0 mmol/L, HDL levels were also above the desired ≥ 1.0 mmol/L (Figure 4.9), resulting in a near normal total cholesterol to HDL ratio of 4.0 (Figure 4.10) [106]. Interestingly, three PRT subjects (subjects, 3, 5, and 7) who were not prescribed cholesterol-lowering medications experienced a 0.8 to 1.1 mmol/L reduction in total cholesterol (Figure 4.8a). Four of five PRT subjects (subjects 1, 2, 4, and 9) taking statin medication had normal baseline cholesterol levels (range 3.6 to 3.9 mmol/L) and experienced a further reduction up to 0.6 mmol/L after 16 weeks. Consistent with a previous report showing beneficial effects of PRT on blood lipids [107], this finding suggests that PRT alone may be an effective therapeutic modality for reducing total cholesterol or possibly as an adjunct therapy for further reductions in those already prescribed statin medications. However, this hypothesis requires corroboration by further investigations with a larger number of participants.

Mean triglyceride levels in the AER group at baseline were within normal limits (≤ 1.7 mmol/L) [106], but significantly increased in all AER subjects after 16 weeks from 1.6 to 1.9 mmol/L, including three subjects who were taking statin medications (Figure 4.12b). The reason for this increase is not clear. While there may be metabolic changes occurring with exercise that could impact triglyceride concentrations, it is not possible to conclude that AER is responsible for this result. First, intraindividual biological variability in triglyceride concentrations has been

shown to be as high as 23% [108] and may partially account for the observed 20% increase from baseline to 16 weeks in the AER group. Second, triglyceride concentrations in both groups were similar at 16 weeks secondary to an increase in the AER group and a reduction in the PRT group, possibly reflecting a regression to the mean [109]. Lastly, several subjects admitted to eating breakfast before arrival to the hospital for the blood draw, at which time they were rescheduled. It is therefore possible some subjects were not fasted, but there is no way to definitively know this. Taken together, this finding should be considered speculative and warrants further investigation.

A key strength of the study was the high ratio of exercise leaders to participants (Chapter 3.5.1), which provided a supportive quasi-personal training environment and ensured 100% compliance with all exercise intervention protocols when subjects were present for training sessions. It further minimised the potential for injury and contributed to the overall safety of the trial. There was only one reported adverse event which spontaneously resolved without sequelae, and lends additional support to previous reports that high-intensity exercise is safe, well-tolerated, and feasible in high-risk individuals with type 2 diabetes [30, 41, 42, 44].

A limitation of this study was the lack of a non-exercising control group. The initial intention was to conduct a randomised controlled trial of resistance training versus a sedentary non-exercise control group. Similar to a previous investigation [32], many potential subjects were acutely aware their diabetes placed them at greater health risk and stated they would drop out unless allocated to the exercise group. The research team convened to discuss alternate interventions that would be acceptable to Māori and Pacific peoples. After further review of the literature and discussions amongst investigators and consultants, the study design was adapted to compare the

differential effects of PRT and AER within the framework of a randomised trial. Both types of exercise have been shown to improve glycaemic control in people with type 2 diabetes [13-15], but no previous studies have evaluated these modalities within a Polynesian cohort with morbid obesity and type 2 diabetes.

Secondly, there were difficulties in monitoring dietary and physical activity habits outside of exercise sessions. A three-day food diary and International Physical Activity Questionnaire (IPAQ) [110] were initially administered to monitor these parameters, but were eventually abandoned due to non-compliance and participant dissatisfaction with these instruments. For example, food diaries did not provide useful data due to difficulties on the part of many subjects with serving size estimation, meals that were not recorded, or forms that were not returned to investigators despite repeated requests. Many subjects found the IPAQ daunting due to its length and confusing answer matrix, resulting in numerous missing values and consequently unusable data. In light of these difficulties, Māori and Pacific allied health consultants affiliated with the study suggested that future investigations should employ more basic, easy to administer questionnaires for monitoring diet and activity habits, but these would likely need to be developed and validated in a Polynesian population. Another option would be to incorporate more advanced objective assessment technologies such as global positioning satellite, inclinometers, and accelerometers to ascertain physical activity habits.

Thirdly, variability in blood outcome measures may have been due to a combination of factors. Though subjects were explicitly instructed to arrive to the hospital for the blood draw after a 12-hour fast, upon questioning several subjects revealed they had eaten breakfast. These subjects were sent home and rescheduled. However, it is possible others had their blood drawn in a non-fasted state. Subjects

were questioned on a weekly basis regarding changes to their current medications. No changes were noted, however in future studies, this should be objectively verified with each subject's diabetes management team.

Fourthly, participant recruitment and dropout were ongoing difficulties which resulted in low subject numbers (n = 9) and, consequently, reduced the extent to which statistical inferences could be made. Due to the small sample size in this study and the inherent potential for large or small intra- and inter-subject variability in some parameters, the acceptance or rejection of the null hypothesis based on *P* value alone may inadvertently expose or mask clinically meaningful physiological effects [111]. For this reason, individual subject data were visually inspected to determine if large or small changes in the mean after 16 weeks of training were influenced by a single outlier or other aberrant finding.

Lastly, the initial sample size calculation based on a study by Castaneda *et al.* [30] assumed a 1% reduction in HbA_{1c} between a resistance training and non-exercise control group and resulted in a required 12 subjects per group. However, with nine subjects per group, the SPIRIT study was likely underpowered and not sensitive enough to detect changes in HbA_{1c} between two exercise groups, both of which were initially hypothesised to experience reductions in HbA_{1c}. A subsequent sample size calculation was performed based on Sigal *et al.* [42] which included resistance and aerobic training groups. Assuming a smallest significant change (effect size) of 0.3 and a coefficient of variance of 0.2, this would have resulted in a required 18 subjects per group [112]. An alternative study design would have been an investigation of resistance training only evaluated *via* repeated measures ANOVA which would have yielded a higher number of subjects, but would not have had a comparator group. Though HbA_{1c} is a key outcome measure in clinically obese subjects with type 2

diabetes, powering the study based on other clinically important outcome measures such as blood pressure with a smallest significant change of 0.5 would have resulted in a total of seven subjects required per group [112]. Taken as a whole, the results of the present investigation must be considered preliminary and await corroboration by future well-powered studies with a larger number of subjects.

In conclusion, the application of 16 weeks of supervised high-intensity resistance or aerobic exercise to Māori and Pacific Islands people with type 2 diabetes and class III obesity was safe and well-tolerated but did not improve glycaemic control. Aerobic exercise resulted in statistically significant reductions in systolic and diastolic blood pressure, hip circumference, GLUT4, capillary density, and power output. Resistance training resulted in a reduction in hip circumference and an increase in upper and lower body strength. Greater attendance at training sessions independent of exercise modality was associated with reduced waist circumference. However, these results must be interpreted with caution due to low subject numbers. Future investigations of longer duration with a greater number of subjects, the addition of a dietary intervention, and improved behavioural techniques to enhance attendance may be required to improve type 2 diabetes outcomes in Māori and Pacific Islands people in New Zealand.

4.5 References

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CHAPTER 5

Effect of Exercise Training on Quality of Life

5.1 Introduction

Type 2 diabetes is an increasingly prevalent condition in a modern world of excess energy intake and physical inactivity [1] and comprises approximately 90% of all diagnosed diabetes cases [2]. Common comorbid conditions such as obesity, cardiovascular disease, neuropathy, and depression not only adversely affect the physical health of individuals with type 2 diabetes, but have also been shown to reduce health-related quality of life (QOL) [3-6]. Therefore, maintenance of optimal glycaemic homeostasis is important for delaying the early onset of diabetic complications and the preservation of QOL [7].

The current trident of type 2 diabetes management consists of a combination of medication, diet therapy, and exercise, with the latter garnering considerable empirical support in recent years [8-11]. While the role of exercise for improved glycaemic control is well-established in individuals with diabetes [8-11], comparatively few studies to date have evaluated its impact on QOL. In a study of 2,056 adults with type 2 diabetes, Glasgow and colleagues found that lower self-reported physical activity levels were associated with lower QOL domain scores (as assessed by the Medical Outcomes Study Short-Form 20), including perceptions of Physical Functioning, Social Functioning, and Mental Health [12]. Further, a few recent exercise intervention studies suggest that aerobic (AER) [13], AER plus diet [14], or exercise consultation [15] can significantly enhance psychological well-being [13] and QOL [14, 15] in adults with type 2 diabetes, while other studies employing AER and progressive resistance training (PRT) protocols have reported equivocal findings [16-18].

Within New Zealand, Māori and Pacific Islands (Polynesian) people suffer disproportionately from type 2 diabetes [19] and its comorbidities [20-24] and complications [25-27] compared to European New Zealanders. Moreover, in a

nationally representative survey of 7,862 New Zealand adults, Polynesian respondents scored lower on most QOL domain scales as compared to those of European origin [28]. Although, the authors did not elaborate on specific reasons for this disparity, it was suggested that cultural differences regarding the definitions and expectations of health might play a role [29]. Other reports have linked greater decrements in Polynesian health status to identified inequalities in income, education, employment, and housing [30], as well as interpersonal and institutional racism and discrimination [30, 31].

At present, there is a need to reduce the disparity in QOL between New Zealanders of Polynesian and European lineage. Therefore, investigations of treatment modalities which can enhance QOL in Polynesian people would be particularly valuable, especially in individuals afflicted with chronic diseases such as type 2 diabetes. There is evidence to suggest that PRT and AER can improve QOL, however no studies to date have evaluated the therapeutic role exercise may play in improving QOL in Māori and Pacific Islands people with type 2 diabetes. Therefore, the purpose of this component of the SPIRIT study was: (1) to determine if a 16 weeks intervention of either progressive resistance training or aerobic exercise could improve health-related QOL domain scores in this cohort; and (2) to determine which exercise modality may be more beneficial for inducing changes in QOL.

5.2 Methods

Specific details regarding exercise protocols and administration of the Medical Outcomes Study Short-Form 36 General Health Survey (SF36) quality of life questionnaire are presented in Chapter 3.

5.3 Results

5.3.1 Quality of life

One subject in the AER group did not complete the SF36 at 16 weeks and was not included in the final analysis. Analysis using pooled data (time effects) for the entire cohort are presented in Table 5.1. Physical QOL scores significantly improved for Physical Functioning ($P = 0.0004$), Role-Physical ($P = 0.02$), Bodily Pain ($P = 0.009$), and General Health ($P = 0.0001$) domains. Moreover, statistically significant improvements were noted in mental domains including Vitality ($P < 0.0001$), Social

Table 5.1: Summary of quality of life outcome measures in total cohort (n = 17)

Outcome Measures	Week 0	Week 16	Change	*P*
Quality of life domain				
Physical Functioning	65.9 ± 27.5	87.9 ± 18.2	22.1 ± 20.2	0.0004
Role-Physical	69.1 ± 35.9	88.2 ± 26.7	19.1 ± 31.3	0.02
Bodily Pain	66.7 ± 16.9	78.8 ± 21.5	12.2 ± 16.7	0.009
General Health	51.1 ± 26.4	70.0 ± 21.3	18.9 ± 15.3	0.0001
Vitality	51.8 ± 19.8	73.8 ± 16	22.1 ± 16.9	<0.0001
Social Functioning	72.8 ± 20.8	90.4 ± 12.9	17.6 ± 21.2	0.003
Role-Emotional	76.0 ± 39.3	98.0 ± 8.1	22.1 ± 41.3	0.04
Mental Health	80.0 ± 10.4	85.4 ± 9.3	5.4 ± 12.2	0.09
Summary scores				
Physical Component	41.0 ± 12.1	49.4 ± 10.1	8.4 ± 4.7	<0.0001
Mental Component	51.5 ± 8.2	56.6 ± 3.8	5.1 ± 8.4	0.02

All data expressed as mean ± SD.

Functioning ($P = 0.003$), and Role-Emotional ($P = 0.04$) scales. Analysis of the physical (PCS) and mental (MCS) component summary scales revealed that PCS ($P < 0.0001$) and MCS ($P = 0.02$) improved significantly over time in the entire cohort.

Within and between group results for all domains and component summary scales are presented in Table 5.2. Repeated measure analysis of variance revealed that the PRT group experienced significant improvements in Physical Functioning ($P = 0.002$), Role-Physical ($P = 0.007$), General Health ($P = 0.008$), Vitality ($P = 0.006$), Social Functioning ($P = 0.007$), and Role-Emotional ($P = 0.04$) subscales (Table 5.2).

Analysis of the component summary scales revealed a significant improvement on the PCS ($P < 0.001$) (Table 5.2).

In the AER group, there were significant improvements on Physical Functioning ($P = 0.05$), Bodily Pain ($P = 0.02$), General Health ($P = 0.01$), and Vitality ($P = 0.002$) and a trend toward statistical significance in Social Functioning ($P = 0.10$) and Mental Health ($P = 0.07$). No significant differences were seen in Role-Physical and Role-Emotional ($P > 0.07$) (Table 5.2). A significant improvement was also observed on the PCS ($P = 0.002$), but not the MCS ($P > 0.07$).

Between group repeated measure analysis of variance revealed no significant differences between groups on any QOL domain score (Table 5.2).

5.3.2 Attendance

Average attendance to the exercise sessions for the entire cohort was only 70%, and only eight of 18 subjects completed at least 36 of the available 48 exercise sessions (75%). Linear univariate regression analyses were conducted using pooled data for the whole cohort to determine if higher attendance was associated with a larger gain in QOL. However, there was no association between the number of sessions attended and change in any QOL domain score ($P = 0.23$ to 0.97) (Table 5.3).

Table 5.2: Summary of within and between group differences for quality of life domains and component summary scores (n = 17)

Outcome Measures	PRT (n = 9)				AER (n = 8)				*P (between groups)*
	Week 0	Week 16	Change	*P*	Week 0	Week 16	Change	*P*	
Quality of life domain									
Physical Functioning	63.3 ± 28.5	86.1 ± 23.6	22.8 ± 15.2	0.002	68.8 ± 28	90.0 ± 10.7	21.3 ± 25.7	0.05	0.88
Role-Physical	61.1 ± 30.9	88.9 ± 18.2	27.8 ± 23.2	0.007	78.1 ± 41.1	87.5 ± 35.4	9.4 ± 37.6	0.50	0.24
Bodily Pain	61.0 ± 19.4	75.6 ± 27.4	14.6 ± 22	0.08	73.0 ± 11.8	82.5 ± 13.2	9.5 ± 8.6	0.02	0.55
General Health	52.7 ± 33.5	71.4 ± 28.7	18.8 ± 15.9	0.008	49.4 ± 17.4	68.4 ± 9.6	19.0 ± 15.8	0.01	0.98
Vitality	52.8 ± 22.2	78.3 ± 17.9	25.6 ± 20.8	0.006	50.6 ± 18.2	68.8 ± 12.7	18.1 ± 11	0.002	0.38
Social Functioning	75.0 ± 15.3	91.7 ± 14	16.7 ± 14	0.007	70.3 ± 26.6	89 ± 12.4	18.8 ± 28.3	0.10	0.85
Role-Emotional	65.7 ± 41.8	100.0 ± 0	34.3 ± 41.8	0.04	87.5 ± 35.4	95.8 ± 11.8	8.3 ± 38.8	0.56	0.21
Mental Health	84.0 ± 9.6	87.6 ± 6.5	3.6 ± 14.2	0.47	75.5 ± 9.9	83.0 ± 11.7	7.5 ± 9.9	0.07	0.52
Summary scores									
Physical Component	39.2 ± 14	48.6 ± 12.9	9.4 ± 5	<0.001	43.1 ± 10.1	50.4 ± 6.4	7.3 ± 4.5	0.002	0.38
Mental Component	52.6 ± 8.5	58.3 ± 3.1	5.7 ± 9.5	0.11	50.2 ± 8.1	54.6 ± 3.6	4.4 ± 7.4	0.14	0.76

Data expressed as mean ± SD. Abbreviations: PRT—Progressive Resistance Training; AER—Aerobic Exercise Training.

Table 5.3: Correlation coefficients for number of sessions attended and quality of life domain change scores (n = 17)

	r	*P*
Quality of Life Domain		
Physical Functioning	+0.09	0.72
Role-Physical	+0.26	0.31
Bodily Pain	−0.01	0.97
General Health	−0.31	0.23
Vitality	+0.09	0.72
Social Functioning	+0.12	0.65
Role-Emotional	−0.14	0.58
Mental Health	−0.04	0.88
Summary Scales		
Physical Component	+0.29	0.26
Mental Component	0.05	0.84

5.4 Discussion

The SPIRIT study is the first randomised trial to demonstrate that PRT and AER are safe and efficacious for improving health-related QOL in morbidly obese (BMI = 43.8 ± 9.5 kg/m^2) Māori and Pacific Islands people with type 2 diabetes. Pooled analysis of the entire cohort (n = 17) revealed statistically significant improvements on all SF36 domains except for Mental Health. Both PCS and MCS scores also significantly improved in the whole cohort after the intervention period. Within groups, PRT significantly improved Physical Functioning, Role-Physical, General Health, Vitality, Social Functioning, and Role-Emotional domain scores. Aerobic training resulted in significant improvements in Physical Functioning, Bodily Pain, General Health, and Vitality subscales. Significant improvements were observed on the Physical Component Summary scale in both groups with a trend toward statistical significance on the MCS in the PRT group. No between group differences were detected on any domain or summary scale suggesting both exercise modalities are

effective for improving QOL.

The finding that both PRT and AER improved virtually all QOL domain scores may have important implications for enhanced diabetes care in this cohort, given that Polynesian people have previously been shown to have lower self-reported QOL than the general New Zealand population [32]. Resistance training offers a variety of exercise movements and appears to be a safe and efficacious alternative to repetitive and aerobic exercises which move through the same motor unit recruitment patterns. Many participants undergoing PRT anecdotally expressed their satisfaction with being assigned to this modality, while a number of AER subjects stated they "wished they were doing the weight lifting exercise."

Low attendance and subject drop-out were issues in the present study. While 18 of 26 subjects completed the study, only eight attended at least 36 (75%) or more of the available 48 sessions over the 16 week intervention. However, linear univariate regression analyses revealed no association between higher attendance levels and QOL subscale change scores. Whilst less than satisfactory attendance is a plausible explanation for the lack of change in HbA_{1c} and other physiological markers (Chapter 4), one to two exercise sessions per week appears to provide adequate stimulus to effect statistically significant improvements in QOL.

Enhanced QOL in this cohort secondary to 16 weeks of high-intensity exercise might also be attributable to social factors and may have important long-term implications for improved glycaemic control. Ligtenberg *et al.* [13] attributed improvements in psychological well-being to an enhanced sense of self-efficacy and self esteem in patients with type 2 diabetes. Although self-efficacy and self-esteem were not formally measured in the present trial, subjects verbally expressed their satisfaction with the exercise setting which may have contributed to the improvements

in QOL. Common reasons cited were the supportive nature of the group exercise sessions, shared culture and language with other participants, and one-on-one supervision. A few subjects were so enthusiastic about exercise that they arranged with investigators to make up missed sessions on non-study days or outside of usual class times. If subject attitudes toward exercise, self-efficacy, and self-esteem improve in tandem with QOL, then this could be a motivating factor to continue exercising on a long-term basis, which may eventually translate into appreciable reductions in HbA_{1c}. However, this hypothesis has yet to be tested.

Participants verbally expressed their satisfaction with the group environment and one-on-one exercise supervision. The exercise room at Porirua City Fitness was an open plan room which facilitated socialisation not only with fellow participants but also with gym members and friends and family who were attending for moral support. It is possible the observed improvements in QOL may have been favourably influenced by the social element of meeting new people, making friends, and interacting with co-participants and exercise leaders three days per week. Consistent with previous reports [33], social support in this cohort appeared to be an inherent and important aspect of exercise and investigators may wish to consider this in developing future Polynesian exercise trials.

The results of the present trial agree with some [13-15] but not all [16-18] studies published on exercise as a QOL intervention in diabetes. In a study by Ligtenberg *et al.*, six weeks of moderate- to high-intensity AER three times per week significantly improved self-reported psychological well-being ($P = 0.02$), anxiety ($P = 0.01$), positive well-being ($P = 0.01$), and energy ($P = 0.03$) in older subjects with type 2 diabetes compared to a non-exercise control group, [13]. In another study, subjects with type 2 diabetes undergoing 18 months of twice-weekly moderate-intensity AER

plus diet significantly improved well-being compared to the diet, exercise, and control groups (all $P = < 0.05$) [14]. Kirk *et al.* [15] reported that subjects with type 2 diabetes receiving a single exercise consultation (with research assistant) plus written exercise guidelines tended to improve on most subscales of the SF36 and Well-Being Questionnaires, but only vitality and mental health scores were significantly higher after five weeks. Between groups, mental health scores were significantly higher compared to a control group receiving written exercise guidelines only. However, care must be taken in comparing the findings from the present study to the results of previous studies due to differences in types of questionnaires administered, exercise protocols, intervention duration, the addition of a dietary arm, and reporting methodologies.

The results of the present study contrast with those of previous reports in type 2 diabetes [16-18]. Tessier and colleagues found that 16 weeks of combined low- to moderate-intensity PRT and AER three times per week did not improve quality of life scores [16]. Holton *et al.* reported no improvement in PCS and MCS scores on the SF36 secondary to 10 weeks of supervised moderate intensity AER for 20 to 45 minutes three times per week [18]. Lambers *et al.* found no improvement in QOL scores in subjects assigned to 12 weeks of three times weekly combined moderate-intensity PRT and AER, AER only, or a non-exercise control group [17]. The reason for lack of agreement with other studies is difficult to determine, but might be explained by the comparatively lower exercise intensities, intervention duration relative to the present investigation, or other factors such as socialisation, group exercise environment, or the support of family and friends.

5.4.1 Limitations

There were a number of limitations to the present study. The SF36 is a general

QOL assessment instrument and only gives an indication of overall physical and mental improvements. While some authors believe a general questionnaire might not be sensitive enough to detect small changes in QOL [34], the magnitude of statistical significance on many of the physical subscales in the present study may have been adequate to override sensitivity concerns. Scott *et al.* [29] suggested that SF36 may not accurately reflect QOL in Pacific Islands people and Māori 45 years or older due to a perceived health paradigm which does not separate physical and mental health domains. However, additional research is necessary to corroborate this hypothesis. To date, no specialised QOL questionnaires have been specifically designed for use in the Polynesian population and, until the development of such an instrument, SF36 represents the most robust and validated QOL tool available [35]. Moreover, because SF36 is a general QOL instrument, the administration of diabetes- [36] and obesity-specific [37] QOL questionnaires, or a combination thereof, in future investigations may provide additional disease-specific information regarding QOL improvements in this cohort.

A second limitation was the lack of participant follow up to determine if these improvements could be sustained on a long-term basis without the group exercise environment, on-site family and friend support, and one-on-one supervision. A study by Ligtenberg *et al.* [13] found that subjects with type 2 diabetes reverted to baseline levels after the supervised six-week exercise program, though the duration of the follow up period was not reported. Future studies should evaluate subjects at various time points after completion of the intervention period.

Lastly, a key strength of the study might also have been a limitation. It is possible that the observed improvement in QOL may have been favourably influenced by the social element of meeting new people, making friends, and interacting with co-

participants and exercise leaders three days per week. However, by nature of the group setting, interpersonal interactions would be difficult to control. Future trials involving a non-exercise control group may be necessary to test this hypothesis.

In conclusion, this study demonstrates that both PRT and AER can significantly improve health-related QOL in Māori and Pacific Islands people with type 2 diabetes. Thus, it is possible that psychological improvements may precede physiological changes in this cohort. Longer intervention periods (> 16 weeks) may be necessary to induce more appreciable changes in physiological outcomes. Relatively few studies have been conducted on the impact of exercise on self-reported QOL in people with type 2 diabetes and, up to this study, none in diabetic Polynesian cohort. Future QOL studies with larger numbers of subjects, better attendance and retention strategies, standardised and thoroughly described exercise protocols, adequate follow-up testing, and which incorporate more disease specific and culturally-appropriate psychometric instruments may help provide a more thorough understanding of the extent to which high-intensity exercise improves health-related QOL in Polynesian New Zealanders.

5.5 References

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CHAPTER 6

Conclusion

6.1 Introduction

The **S**outh **P**acific **I**slands **R**esist diabetes with **I**ntense **T**raining (SPIRIT) study investigated the effects of 16 weeks of high-intensity progressive resistance training (PRT) versus aerobic exercise (AER) on glycaemic control and associated metabolic, anthropometric, and psychological outcomes in morbidly obese Māori and Pacific Islands people with type 2 diabetes. This study is novel because it is the first clinical exercise investigation in Polynesian people with type 2 diabetes and included the most obese cohort (body mass index 43.8 ± 9.5 kg/m^2) of any clinical exercise trial to date for the treatment of type 2 diabetes. In order to develop and implement this research project, extensive cultural, medical, and organisational consultation was undertaken to assure that study protocols were safe and acceptable to Polynesian people.

The principal findings from the SPIRIT study indicate the following: 1) high-intensity PRT and AER were safe and well-tolerated by Māori and Pacific Islands people, but did not result in improved glycaemic control; 2) AER training induced statistically significant reductions in systolic and diastolic blood pressure, increased GLUT4 and capillary density, and a trend toward a reduction in fasting plasma insulin; and 3) both PRT and AER significantly enhanced many components of self-reported quality of life.

The SPIRIT trial was the first investigation to provid8e a preliminary empirical foundation that may aid in the development of future structured exercise trials in Māori and Pacific Islands people with type 2 diabetes. The purpose of this chapter is to discuss the principal findings and limitations of the study, and implications and recommendations for ongoing research in this high risk cohort.

6.2 Cultural, medical, and organisational consultation

6.2.1 Cultural consultation

Research in New Zealand must be carried out in a culturally-sensitive manner with respect to the well-being of Māori and Pacific Islands people. Cultural consultation was not only a required part of the ethics approval process for the SPIRIT study, but the input received from cultural and religious leaders played a valuable role in establishing and carrying out the study protocols.

Consultation entailed numerous personal meetings and presentations to church leaders and liaisons within Pacific health organisations such as Pacific Health Services in Porirua and Wellington and the National Heart Foundation's Pacific Heart Beat program. Question and answer sessions with cultural leaders were important because they provided an opportunity for interested parties to voice their concerns regarding the exercise protocols, participant safety, and the potential benefits to the community at large.

6.2.1.1 SPIRIT study acceptability to Māori and Pacific Island people

6.2.1.1.1 Exercise venue

The exercise training venue was important for preserving and reinforcing cultural and ethnic identities. The Marae (sacred Māori meeting place for religious and social gatherings) or Pacific church might be considered the ideal location, but for the purpose of a clinical exercise investigation, this may not be feasible without the necessary exercise equipment for quantifying exercise workloads. In the development phase of the study, one consultant of European origin thought a commercial fitness centre would be a barrier to Polynesian participants. However, the decision to conduct the study at City Fitness gym in Porirua, a predominantly Polynesian community, was

met with approval by cultural leaders due to the gym's high Māori and Pacific membership base and provided a welcoming and supportive group atmosphere acceptable to participants. Participants spoke their own language with staff, club members, and fellow subjects, dressed in traditional clothing if desired (as opposed to athletic clothing), and sometimes prayed together. Furthermore, some cultural leaders involved in the consultation process were also members at the gym and provided on-site encouragement to study participants during exercise sessions. The present study demonstrates that a commercial fitness centre within a Polynesian community is an acceptable and feasible alternative to the Marae and Pacific church setting.

6.2.1.1.2 Exercise leaders

There were eight exercise leaders in total, comprised of four advanced exercise science students from Massey University, three qualified personal trainers, and the principal investigator (WRS, a clinical exercise physiologist). The high ratio of exercise leaders to participants resulted in one-on-one support during most exercise sessions and provided a quasi-personal training environment. Exercise staff and supporting research team members maintained a high-level of commitment and made every effort to accommodate participants' needs. For example, exercise sessions were provided outside usual class times if needed to allow for subjects to meet pre-existing family, religious, or employment commitments.

6.2.1.1.3 Exercise protocols

The PRT and AER exercise modalities employed in the study (i.e., adjustable weight resistance training machines and stationary cycle ergometers) were selected in order to quantify workloads and make precise adjustments in training intensity. This

allowed the exercise leaders to gradually progress participants from lower to higher intensities per study protocols which also reduced the risk of muscle soreness. Despite the lack of a cultural element to the training modalities (i.e., traditional Māori song and dance (*kapa haka*) or other Pacific dance movements), many participants verbally expressed their satisfaction with the high-intensity, gym-based exercise regimen.

6.2.1.1.4 Social support

Social support was an important aspect of the SPIRIT study. Family, friends, and co-workers without diabetes were encouraged by investigators to attend and participate in exercise sessions to motivate and support subjects' efforts. Some participants verbally expressed that this provision played an integral role in their attendance and stated it would have been difficult without this support. A high level of camaraderie also developed amongst participants, as they spoke freely about their health, championed each others' successes, and offered genuine and empathetic encouragement to each other. A number of subjects exchanged phone numbers and email addresses to maintain contact outside study hours and organise carpools to exercise sessions if necessary.

6.2.2 Medical consultation

Extensive consultation was also undertaken with regional medical and allied health professionals as well as commercial and tertiary institutions. Doctors and diabetes nurse specialists provided technical advice regarding interpretation of outcome measures most pertinent to diabetes care and management (i.e., HbA_{1c}, fasting glucose, insulin), as well as advice regarding necessary medical supplies (i.e., blood vials, glucose meters and strips, etc). Endocrinologist Dr. Jeremy Krebs not only provided

valuable clinical information regarding study design and diabetes outcome measures during the consultation process but also joined the study as a medical research collaborator. Renal specialist Dr. Murray Leikis provided important information regarding the muscle biopsy procedure, development of the biopsy informed consent, and was responsible for performing the actual muscle biopsy harvest.

6.2.3 Organisational consultation

Diabetes organisations such as the New Zealand Society for the Study of Diabetes invited WRS to give a presentation on the SPIRIT study at the Wellington forum meeting at Hutt Hospital in Lower Hutt. It provided an opportunity to present the study protocols to a large audience of doctors, nurses, and diabetes educators, as well as commercial organisations such as Roche Diagnostics. Roche later donated Accu-check glucose meters which were important for monitoring pre- and post-exercise capillary blood glucose levels. Presentations were also delivered to members of Diabetes New Zealand's Wellington and Kapiti chapters which offered exposure to potential subjects with type 2 diabetes.

6.3 Principal findings of the SPIRIT study

Previous high-intensity exercise training studies of at least 16 weeks and without dietary treatment demonstrated a reduction in HbA_{1c} ranging from 0.4 to 1.0% [1-3]. In the SPIRIT study, exercise was expected to reduce HbA_{1c} levels to a similar or greater extent. It was thought that the high degree of obesity and physical deconditioning secondary to a prolonged sedentary lifestyle might have created a higher physiological margin for improvement in clinical outcome measures. However, despite the high-intensity nature of both exercise modalities in the present study, there were no

statistically significant improvements in glycaemic control. The SPIRIT cohort exhibited class III obesity as defined by the World Health Organisation [4] thereby making it the most obese cohort (body mass index $\geq 43.8 \pm 9.5$ kg/m^2) of any exercise study for the treatment of type 2 diabetes to date. As discussed in Chapter 4, it is possible the level of obesity in this group may have been so extreme as to minimise or delay the potential for improvement in glycaemic control and many associated metabolic aberrations.

The significant reduction in both systolic and diastolic blood pressure after 16 weeks of AER is a clinically important finding (Chapter 4). Māori and Pacific Islands people are not only disproportionately afflicted with type 2 diabetes [5] but also have a higher incidence of hypertension [6] and cardiovascular disease [7, 8] compared to European New Zealanders. Thus, any treatment modality which can reduce arterial blood pressure in Polynesian people warrants further investigation. The incorporation of regular aerobic activity as part of a culturally-appropriate hypertension management program, in conjunction with standard diabetes and obesity medical care, may help reduce morbidity and mortality in Māori and Pacific Islands people.

Despite no statistically significant improvement in glycaemic control in this study, there were significant within and between group improvements in health-related quality of life secondary to 16 weeks of both PRT and AER (Chapter 5.3.1). These findings suggest that even with less than optimal subject attendance, exercise still significantly increased most quality of life domain sub-scales and the physical and mental component summary scores. It is possible these psychological improvements may serve as a motivating force to continue with exercise which may eventually translate into quantifiable physiological adaptations. However, because these results are based on a small number of subjects, further investigation is necessary to explore the

link between exercise and quality of life improvements and the potential impact these psychological improvements may have on long-term exercise adherence in Māori and Pacific Islands people.

6.4 Limitations and difficulties of the SPIRIT study

There were a number of limitations and difficulties in the development and execution of the SPIRIT study pertaining to subject recruitment, establishing a non-exercise control group, and subject attendance issues.

6.4.1 Recruitment and subject numbers

In spite of receiving 18 months of cultural consultation and promotion of the study through local Marae, Pacific churches, and Porirua medical clinics, the overall number of subjects recruited was low. In fact, many potential participants did not find out about the study through advertisements but were instead recruited by family members, friends, and co-workers who were already enrolled in the study, similar to the "snowball" effect described by Murphy *et al.* [9]. This suggests that recruitment for Polynesian research may also need to be tailored to facilitate referrals through existing study participants, many of whom are trusted personal contacts, in addition to traditional advertising methods (i.e., newspaper, flyers, and referrals from health professionals).

A multi-centre trial conducted across New Zealand and other island nations of the South Pacific Ocean is another option for enhancing recruitment. In the present study, the research team considered offering training sessions at both Massey University's Wellington campus and City Fitness in Porirua. However, this option would have introduced a significant increase in both cost and staffing requirements beyond funding levels already allocated to the study. Future well-funded Polynesian

exercise trials with ample staffing resources may be a feasible alternative to increase overall number of subjects.

As discussed in Chapter 4, the low number of subjects per group in this study clearly introduces limitations in statistical power and, consequently, the extent to which inferences can be made based on these data. For this reason, individual subject results (discussed in Chapter 4.3.7 and presented in Appendix E) were evaluated for each outcome measure in order identify anomalously high or low values which might have unduly influenced mean change scores and standard deviations. Therefore, the finding of no statistically significant reduction in HbA_{1c} in both groups must be interpreted with caution due to low subject numbers and heterogeneity in individual results and await corroboration by future studies with a larger number of subjects and adequate statistical power.

Variability between groups in baseline HbA_{1c}, systolic and diastolic blood pressure values, and medications prescribed was a potential limitation which was created at the time of initial randomisation. Combined with the fact that small numbers minimise the extent to which statistical inferences can be made, a minimisation approach [10] which matches subjects based on predefined subject factors could have dispersed this variability. This would have reduced the likelihood of introduced bias at the start of the trial.

6.4.2 Lack of control group

The initial intention of carrying out a trial of PRT versus a non-exercise control group was met with resistance from potential participants during the recruitment phase. Numerous volunteers explicitly stated they would immediately drop out of the study if randomised to a non-exercise control group because they knew exercise could

potentially improve their diabetes and should therefore be allocated to an intervention group. Upon consultation with cultural liaisons, the substitution of an aerobic intervention group in place of the control group was deemed a robust alternative and was acceptable to potential participants. Other researchers conducting Polynesian lifestyle interventions reported a similar experience [11, 12]. For example, in one study, participants refused to be randomised to a control group [11] while others were so upset about being allocated to a non-exercise group that they formed their own exercise group outside of the study [12]. In another study with the aim of predicting insulin resistance in Māori participants, Bell *et al.* [13] reported it was culturally inappropriate to exclude participants after they'd already volunteered. This is an interesting observation but it is not known if this phenomenon is limited to Polynesian participants.

A potential alternative to a non-exercise control group in future studies may be to allocate subjects to a sham control group entailing light stretching or relaxation movements similar to that employed by Van Rooijen *et al.* [14]. This modality would be expected to mildly improve flexibility and is unlikely to elicit any significant metabolic improvements similar to high-intensity strength or aerobic training modalities. However, this may also be deemed deceptive and unacceptable by Māori and Pacific Islands people. Another option would be to employ a randomised cross-over study design whereby subjects receive both modalities for 16 weeks with a wash out period in between interventions, though there is no way to ascertain the optimal length of the wash out period [15]. A second limitation of this approach might be a "period effect" whereby the progression of type 2 diabetes may impact the efficacy of the treatments over time [15].

6.4.3 Attendance

Only eight of 18 subjects that completed the study attended at least 36 of 48 (75%) available exercise sessions. This may have resulted in a less than optimal training stimulus required for appreciable changes in glycaemic control and associated metabolic outcomes. However, statistically significant improvements were observed in health-related quality of life for both PRT and AER, suggesting that even with less than optimal attendance, participants felt positive about their health outlook. Because exercise was shown to exert a strong beneficial effect on quality of life in participants in the present study, it is possible that this effect may motivate individuals to continue with their exercise regimen which could eventually translate into measurable improvements in metabolic outcomes. This hypothesis warrants confirmation by future investigations.

6.5 Considerations for future research

6.5.1 Follow-up

Participants verbally expressed their satisfaction with the high-intensity nature of the gym-based program, but acknowledged this would be difficult to maintain without the level of supervision provided during the SPIRIT study. Ongoing supervised training sessions and continued follow up (> 1 year) were not feasible due to funding and staffing limitations (i.e., exercise leaders graduated from university). Participants were offered discounted memberships to Porirua City Fitness gym, but only five subjects purchased memberships and continued exercising on their own. Five other subjects continued exercising either at a different fitness centre or independently (i.e., walking in their neighbourhood). Though long-term monitoring after the 16 week intervention was beyond the scope of the SPIRIT study, future investigators conducting exercise research in Polynesian cohorts may wish to incorporate a more robust follow-up period to assess both long-term adherence to high-intensity exercise and its impact

on glycaemic control.

6.5.2 Cross-ethnic studies

The SPIRIT study sought to determine the efficacy of PRT and AER on glycaemic control and associated metabolic outcomes within a diabetic Polynesian cohort, but did not include a parallel New Zealand European cohort for ethnic comparisons. Two studies published during the implementation of the SPIRIT study [16, 17] evaluated the impact of exercise on a Caucasian group versus Middle-Eastern [16] or African-American [17] subjects. As discussed in Chapter 2, the physiological response to exercise may have been influenced by ethnicity in these studies [16, 17] but, due to limitations in methodology and reporting, further research is required to confirm these findings. Furthermore, even when there may be statistically significant physiological differences in the exercise response to a given exercise prescription between two or more ethnic groups, it is not known how such a difference relates to the actual population variance in a particular outcome measure. In addition to the possible interethnic difference in exercise response, there is also the potential for intraethnic variation which may enhance or lessen the appearance of ethnic differences in exercise response. Subsequent studies should examine the physiological impact of precise exercise prescriptions on Polynesian and European New Zealanders with respect to training modality, frequency, intensity, duration, volume, specific exercises performed, equipment used, and training supervision. These data are necessary to establish a dose-response relationship of exercise required for improving clinical outcomes in this group and may elucidate the potential impact of ethnicity on the exercise response.

6.5.3 Increased funding and staffing

The entirety of the SPIRIT study was financed by start-up funding through the Massey University Research Fund and was spent mainly on the blood analyses at Capital and Coast District Health Board, miscellaneous sundries, and expenses associated with analysing the muscle biopsy samples at University of Otago at Dunedin. More sensitive, and consequently more expensive, outcome assessment methods such as the hyperinsulinaemic euglycaemic clamp for determining insulin sensitivity or dual-energy x-ray absorptiometry for determining body composition were not fiscally viable, so more readily available options (i.e., homeostasis modelling assessment and bioelectrical impedance analysis) were selected. However, there was a considerable amount of goodwill generated towards the study from the extensive medical consultation that was undertaken during the development of the SPIRIT study. For example, Roche Diagnostics donated Accu-Chek Performa capillary blood glucose meters and general practitioners and pharmacies located in the Porirua community donated glucose strips. Outpatient exam rooms at Kenepuru and clinician labour hours for the muscle biopsy harvest (Dr. Murray Leikis), as well as liquid nitrogen (for biopsy samples) and blood vials were all donated to the study free of charge. Future studies are needed to confirm the preliminary findings of the present investigations and would require adequate funding and staffing resources to accommodate more sensitive outcome measure assessments and ongoing support and supervision during longer follow up periods.

6.5.4 Ongoing SPIRIT research

Other investigators affiliated with the SPIRIT study in New Zealand and the United States are conducting ongoing analyses on the muscle biopsy samples evaluating key glycolytic and oxidative enzymes associated with substrate utilisation and energy

metabolism, as well as epigenetic analyses such as microRNA, mRNA, and SNPS. It is possible that these analyses may yield more specific information pertinent to molecular-level adaptations which may potentially precede metabolic and anthropometric changes. If this is the case, then it may lend support to the hypothesis that studies of longer duration (≥ 16 weeks) are required to effect more significant changes in glycaemic control and associated outcome measures.

6.6 Opportunity for action

There is a paucity of empirical evidence on exercise management of diabetes in Māori and Pacific Islands people in New Zealand. This gap in the literature remains virtually ignored despite the clear and present public health epidemic of diabetes and obesity in Polynesian people. SPIRIT study is the first clinical exercise trial to date conducted in this high risk cohort. It is hoped that this preliminary research will provide the necessary impetus to spawn more large-scale, well-funded studies using more sensitive and refined methods for assessing key outcome measures, which may eventually provide more data on the impact of exercise on glycaemic control and associated cardiometabolic disruptions. Māori and Pacific investigators should not only be involved, but also maintain an ownership stake in the development, implementation, refinement, and ongoing monitoring of Polynesian exercise and lifestyle programs.

6.7 Conclusion

In conclusion, the successful development and implementation of the SPIRIT study demonstrates for the first time that a structured clinical exercise trial is feasible and acceptable to Māori and Pacific Islands people with type 2 diabetes and morbid obesity. The main findings of this investigation show that 16 weeks of high-intensity

gym-based exercise is safe and well-tolerated in Polynesian New Zealanders, but is insufficient to improve glycaemic control. There were significant improvements in health-related quality of life after PRT and AER, reductions in systolic and diastolic blood pressure, and increases in GLUT4 and capillary density after AER. Further large-scale clinical exercise trials with more subjects are required to corroborate these findings and advance the overall knowledge in this research area which may potentially minimise or eradicate ethnic health disparities in New Zealand. Strategies should be developed so that effective and targeted exercise interventions may be adapted into self-governed and culturally acceptable comprehensive lifestyle programs by which Māori and Pacific communities may benefit.

6.8 References

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APPENDIX A

Information Sheets and Consent Forms

INFORMATION SHEET

Study title
SPIRIT Study: South Pacific Islanders Resist diabetes with Intense Training

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Introduction
Hello and thank you for your interest. We would like to invite you to take part in a research study looking at the effects of weight lifting exercise in people with type 2 diabetes. This information sheet is meant to inform you of all possible benefits and risks. It is important that you read the following information. Please ask as many questions as possible to ensure you understand the procedures involved. Your participation is voluntary. You are free to withdraw from the study at any time.

About the study
Type 2 diabetes is a condition in which your body either doesn't produce enough insulin or your body is resistant to the effects of insulin (insulin resistance). Weight lifting and aerobic exercise have been shown to safely reduce fat, improve blood sugar control, and improve insulin resistance in people with type 2 diabetes. The goal of this study is to improve your diabetes control and overall health with weight lifting exercise or aerobic exercise.

Screening
Your safety is our top priority. You will be screened to make sure exercise is safe for you. We will contact your doctor only with your consent. We will request medical information that relates to your diabetes. We will also ask the doctor to sign a form which gives you permission to take part in the study.

Exercise vs. Control Group Assignment
In this study, you will be randomised (like the flip of a coin) to receive either resistance exercise training **or** aerobic exercise training

Resistance exercise group
The resistance exercise programme will consist of 16 weeks of weight lifting at City Fitness in Porirua. Exercise sessions will take place on Monday, Wednesday, and Friday. For your convenience, a variety of 1-hour time slots will be available. Each session will last approximately 45 minutes to 1 hour. A qualified exercise physiologist will supervise all exercise sessions.

Aerobic exercise group
The aerobic exercise programme will consist of 16 weeks of weight lifting at City Fitness in Porirua. Exercise sessions will take place on Monday, Wednesday, and Friday. For your convenience, a variety of 1-hour time slots will be available. Each session will last approximately 45 minutes to 1 hour. A qualified exercise physiologist will supervise all exercise sessions.

Health and fitness testing
Health and fitness tests will be done before and after the study. These tests will be done on 2 different days. Day 1 testing will take about 1 hour and 50 minutes. Day 2 testing will take about 45 minutes. Two (2) hours and 35 minutes of your time will be needed in total. These tests are important to help us understand the ways in which weight lifting improves diabetes control. All tests will be performed by qualified doctors, nurses, and exercise physiologists. After testing, you will be randomised (like the flip of a coin) to the resistance exercise or aerobic exercise group.

Day 1 testing:
Day 1 testing will take place at City Fitness in Porirua. You will undergo a number of tests as follows:

Questionnaires
You will be asked to fill in questionnaires about your personal information, physical activity level, physical well-being, and quality of life. You do not have to answer all the questions and you are free to stop at any time.

Body measurements
We will measure your height and weight with a standard hospital-grade scale. We will measure your waist and hip circumference with a tape measure. We will check your body fat levels with a bioelectrical impedance machine. This machine sends a harmless electrical impulse through your body. This impulse gives an estimation of your body fat. Your upper and lower body strength will be assessed on exercise weight machines.

Heart rate and blood pressure
We will check your resting heart rate by checking the pulse on your wrist. We will measure your blood pressure with a standard blood pressure cuff and stethoscope.

Urine sample
We will provide you with a special urine collection bottle. We will ask you to collect urine samples for a 24-hour period. We will ask you to return the urine on day 2 day two of testing.

Day 2 testing:
Day 2 testing will take place at Kenepuru Hospital. A trained doctor will take a small sample of muscle tissue (about the size of a grain of rice). These samples will be frozen for later testing

Blood draw
We will draw approximately 35-45 millilitres of blood from your arm. Your blood samples will be sent to Wellington Hospital laboratory services for analysis. Some blood may be frozen for later testing.

Benefits
Your participation in this study may improve your blood sugar control. Your doctor may decide to reduce the dosage of your diabetes medication, but this cannot be guaranteed. You may also see increases in your energy levels, improved muscle strength, loss of body fat, improved mood and outlook on life.

Risks and safety
1. There are risks associated with all forms of exercise. You will be supervised by a qualified exercise physiologist in order to minimise risks. Weight lifting and aerobic exercise may cause injury to your joints, muscles, tendons, or ligaments. There is a chance you may experience mild muscle soreness at the beginning. This is common and the discomfort usually disappears with rest after a few days. We will start with light weights or slow aerobic exercise to minimise this risk.

   Although uncommon, there is always a risk heart attack or stroke. We will try to minimise this risk by pre-screening all study participants. We also require that your doctor consent to your participation. If you qualify for the study, we will regularly monitor you for signs and symptoms. If you experience any serious symptoms, we will call for immediate emergency medical attention. All exercise training staff will be certified in first aid and basic life support.

2. Weight lifting and/or aerobic exercise may cause your blood sugar to drop. Symptoms of low blood sugar include the following:

   - Hunger
   - Dizziness
   - Weakness
   - Sweaty (more than usual)
   - Shaky (loss of coordination)

   We will closely monitor your blood sugar before and after exercise with a glucose meter. If you experience these symptoms, we will provide you with glucose to raise your blood sugar. You will be closely monitored until your blood sugar returns to normal and symptoms have disappeared.

3. You may experience arm pain and bruising from the blood draw. This should disappear within several days. Some people faint when having a blood test. We will make every effort to ensure this does not happen. Blood will be drawn by a trained person prepared to handle such situations.

4. The muscle biopsy will be done on your thigh by a trained doctor. It will be performed under local anaesthetic (pain killer). You may have some minor discomfort and bruising when the anaesthetic wears off. There is a risk of fainting. There is also a risk of infection any time a cut is made to the skin. You will be provided with instructions for care to reduce this risk.

5. You will answer a series of questionnaires relating to your health, activity, and outlook on life. The questions should not upset you. You do not have to answer any question that upsets you.

Payments

You do not have to pay anything to take part in the study. You will not be charged for doctor's visits, blood tests, or any other tests. All exercise training will be provided for free. No reward or compensation is paid to participate in this study. However, some monetary support will be offered to offset costs for travel to Kenepuru hospital for day 2 of testing.

Participation

- Your participation is entirely voluntary. You do not have to take part in this study, and if you choose not to take part you will still receive your usual diabetes treatment.
- If you need an interpreter, we will make every effort possible to provide one for you.
- If you do agree to take part you are free to withdraw from the study at any time, without having to give a reason and this will in no way affect your continuing health care**.**
- Participation in this study will be stopped should any harmful effects appear or if the study's doctor feels it is not in the participant's best interests to continue.
- If you have any questions or concerns about your rights as a participant in this research study you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.
  Telephone: (NZ wide) 0800 555 050
  Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)
  Email (NZ wide): advocacy@hdc.org.nz

Confidentiality and Information Protection

No material which could personally identify you will be used in any reports on this study. All information collected about you during the course of this study will be held strictly confidential and will only be used for purposes related to the study. Raw data will be kept in a locked file cabinet in Dr. Cheema's office on the Massey University campus. It will be secured for a period of 10 years as is required by law, after which it will be properly disposed in a secure manner. Upon completion of the study, a report of the findings will be made publicly available. Please feel free to contact William Sukala or Dr. Bobby Cheema (contact details written on page 1) if you have any questions about this study.

What happens if there are ill effects from the study? Is there compensation?

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

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

Potential medical insurance conflict

If you have private medical insurance, please check with your insurance company before agreeing to take part in the study. You should do this to ensure that your participation will not affect your medical insurance.

Statement of Approval

This project has been reviewed and approved on 16/10/2007 by the Central Regional Ethics Committee, Wellington Application CEN/07/08/054. If you have any concerns about the ethics of this study, please contact Claire Yendoll telephone (04) 496-2405 or by email claire_yendoll@moh.govt.nz

PARTICIPANT CONSENT FORM

Study Title: SPIRIT: South Pacific Islanders Resist diabetes with Intense Training

Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
English	I wish to have an interpreter.	Yes	No

I have read and I understand the information sheet dated 11/03/2008 for volunteers taking part in the above named study. ☐Yes ☐No

I have had the opportunity to discuss this study and I am satisfied with the answers I have been given. ☐Yes ☐No

I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study. ☐Yes ☐No

I understand that taking part in this study is voluntary (my choice). ☐Yes ☐No

I understand that I may withdraw from the study at any time. ☐Yes ☐No

I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study. ☐Yes ☐No

I understand that the treatment, or investigation, will be stopped if it should appear harmful to me. ☐Yes ☐No

I understand the compensation provisions for this study. ☐Yes ☐No

I have had time to consider whether to take part. ☐Yes ☐No

I know who to contact if I have any adverse effects to the study. ☐Yes ☐No

I know who to contact if I have any questions about the study	☐Yes ☐No
I agree to my blood being taken.	☐Yes ☐No
I agree to my blood being stored after collection for later testing.	☐Yes ☐No
I agree to a muscle biopsy sample being taken	☐Yes ☐No
I agree to my muscle biopsy sample being stored for later testing	☐Yes ☐No
I understand that some of the muscle biopsy analysis may be conducted in a laboratory overseas.	☐Yes ☐No
I wish to receive a copy of the results or have the researcher discuss the results with me.	☐Yes ☐No
I agree to my GP or other current provider being informed of my participation in this study.	☐Yes ☐No
I authorise my GP to release my medical information to study researchers.	☐Yes ☐No

I _____ (full name) hereby consent to take part in this study.

Date	
Signature	
Full names of Researchers	
Contact Phone Number for researchers	
Project explained by	
Project role	
Signature	
Date	

MUSCLE BIOPSY INFORMATION SHEET

Introduction
You have volunteered to take part in a research study that requires you to undergo a muscle biopsy. This is a commonly performed procedure in medicine and research. The procedure will be performed by a medical doctor trained to perform muscle biopsies or a specially trained researcher directly supervised by a medical doctor.

What is a muscle biopsy?
A muscle biopsy is an outpatient procedure to remove a small muscle sample, about the size of a grain of rice.

Why is a muscle biopsy performed?
The muscle cells of people with diabetes become resistant to the effects of insulin which leads to elevated blood sugar levels. Exercise has been shown to improve this condition, resulting in better blood sugar management. Muscle biopsy analysis allows researchers to directly study the components of muscle cells involved in insulin resistance and the ways in which exercise training may enhance their functioning.

In which muscle will the biopsy take place?
We will take a sample from your top/outer thigh muscle.

How is the biopsy performed?
The procedure is performed under local anaesthetic. You will be asked to lie down, and a local anaesthetic will be given in the site from which the biopsy will be taken. A small cut (incision) of 4-5mm is made, and the muscle is carefully exposed. The sample of muscle is then taken with a special needle designed for biopsies. The incision site will be sealed with a butterfly strip (instead of stitches). Although it is not necessary to avoid eating before the procedure, as there is no general anaesthetic, it is better not to eat immediately before (1-2 hours) the procedure in case you feel sick. The procedure takes around 30 minutes.

What do I do after the biopsy?
The incision will be closed with a suture strip and then covered with a good quality band-aid. Use an ice pack and bandage to reduce local inflammation for the first two (2) hours after the procedure. If possible, you should rest your leg for the first day if possible. Do your best to keep the site clean. First, wash it with warm water and soap, and then thoroughly dry the area with a clean towel. A topical antiseptic may be used as well. The site will gradually heal on its own.

What problems may there be with the biopsy?
The incision site may ooze a little, and this is normal. If there is excessive bleeding, you should contact the researchers. There is a small risk of the site becoming infected. If you experience excessive redness, swelling, or infection around the biopsy site or excessive pain or stiffness in your leg, you should consult your GP immediately. Treatment with antibiotics may be appropriate.

What are the side effects of a muscle biopsy?
As indicated above, there may be problems with bleeding or healing at the incision site. There

will be a small scar at the site of the procedure, which will heal gradually. If there is any pain or discomfort in the skin or muscle immediately following the procedure after the local anaesthetic has worn off, simple pain killing medication such as paracetamol may be taken.

What happens to the muscle biopsy?
The muscle sample is immediately frozen and stored at -70°C. It will later be processed and evaluated for markers related to the structure and function of muscle in people with diabetes. Some of the analyses may be conducted overseas. Any sample remaining after this analysis is stored, in case further analysis, or reanalysis is required in the future.

Do you have any further questions?
When you come into the hospital for the muscle biopsy, the doctor will seek your consent to the biopsy and provide further information. This is also a chance to ask any further questions you may have.

Statement of Approval

This project has been reviewed and approved by the Central Regional Ethics Committee, Wellington Application CEN/07/08/054. If you have any concerns about the ethics of this study, please contact Claire Yendoll telephone (04) 496-2405 or by email claire_yendoll@moh.govt.nz

MUSCLE BIOPSY CONSENT FORM

Study Title: SPIRIT: South Pacific Islanders Resist diabetes with Intense Training

Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
English	I wish to have an interpreter.	Yes	No

I have read and I understand the muscle biopsy information sheet dated 11/03/2008 for volunteers taking part in the above named study. ☐Yes ☐No

I have had the opportunity to discuss the muscle biopsy procedure and I am satisfied with the answers I have been given. ☐Yes ☐No

I have had the opportunity to use whanau support or a friend to help me ask questions and understand the muscle biopsy procedure. ☐Yes ☐No

I understand that undergoing the muscle biopsy procedure is voluntary (my choice). ☐Yes ☐No

I understand that I may withdraw my consent for the muscle biopsy at any time. ☐Yes ☐No

I agree to a muscle biopsy sample being taken ☐Yes ☐No

I agree to my muscle biopsy sample being stored for later testing subject to ethical approval. ☐Yes ☐No

I understand that some of the muscle biopsy analysis may be conducted in a laboratory overseas.	☐Yes ☐No
I understand that muscle tissue remaining after analyses will be destroyed via appropriate biohazard disposal procedures.	☐Yes ☐No
I have had time to consider whether to undergo the muscle biopsy procedure.	☐Yes ☐No
I know who to contact if I have any adverse effects to the muscle biopsy.	☐Yes ☐No
I know who to contact if I have any questions about the muscle biopsy.	☐Yes ☐No

I _____ (full name) hereby consent to take part in this study.

Date	
Signature	
Full names of Researchers	
Contact Phone Number for researchers	
Project explained by	
Project role	
Signature	
Date	

SPIRIT Confirmation Cards

Participant Confirmation Card

Name:

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APPENDIX B

Subject Screening and Data Sheets

SPIRIT TELEPHONE SCREENING FORM

Name_____ Phone_____
Address_____ Cell_____
_____ Email_____

1) Self-identified Maori or Pacific Islands descent? **Y or N**

2) Age and date of birth?_____

3) Diagnosed type 2 diabetes? **Y or N**

4) Waist circumference (if known):_____Pants waist size:_____

5) Are you currently taking oral medications? **Y or N**
Med names:_____

6a) Have there been any changes in your medications? **Y or N**
If so, how long ago (date)_____

7) Are you currently receiving insulin injections? **Y or N**

8) Any diagnosed heart issues (heart attack, angioplasty, open heart surgery)? **Y or N**
If yes, what condition?_____

9) Are you currently engaged in any structured exercise programme? **Y or N**

10) Are you available for the 16 week duration of the study in Porirua? **Y or N**

Other notes:_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Patient Name:_____

DOB : _____

Medical Screening Form

• **Checklist of conditions and events, which would require temporary exclusion from study:**

STOP! Permanent Exclusion	**WAIT! Temporary Exclusion**	**GO! Exercise Recommended**
If any boxes in this column are checked, subject is ineligible to participate in study.	If any boxes in this column are ticked, follow protocols for further evaluation of these concerns with medical staff prior to reevaluating for appropriateness or modification of exercise prescription.	If only boxes in this column are checked, resident is suitable for exercise program without additional evaluation by medical staff at this time.
❑ End-stage congestive heart failure ❑ Permanent bed-bound status ❑ Severe cognitive impairment or behavioral disturbance ❑ Unstable abdominal, thoracic or cerebral aneurysm ❑ Untreated severe aortic stenosis ❑ Other_____	❑ Acute change in mental status or delirium ❑ Cerebral hemorrhage within the past 3 months ❑ Exacerbation of chronic inflammatory joint disease or osteoarthritis ❑ Eye surgery within the past 6 weeks ❑ Fracture in healing stage _____ ❑ Hernia, symptomatic (abdominal or inguinal) ❑ Myocardial infarction or cardiac surgery within past 6 months ❑ Other acute illness or change in symptoms _____ ❑ Proliferative diabetic retinopathy or severe non-proliferative retinopathy ❑ Pulmonary embolism or deep venous thrombosis within 3 months ❑ Soft tissue injury, healing ❑ Systemic infection_____ ❑ Uncontrolled blood pressure (>180/100) ❑ Uncontrolled diabetes mellitus (FBS >250mg/dl) ❑ Uncontrolled malignant cardiac arrhythmia (ventricular tachycardia, complete heart block, atrial flutter, symptomatic bradycardia) ❑ Unstable angina (at rest or crescendo pattern, ECG changes) ❑ Other_____	❑ Arthritis ❑ Chronic obstructive pulmonary disease, asthma ❑ Congestive heart failure ❑ Coronary artery disease ❑ Chronic renal failure ❑ Cancer (history or current) ❑ Chronic liver disease ❑ Chronic venous stasis ❑ Dementia ❑ Depression, anxiety, low morale ❑ Diabetes ❑ Drugs causing muscle wasting (steroids) ❑ Frailty ❑ Falls, history of hip fracture ❑ Gait and balance disorders, mobility impairment ❑ Hypertension ❑ HIV infection ❑ Hyperlipidemia ❑ Malnutrition, poor appetite ❑ Neuromuscular disease ❑ Obesity ❑ Osteoporosis ❑ Parkinson's disease ❑ Peripheral vascular disease ❑ Stroke

Physician Signature:_____Date:_____

William R. Sukala, MSc, PhD Candidate
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The SPIRIT Study

South **P**acific **I**slanders **R**esist diabetes with **I**ntense resistance **T**raining

Dr.XXXX XXXXXXXXX
Takapuwahia Medical Centre
Porirua

Dear Dr. XXXXXXXXX,

Your patient, **Joe Blogs**, has expressed interest in participating in the SPIRIT study. To further the medical screening process, please complete the attached checklist for your patient and return this form to me using the pre-paid envelope provided. Alternatively, you may fax to (04) 801-4994. Your assistance is greatly appreciated.

The purpose of the SPIRIT study is to evaluate the efficacy of 16 weeks of resistance training vs. aerobic exercise on glycaemic control in Polynesian New Zealanders with type 2 diabetes. We will also evaluate insulin sensitivity, body composition, inflammatory adipocytokines, muscle histology, and quality of life. I have enclosed a copy of a recent press article which you may reproduce for your patients. Entry criteria for the study are:

- Self-identified adult Polynesian with diagnosed type 2 diabetes
- Elevated waist circumference (88cm for women; 102 for men)
- Medically stable: no changes in diabetes medications in previous two months

I would be grateful if you could advise us if you have any concerns about your patient's participation in the study. I am hopeful that you will recommend participation in this research trial to other Polynesian diabetic patients meeting eligibility requirements. Please feel free to contact me if you require further information about the study.

Sincerely,

William R. Sukala, MSc, PhD Candidate
Principal Investigator
Clinical Exercise Physiologist

Name : _____

DOB : _____ Age :_____

SPIRIT ID number : _____

Date : _____

☐ baseline ☐ 16 weeks

Examiner : _____

Demographic information

	Patient details	Person for Notification
Name		**Relationship**
Address		
Telephone		**H:** **W:**

Gender

☐ Male
☐ Female

Race / Ethnic background
With which ethnicity do you most closely identify?

☐ Samoan
☐ Cook Islander
☐ Tongan
☐ Niuean
☐ Tokelauan
☐ Tuvaluan
☐ Fijian
☐ Other Pacific
☐ Various Pacific (2+ ethnicities)
☐ Maori
☐ Asian
☐ Caucasian
☐ Other _____

Marital status
Are you married, widowed, divorced, separated, never married?

☐ married / defacto
☐ widowed
☐ divorced
☐ single/ never married
☐ separated

Residence
In what type of accommodation do you live?

☐ house (own)
☐ house (rented)
☐ unit (own)

□ unit (rented)
□ retirement village
□ hostel
□ nursing home
□ board/rooming house

How long have you lived at this address? Years _____Months _____

Living Situation

With whom do you live?
□ alone
□ spouse / partner
□ family
□ paid care giver
□ friend
□ other residents

Total number of persons in the household _____ people

Education

What is the highest grade or year of school you completed?

□ never /kindergarten	0
□ primary school	1 2 3 4 5 6
□ high school	7 8 9 10 11 12
□ tertiary	13 14 15 16
□ post graduate	17 18 19 20

Work

Do you currently work for pay either for yourself or someone else?
□ yes
□ no

How many hours per week do you work for pay? _____hours / week

Do you currently work as a volunteer?
□ yes
□ no

How many hours volunteer hours / week do you work? _____hours / week

Pension

Do you receive a pension?
□ Nil
□ Age pension
□ Widows pension
□ Disability Pension

Hospital admissions

During the past 12 months, how many different times did you stay in hospital over night? _____ number of times

_____ number of days in hospital

Smoking

Have you ever smoked cigarettes, cigars or a pipe on a daily basis?	□ yes □ no
Do you currently smoke at least 1 cigarette, cigar or pipe per day?	□ yes □ no
If yes, how many cigarettes, cigars or pipes do you smoke on an average day?	_____ per day

Alcohol

During the past 30 days, about how many days did you drink any alcoholic beverages (beer, wine, liquor)	□ almost every day □ 3-4 times a week □ once or twice a week □ 2-3 times a month □ once a month □ none

Comments : _____
_____
_____
_____

Name: _____

DOB : _____ **Age :**_____

Date : _____

☐ baseline ☐ 16 weeks

Examiner : _____

Diabetes • Health Questionnaire

Diabetes History

- Type of diabetes: ☐ Type 1 ☐ Type 2
- Years with diabetes: _____
- Current diabetes management regimen:
  ☐ Insulin ☐ Hypoglycaemic Pills ☐ Diet ☐ Exercise
- Date of last change in diabetes medication: _____
- Known diabetic complications:
  ☐ Neuropathy ☐ Nephropathy ☐ Retinopathy ☐ Other

Other Diagnoses

	Type	Date
Active malignancy:		
Gastrointestinal disease:		
History of heart attack:		
History of cardiac surgery:		
History of hernia:		
Alcohol or drug use:		
Inability to use arm or leg (i.e. stroke,neuromuscular disease):		
Other (surgeries, procedures, etc):		
Number of visits to GP or hospital over previous 3 months:		

Family Health History

Please tick and indicate which family member(s) have had the following health problems:
Key: (m-mother, f-father, b-brother, s-sister, a-aunt, u-uncle, g-grandparent)

☐Heart disease	☐Kidney disease	☐Alzheimer's
☐High blood pressure	☐Stroke	☐Tuberculosis
☐Diabetes	☐Glaucoma	☐Bleeding tendency
☐Lung disease	☐Other	

Medications: include prescription, over-the-counter, and supplements

Medication Name	Dosage

Participant Master Kardex

Participant Details

First Name		Consult Date		GP	
Last Name		Start Date		Address	
Address		DOB		Phone	
		Age		Fax	
		Gender	☐♂ ☐♀		
Phone		Weight		Specialist	
Cellular		Height		Address	
Spouse/Partner		Language 1		Phone	
Emergency Phone		Language 2		Fax	

Medical History

Diagnoses/Event		Date	CAD Risk Factor Profile		Reference Range	Actual	Detailed Medical History
CAD	☐		Family History	☐	M<55; F<65		
MI	☐		Cigarette Smoking	☐	Quit < 6 mo		
CABG	☐		Hypertension	☐	140/90		
PTCA	☐		Dyslipidaemia	☐	LDL 3.4; TC 5.2		
Stent	☐		IFG/DM	☐	BG 5.6		
Valve	☐		Obesity	☐	BMI 30; w:h .95/.86; girth 102/88		
Transplant	☐		Sedentary Lifestyle	☐	Physical inactivity		
DM	☐		HDL Cholesterol (+)	☐	1.6mmol		
CVA	☐						
COPD	☐		Ejection Fraction				
Other	☐		ICD/PPM Limits				

Medications

Name	dose	x/day	dc date	Name	dose	x/day	dc date	Name	dose	x/day	dc date

SPIRIT ID : _____

DOB : _____ **Age :** _____

Date : _____

☐ baseline ☐ 16 weeks

Examiner : _____

Anthropometric, Haemodynamic, Composition, Strength Measurements

Measurement	Trial 1	Trial 2	Trial 3	Average
Body Weight (kg)				*Corrected Weight:*
Standing Height (cm)				
Body Mass Index (kg/m^2)				
Heart Rate (bpm)				
Blood Pressure (R or L)				
Waist Circumference (cm)				
Hip Circumference (cm)				
Waist to Hip Ratio				
Bioelectrical Impedance Analysis	Lean Mass	Fat Mass	% Fat	Total Body Water (or %) if given.
Upper Body Strength 10-RM Bench Press				
Lower Body Strength 10-RM Leg Press				

Comments:_____

_____

_____

- ❑ Protocol completed
- ❑ Not completed due to refusal, drop-out or loss to follow up
- ❑ Not completed due to medical illness or incapacity
- ❑ Not completed due to equipment failure or examiner error
- ❑ Not completed due to other cause (specify)

SPIRIT ID : _____

DOB : _____ **Age :** _____

Date : _____

☐ baseline ☐ 16 weeks

Examiner : _____

Strength Testing

Measurement	Load	Reps	Adjusted 1RM
Upper Body Strength: 10-RM Bench Press			
Lower Body Strength: 10-RM Leg Press			

Comments: _____

_____

_____

- ❑ Protocol completed
- ❑ Not completed due to refusal, drop-out or loss to follow up
- ❑ Not completed due to medical illness or incapacity
- ❑ Not completed due to equipment failure or examiner error
- ❑ Not completed due to other cause (specify)

SPIRIT ID: _____

DOB : _____ **Age :** _____

Date : _____

☐ baseline ☐ 16 weeks

Examiner : _____

SF-36 Health Status Survey

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

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

Excellent	Very Good	Good	Fair	Poor
○	○	○	○	○

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

- ○ Much better now than 1 year ago
- ○ Somewhat better now than 1 year ago
- ○ About the same as 1 year ago
- ○ Somewhat worse now than 1 year ago
- ○ Much worse now than 1 year ago

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

Activities	**Yes, Limited A Lot**	**Yes, Limited A Little**	**No, Not Limited At All**
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	○	○	○
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	○	○	○
Lifting or carrying groceries	○	○	○
Climbing **several** flights of stairs	○	○	○
Climbing **one** flight of stairs	○	○	○
Bending, kneeling or stooping	○	○	○
Walking **more than a mile**	○	○	○
Walking **several blocks**	○	○	○
Walking **one block**	○	○	○
Bathing or dressing yourself	○	○	○

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

	Yes	**No**
Cut down on the **amount of time** you spent on work or other activities	○	○
Accomplished less than you would like	○	○
Were limited in the **kind** of work or other activities	○	○
Had **difficulty** performing the work or other activities (for example, it took extra effort)	○	○

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

	Yes	No
Cut down on the **amount of time** you spent on work or other activities	○	○
Accomplished less than you would like	○	○
Didn't do work or other activities as **carefully** as usual	○	○

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

- ○ Not at all
- ○ Slightly
- ○ Moderately
- ○ Quite a bit
- ○ Extremely

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

- ○ None
- ○ Very mild
- ○ Mild
- ○ Moderate
- ○ Severe
- ○ Very severe

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

- ○ Not at all
- ○ A little bit
- ○ Moderately
- ○ Quite a bit
- ○ Extremely

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

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little Bit of the Time	None of the Time
Did you feel full of pep?	○	○	○	○	○	○
Have you been a very nervous person?	○	○	○	○	○	○
Have you felt so down in the dumps that nothing could cheer you up?	○	○	○	○	○	○
Have you felt calm and peaceful?	○	○	○	○	○	○
Did you have a lot of energy?	○	○	○	○	○	○
Have you felt downhearted and blue?	○	○	○	○	○	○
Did you feel worn out?	○	○	○	○	○	○
Have you been a happy person?	○	○	○	○	○	○
Did you feel tired?	○	○	○	○	○	○

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

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

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

	Definitely True	**Mostly True**	**Don't Know**	**Mostly False**	**Definitely False**
I seem to get sick a little easier than other people	○	○	○	○	○
I am as healthy as anybody I know	○	○	○	○	○
I expect my health to get worse	○	○	○	○	○
My health is excellent	○	○	○	○	○

SPIRIT ID : _____

DOB : _____ Age :_____

Date : _____

☐ baseline ☐ 16 weeks

Examiner : _____

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

☐ Yes

☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

_____ **days per week**

☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

_____ **days per week**

☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Weekly Status Check

Study ID		
Date		**Week**
Interviewer		**❒ Telephone ❒ In-person**

During the past week have you had any of the following?

	Yes	**No**
1. Acute illnesses Specify_____ _____	❒	❒
2. Change in medication (prescribed, over-the-counter, herbal, nutritional supplement) Specify _____ _____	❒	❒
3. Visits to a health care professional Kind_____ Indication_____ Treatment_____	❒	❒
4. New physical, mental, or emotional symptoms of any kind Describe:_____ _____ _____	❒	❒
5. Falls Number_____ Circumstance(s)_____ _____	❒	❒
Injury_____	❒	❒
6. Have you attended all exercise sessions? If not, number attended_____ Reason for missed session(s)_____ _____	❒	❒

7. Other Questions or Comments of subject:

_____
_____
_____

Comments :

- ❑ protocol completed
- ❑ not completed due to death
- ❑ not completed due to refusal, drop-out or loss to follow-up
- ❑ not completed due to medical illness or incapacity
- ❑ not completed due to examiner failure or error
- ❑ not completed due to other :_____

Resistance Training Vitals

Name: ______________________ **Age** __________

Med hx: ______________________ **Meds:** ______________________

	Resting			Exercise (as needed per symptoms)			Recovery		
Date	HR	BP	BG	Peak HR	Peak BP	BG	HR	BP	BG

Signs/symptoms:

SPIRIT Study Aerobic Exercise Log

Name: ______________________ Age ________

Med hx ______________________ Meds: ______________________

	Resting			Exercise						Recovery		
Date	HR	BP	BG	Mode	Workload	Duration	Peak HR	Peak BP	BG	HR	BP	BG

Signs/symptoms:

SPIRIT Study
Aerobic Exercise Log

First Name
Last Name
Age

Med History:
Risk Factors:
Medications:

Target HR Range: Date
Date
Date

Date				Wt	HR	BP	BG	O2
		Resting						
Mode	Min	Total Min	Work load	METS	HR	BP	BG O2	RPE
Session#					HR	BP	BG	O2
			Recovery					
S/Sx Progress Notes								

Date				Wt	HR	BP	BG	O2
		Resting						
Mode	Min	Total Min	Work load	METS	HR	BP	BG O2	RPE
Session#					HR	BP	BG	O2
			Recovery					
S/Sx Progress Notes								

Date				Wt	HR	BP	BG	O2
		Resting						
Mode	Min	Total Min	Work load	METS	HR	BP	BG O2	RPE
Session#					HR	BP	BG	O2
			Recovery					
S/Sx Progress Notes								

Date				Wt	HR	BP	BG	O2
		Resting						
Mode	Min	Total Min	Work load	METS	HR	BP	BG O2	RPE
Session#					HR	BP	BG	O2
			Recovery					
S/Sx Progress Notes								

Date				Wt	HR	BP	BG	O2
		Resting						
Mode	Min	Total Min	Work load	METS	HR	BP	BG O2	RPE
Session#					HR	BP	BG	O2
			Recovery					
S/Sx Progress Notes								

Date				Wt	HR	BP	BG	O2
		Resting						
Mode	Min	Total Min	Work load	METS	HR	BP	BG O2	RPE
Session#					HR	BP	BG	O2
			Recovery					
S/Sx Progress Notes								

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 1

	Adjustments		Date:				Date:				Date:			
				Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load				
	Leg	Reps				Reps				Reps				
Leg Extension	Seat	Load				Load				Load				
	Leg	Reps				Reps				Reps				
Leg Curl	Seat	Load				Load				Load				
	Leg	Reps				Reps				Reps				
Chest Press	Seat	Load				Load				Load				
	Arms	Reps				Reps				Reps				
Lat Pulldown	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Shoulder Press	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Biceps Curl	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Triceps Curl	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Abdominals		Load				Load				Load				
		Reps				Reps				Reps				

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 2

	Adjustments		Date:				Date:				Date:			
				Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load				
	Leg	Reps				Reps				Reps				
Leg Extension	Seat	Load				Load				Load				
	Leg	Reps				Reps				Reps				
Leg Curl	Seat	Load				Load				Load				
	Leg	Reps				Reps				Reps				
Chest Press	Seat	Load				Load				Load				
	Arms	Reps				Reps				Reps				
Lat Pulldown	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Shoulder Press	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Biceps Curl	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Triceps Curl	Seat	Load				Load				Load				
		Reps				Reps				Reps				
Abdominals		Load				Load				Load				
		Reps				Reps				Reps				

Comments/ Subject Complaints/ Adverse Events:

SPIRIT

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 3

	Adjustments	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

SPIRIT

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 4

	Adjustments	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 5

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 6

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 7

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 8

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 9

	Adjustments	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 10

	Adjustments	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3	Date:	Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 11

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 12

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 13

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 14

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 15

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

Training Log

Name : _____
DOB : _____ Age : _____
ID number : _____
Date : _____
Trainer: _____

Week: 16

	Adjustments	Date:				Date:				Date:			
			Set 1	Set 2	Set 3		Set 1	Set 2	Set 3		Set 1	Set 2	Set 3
Leg Press	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Extension	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Leg Curl	Seat	Load				Load				Load			
	Leg	Reps				Reps				Reps			
Chest Press	Seat	Load				Load				Load			
	Arms	Reps				Reps				Reps			
Lat Pulldown	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Shoulder Press	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Biceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Triceps Curl	Seat	Load				Load				Load			
		Reps				Reps				Reps			
Abdominals		Load				Load				Load			
		Reps				Reps				Reps			

Comments/ Subject Complaints/ Adverse Events:

SPIRIT

Master Attendance Sheet

Month ____________________

	M	T	W	Th	F	M	T	W	Th	F	M	T	W	Th	F	M	T	W	Th	F	M	T	W	Th	F
Name																									

APPENDIX C

Ethics Approval Forms

Health and Disability Ethics Committees

Central Regional Ethics Committee
Ministry of Health
Level 2, 1-3 The Terrace
PO Box 5013
Wellington
Phone (04) 496 2405
Fax (04) 496 2191

16 October 2007

William Sukala
Institute of Food Nutrition & Human Health
Massey University
P O Box 756
Wellington

Dear William

The SPIRIT study: South Pacific Islanders Resist diabetes with intense resistance training: a randomised controlled trial
William Sukala
Capital & Coast DHB, City Fitness
CEN/07/08/054

The above study has been given ethical approval by the **Central Regional** Ethics Committee. A list of members of this committee is attached.

Approved Documents

- Information Sheet Version 1.01, dated 14 September 2007
- Muscle Biopsy Information sheet Version 1.01, dated 14 September 2007
- Participant Consent Form Version 1.01, dated 14 September 2007
- Muscle Biopsy Consent Form Version 1.01, dated 14 September 2007
- SPIRIT Advertisement sheet.
- Dear Colleague Letter dated July 2007
- Dear Dr Letter dated July 2007
- Dear Mr Sukala Letter
- Questionnaires, 1 Demographic Information, 2 Diabetes Health, 3 SF-36 Health Status Survey, 4 International Physical Activity Questionnaire

Certification
The Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out.

Accreditation
The Committee involved in the approval of this study is accredited by the Health Research Council and is constituted and operates in accordance with the Operational Standard for Ethics Committees, April 2006.

Progress Reports
The study is approved until October 2011. The Committee will review the approved application annually and notify the Principal Investigator if it withdraws approval. It is the Principal Investigator's responsibility to forward a progress report covering all sites prior to ethical review of the project in. The report form is available on http://www.newhealth.govt.nz/ethicscommittees. Please note that failure to provide a progress report may result in the withdrawal of ethical approval. A final report is also required at the conclusion of the study.

Requirements for SAE Reporting
The Principal Investigator will inform the Committee as soon as possible of the following:

- Any related study in another country that has stopped due to serious or unexpected adverse events
- withdrawal from the market for any reason

- All serious adverse events occurring during the study in New Zealand which result in the investigator breaking the blinding code at the time of the SAE or which result in hospitalisation or death.
- All serious adverse events occurring during the study worldwide which are considered related to the study medicine. Where there is a data safety monitoring board in place, serious adverse events occurring outside New Zealand may be reported quarterly.

All SAE reports must be signed by the Principal Investigator and include a comment on whether he/she considers there are any ethical issues relating to this study continuing due to this adverse event. It is assumed by signing the report; the Principal Investigator has undertaken to ensure that all New Zealand investigators are made aware of the event.

Amendments
All amendments to the study must be advised to the Committee prior to their implementation, except in the case where immediate implementation is required for reasons of safety. In such cases the Committee must be notified as soon as possible of the change.

Please quote the above ethics committee reference number in all correspondence.

The Principal Investigator is responsible for advising any other study sites of approvals and all other correspondence with the Ethics Committee.

It should be noted that Ethics Committee approval does not imply any resource commitment or administrative facilitation by any healthcare provider within whose facility the research is to be carried out. Where applicable, authority for this must be obtained separately from the appropriate manager within the organisation.

Yours sincerely

Jiska van Bruggen
Central Regional Ethics Committee Administrator

Email: jiska_van_bruggen@moh.govt.nz

Health and Disability Ethics Committees

Central Regional Ethics Committee
Ministry of Health
Level 2, 1-3 The Terrace
PO Box 5013
Wellington
Phone (04) 496 2405
Fax (04) 496 2191

16 October 2007

CEN/07/08/054

The SPIRIT study: South Pacific Islanders Resist diabetes with intense resistance training: a randomised controlled trial

William Sukala
Capital & Coast DHB, City Fitness

Central Regional Ethics Committee Members		
Name	**Member category**	**Term (Appointed)**
Trevor James (Chair)	Community representative	3 years (Dec 04)
Helen Colebrook	Lawyer	3 years (Dec 06)
Matire Harwood	Biostatistician	3 years (Dec 04)
John Kleinsman	Ethicist	3 years (Dec 04)
Elaine Papps	Health practitioner	3 years (Dec 06)
Jacqueline Virtue	Health practitioner	3 years (Dec 04)
Joe Asghar	Pharmacist/pharmacologist	3 years (Dec 06)
Maureen Holdaway	Researcher	2 years (Dec 06)
Guy Taylor	Researcher	3 years (Dec 04)
Jacqueline Renouf	Consumer Representative	3 years (July 05)
Dianne Wepa	Consumer Representative	3 years (Dec 04)
Anne Tuffin	Community Representative	3 years (Dec 06)

Yours Sincerely

Jiska van Bruggen
Central Regional Ethics Administrator

Health and Disability Ethics Committees

Central Regional Ethics Committee
Ministry of Health
Level 2, 1-3 The Terrace
PO Box 5013
Wellington
Phone (04) 496 2405
Fax (04) 496 2191

27 May 2008

William Sukala
Institute of Food Nutrition & Human Health
Massey University
P O Box 756
Wellington

Dear William

CEN/07/08/054
The SPIRIT study: South Pacific Islanders Resist diabetes with intense resistance training: a randomised controlled trial

Thank you for your letter dated 9 May 2008 with enclosed amendment for the above study. Your correspondence has been reviewed and approved by the Chairperson of the Central Regional Ethics Committee.

Approved documents:
- Participant Information Sheet version 1.03, dated 9 May 2008
- SPIRIT Study Aerobic Exercise Log Submitted 9 May 2008

Ethical approval is confirmed by the Chairperson of the Central Regional Ethics Committee under delegated authority.

If you have any further questions please feel free to contact me.

Yours sincerely

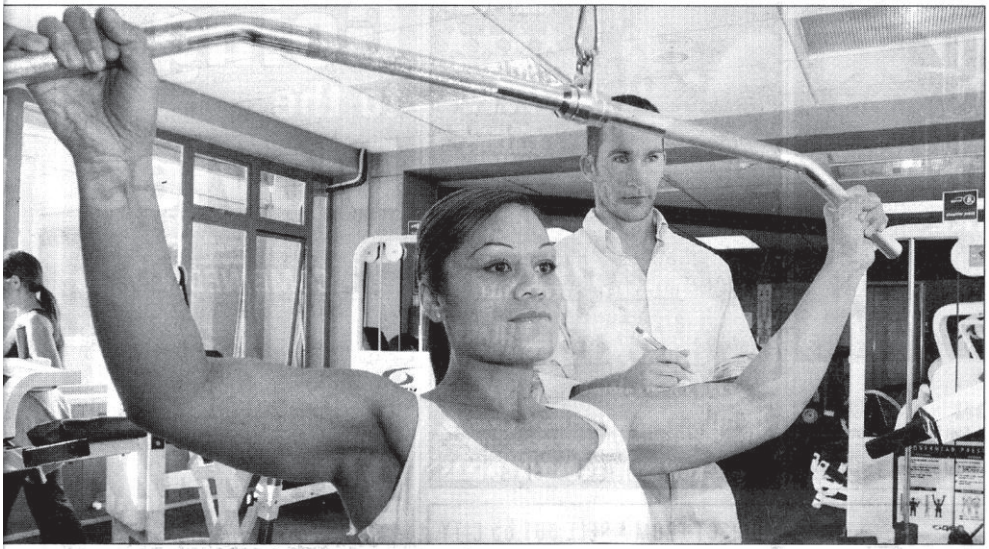
Jiska van Bruggen
Central Regional Ethics Committee Administrator

APPENDIX D

SPIRIT Media Coverage

HIGHER EDUCATION

Putting their weight behind diabetes study



Research given lift: William Sukala assesses volunteer Rachel Osman's weight training.

DIABETES can be a weighty topic for those who suffer from it, but a new study is examining the benefits of weightlifting in combating the disease among Pacific Islanders.

PhD candidate William Sukala and a team of Massey University health researchers will conduct the first controlled trial among Pacific Islanders, using a programme of supervised weightlifting known as progressive resistance training.

The study is called Spirit — South Pacific Islanders Resist diabetes with Intense Training. Forty participants with type 2 diabetes will be drawn from church groups and diabetes healthcare professionals, most in the Porirua area. All will be tested and assessed. Twenty will take part in supervised weightlifting for 16 weeks — the rest will receive usual care. The weightlifting will involve nine exercises, targeting all major muscles of the body, performed three times a week.

Mr Sukala said it was well established that, compared with Europeans, Pacific Islanders were disproportionately affected by type 2 diabetes and obesity.

"Other international studies conducted in high-risk groups have indicated that weightlifting is both safe and effective in improving blood sugar control and other factors in type 2 diabetes management," he said.

The sport encouraged the healthy use of both lower and upper-body muscles.

Structures in the muscles independent of insulin became active with physical exercise, he said. It allowed blood sugar to be poured out of the blood into the muscle, and reduced the risk of long-term complications with diabetes and associated ailments such as heart disease.

"At present, the generic advice given to people with diabetes is usually a vague 'get out and take a walk'. At this point, nobody even considers the therapeutic value of weightlifting," Mr Sukala said.

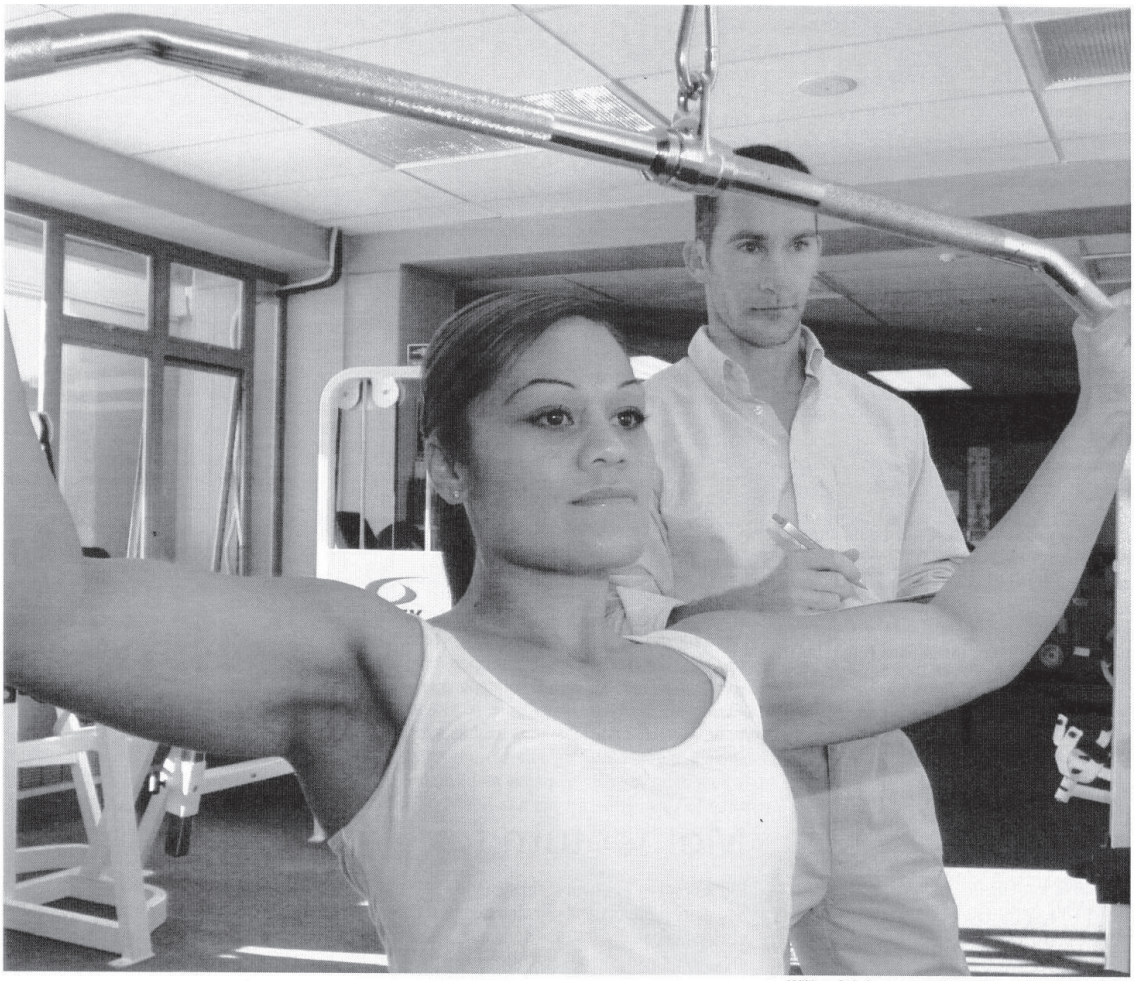
The sport was not all about heavy-duty lifting and "pumping iron", he said. "It can be done within reason by most people. Where I come from we had a 95-year-old lady doing weightlifting and she had a heck of a lot more wrong with her than someone with just diabetes."

Mr Sukala believes the benefits of the study can be exported to the Islands. "The objective is to first run the study as a strictly controlled trial and then adapt it into a self-determined, community-based fitness programme that people want to take part in, that can be encouraged and taken forward by Pacific Island churches and community centres, not just within New Zealand, but back to the islands as well."

Researchers from Massey's institute of food, nutrition and human health have partnered with the National Heart Foundation, Capital and Coast District Health Board, Porirua-based City Fitness, Pacific Island churches and diabetes health specialists for the project.

Before arriving at Massey, Mr Sukala completed a masters in exercise physiology at San Diego State University.

■ *For further information e-mail W.R.Sukala@massey.ac.nz*



William Sukala assesses Rachel Osman's weight training.

Weightlifting raised as answer to diabetes

A new study will be the first to establish the value of weightlifting in combating diabetes among Pacific Islanders.

PhD candidate William Sukala and a team of Massey University health researchers will conduct the first randomised, controlled trial among Pacific Islanders, using a programme of supervised weightlifting known as progressive resistance training.

Their study is called SPIRIT – South Pacific Islanders Resist Diabetes with Intense Training. Forty participants with type-2 diabetes will be drawn from church groups and diabetes health care professionals, most in the Porirua area.

All will be tested and assessed. Twenty will take part in supervised weightlifting for 16 weeks while the rest will have usual care. The weightlifting will involve nine exercises, targeting all major muscles of the body, performed three times a week.

Mr Sukala says it is well established that Pacific Islanders are disproportionately affected by type-2 diabetes and obesity, compared with Europeans.

"The epidemic of diabetes within the Pacific Islands community is a major public health concern that must be addressed with appropriate interventions," he says.

"Other international studies conducted in high-risk groups have indicated that weightlifting is both safe and effective in improving blood sugar control and other factors in type-2 diabetes management.

"However, there has been very little advocacy for its use in the medical management of Pacific Islanders diagnosed with diabetes. This is likely to be because no clinical trials have been conducted within the Pacific island group.

"At present the generic advice given to people with diabetes is usually a vague 'get out and take a walk'. At this point, nobody even considers the therapeutic value of weightlifting."

Researchers from the University's Institute of Food, Nutrition and Human Health have partnered with the National Heart Foundation, the Capital and Coast District Health Board, Porirua-based City Fitness, Pacific Island churches and diabetes health specialists.

"We know that earlier studies support the value of physical exercise in preventing and mitigating both diabetes and obesity in Māori and Pacific Island people.

But this is the first randomised, controlled study – and the first New Zealand study – to focus specifically on weightlifting. We intend to prove its value with this research," says Mr Sukala.

"The objective is to first run the study as a strictly controlled trial, and then adapt it into a self-determined, community-based fitness programme that people want to take part in. That can be encouraged and taken forward by Pacific Island churches and community centres, not just within New Zealand, but back to the islands as well."

Mr Sukala expects the study will also bring benefits to the wider community.

"The fact that it is taking place will raise awareness within the scientific community and the public of the value of weightlifting as a safe and effective weapon in the fight against diabetes and its close ally, obesity."

LIFT FOR POLYNESIANS

New study adds weight to fight against diabetes

By TAMMY BUCKLEY

THE weight-ing game could be over for obese Pacific Islanders who suffer from diabetes.

Massey University researchers are conducting a study to gauge if Pacific Islanders who lift weights can control their diabetes.

The study, called SPIRIT – South Pacific Islanders Resist Diabetes with Intense Training – will see 40 participants from Wellington's Porirua who have type-2 diabetes divided into two groups, with 20 taking part in supervised weightlifting for 16 weeks while the rest have normal care.

> "It doesn't require a long, boring walk"

The weightlifting will involve nine exercises, targeting all major muscles of the body, performed three times a week.

PhD candidate William Sukala told *Sunday News* the normal recommendation for diabetics was to "simply go out and take a walk" but for some it wasn't something they wanted to or could do.

"Weightlifting, on the other hand, is an appealing alternative because it doesn't require the long, boring walk on the treadmill staring at the wall or potentially walking in a dangerous neighbourhood.

"It also works a variety of muscles, not just the legs."

Sukala said Pacific Islanders had a much higher body-mass index than Europeans.

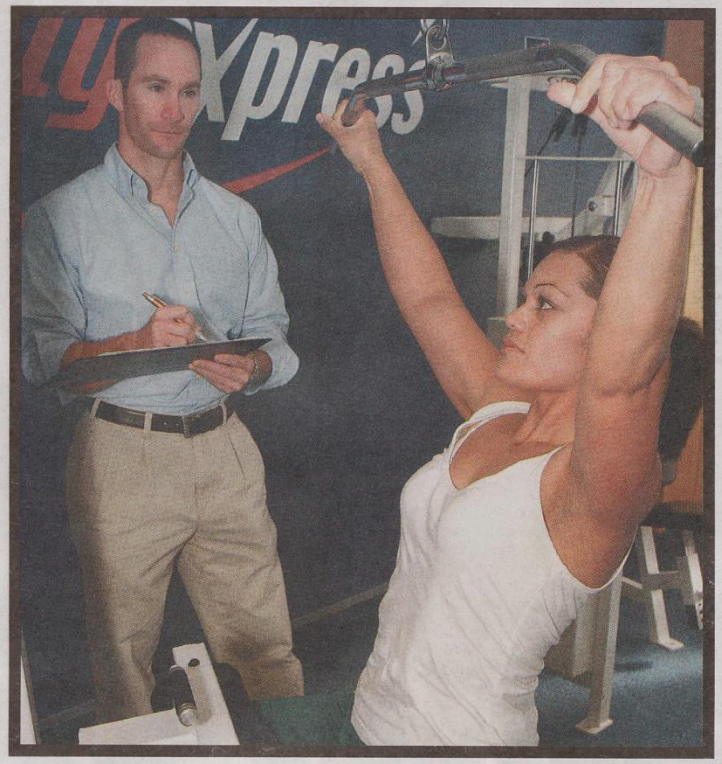
And statistics showed Pacific Islanders' rates of type-2 diabetes and obesity were among the highest in the world.

International studies have indicated weightlifting is safe and effective in improving blood-sugar control and other factors in type-2 diabetes management.

But this will be the first controlled trial of supervised weightlifting for Polynesians.

After the trial is finished the research team then plan to adapt it into a community-based fitness programme.

■ **People with type-2 diabetes interested in taking part in the study can contact William Sukala on 04 801 2794 ext 6801 or email w.r.sukala@massey.ac.nz**



TRAINING DAY: William Sukala ticks off the stats as Rachel Osman works out.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Tens of thousands of New Zealanders with diabetes are being urged to use their extra muscle to combat the disease.
Diabetics are traditionally told to go for a walk or bike ride. But Massey University PHD student William Sukala has taken this one step further, with a closely monitored weights regime that has got a group of afflicted Pacific Islanders into building muscle to burn calories. The programme is proving popular with a small group in Porirua, who want to see it go global.
"It has structures inside the muscle that are kind of like sponges so they help pull the blood sugar out of the blood and into the muscle. People that manage their blood sugar better will often have a reduced risk of diabetic complications," says Sukala, Spirit Study co-ordinator.
Every Monday, Wednesday and Friday from 7am 24 people will make their way though an hour long circuit and their blood pressure, blood sugar and heart rate will be tested throughout.
The results of Sukala's number crunching will not be known until next year.
However, the effectiveness of the weight training can already be measured in enthusiasm.
"When I first started the Spirit Study I could tell that they were thinking 'oh here we go Nick's been down this path before - we'll give him a couple of days and he'll quit', but that hasn't happened yet," says Nick Lopa, diabetic.
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The Spirit Study training programme has gained momentum through a key partnership with a Porirua Pacific community stronghold - the church.
Local Pastor Teremoana Tauira has already shed 20 kilograms.
"Over 50% of my church members are now coming to the gym!" says Tauira.
And he says as waistelines contract the programme will only expand.
"I believe it has the potential to go nationwide, and not only nationally I believe also internationally because a lot of our people are still connected back to our home islands," says Tauira.
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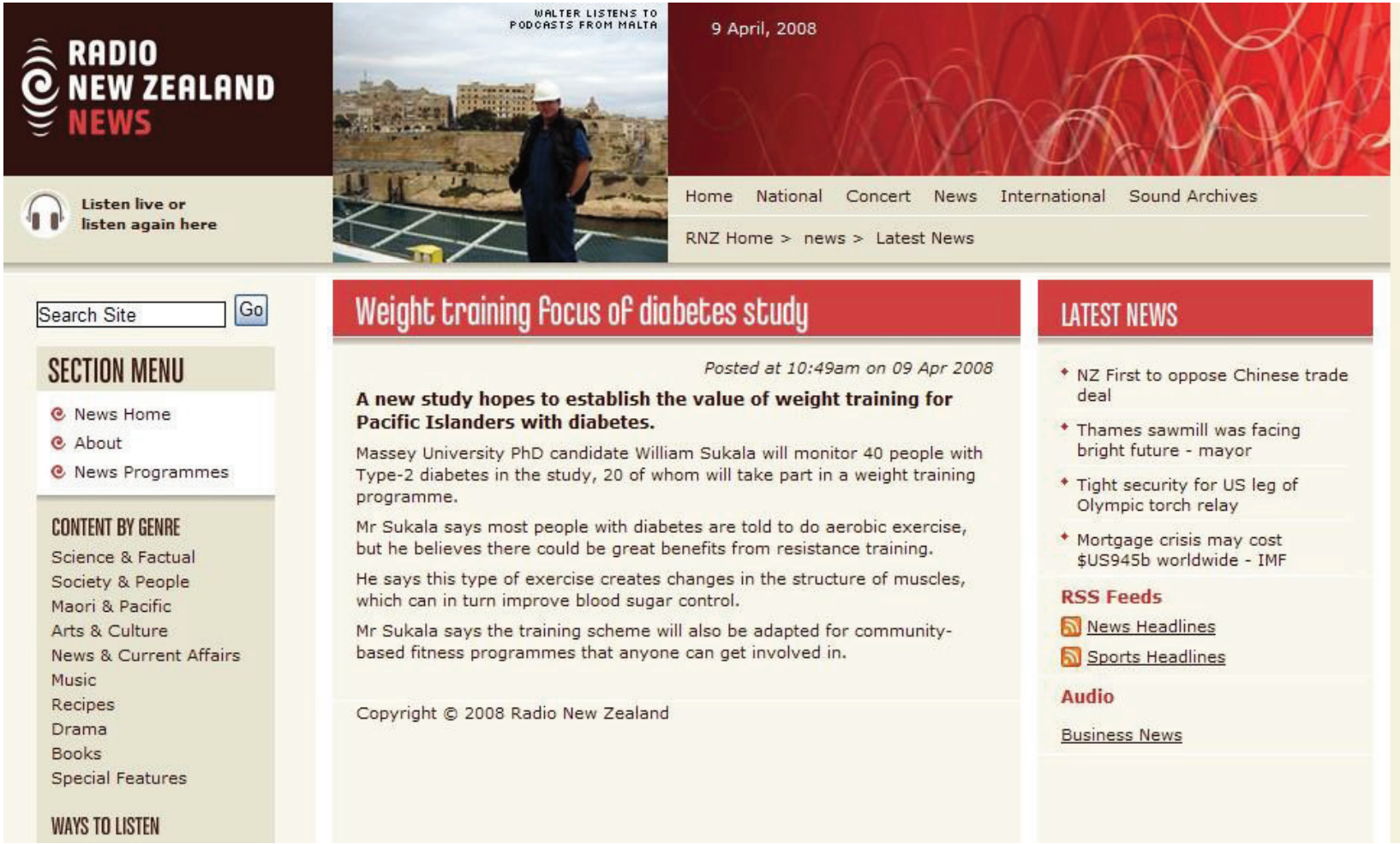
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WAYS TO LISTEN
Weight training focus of diabetes study
Posted at 10:49am on 09 Apr 2008
A new study hopes to establish the value of weight training for Pacific Islanders with diabetes.
Massey University PhD candidate William Sukala will monitor 40 people with Type-2 diabetes in the study, 20 of whom will take part in a weight training programme.
Mr Sukala says most people with diabetes are told to do aerobic exercise, but he believes there could be great benefits from resistance training.
He says this type of exercise creates changes in the structure of muscles, which can in turn improve blood sugar control.
Mr Sukala says the training scheme will also be adapted for community-based fitness programmes that anyone can get involved in.
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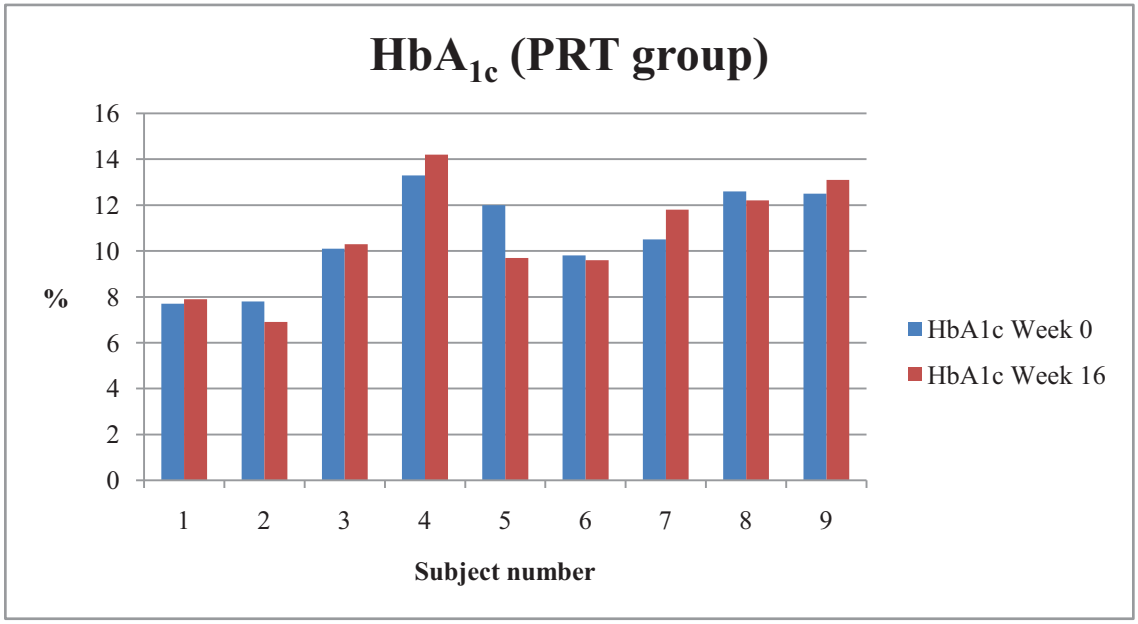
APPENDIX E

Subject Raw Data Graphs


HbA1c (PRT group)
16
14
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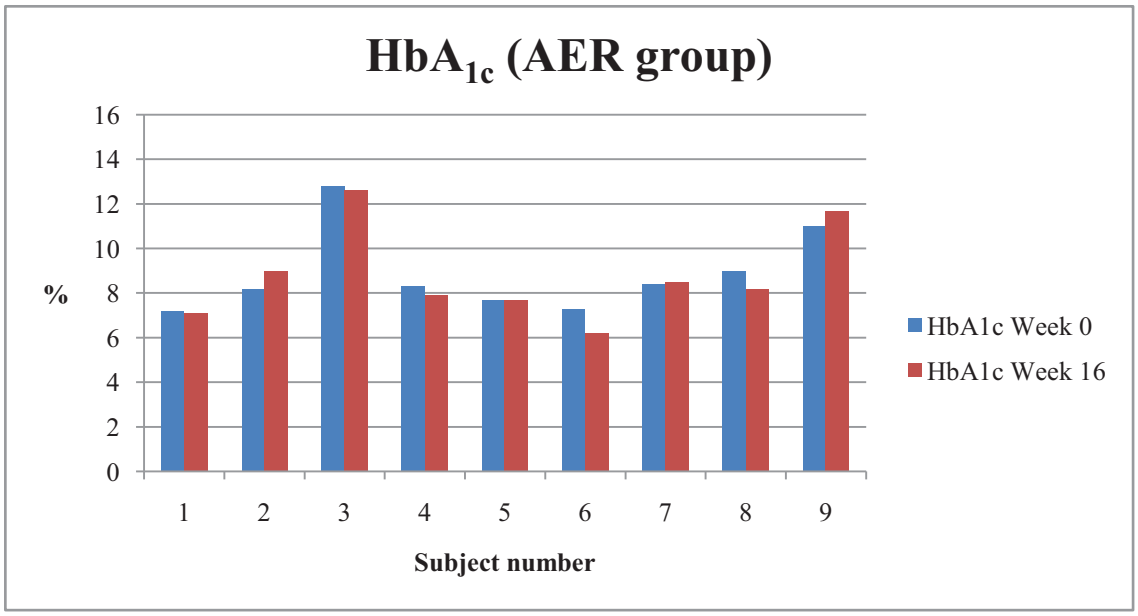
Subject number
HbA1c Week 0
HbA1c Week 16


HbA1c (AER group)
16
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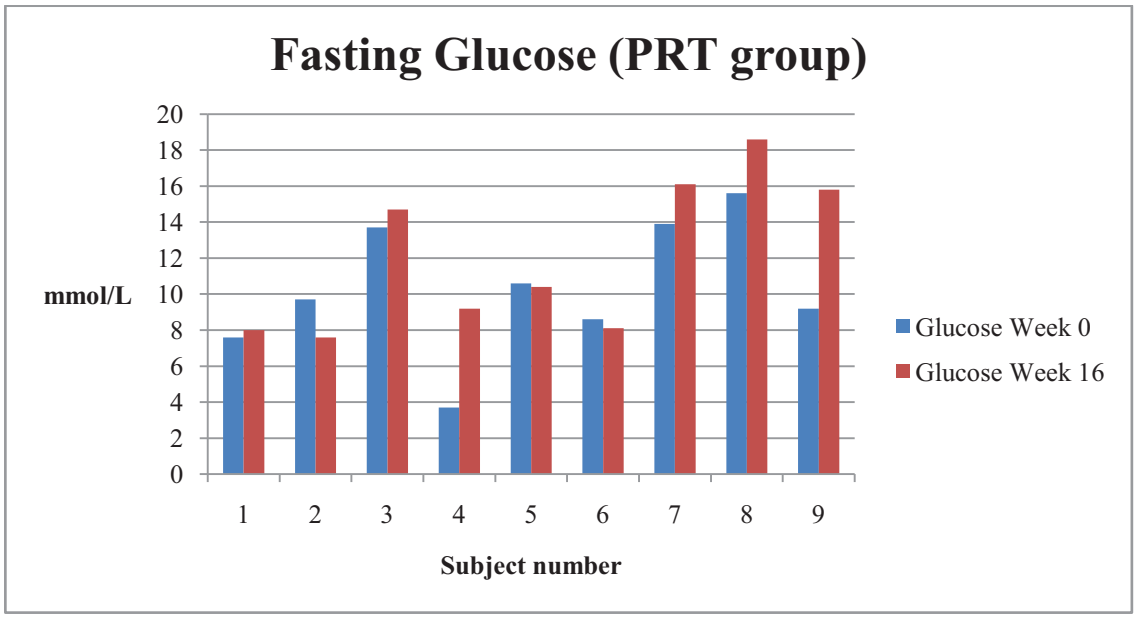
HbA1c Week 0
HbA1c Week 16


Fasting Glucose (PRT group)
mmol/L
20
18
16
14
12
10
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2
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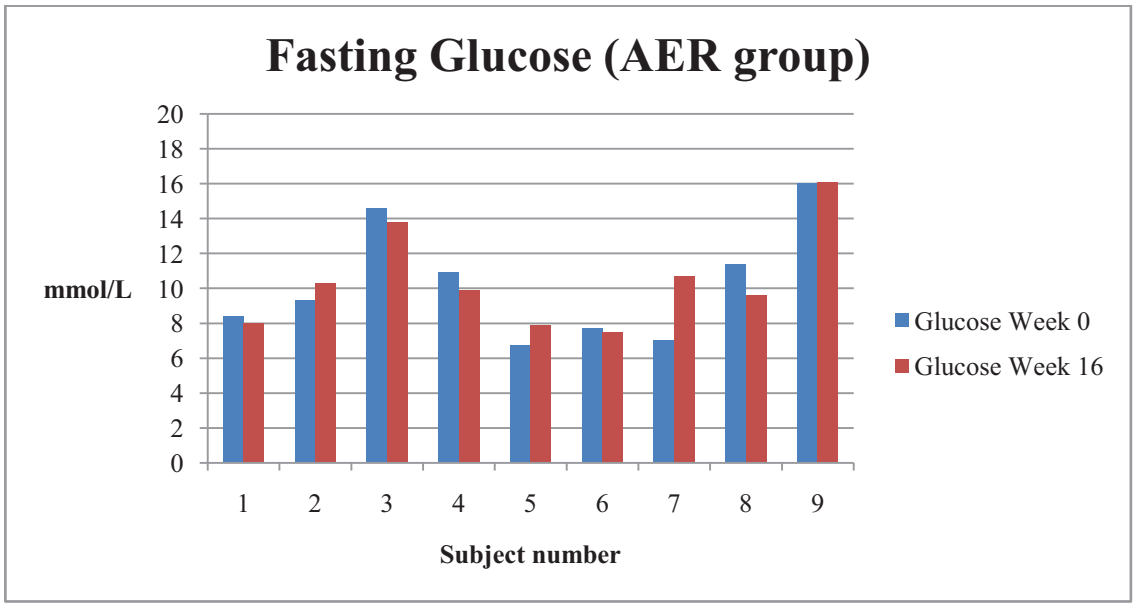
Subject number
Glucose Week 0
Glucose Week 16


Fasting Glucose (AER group)
mmol/L
20
18
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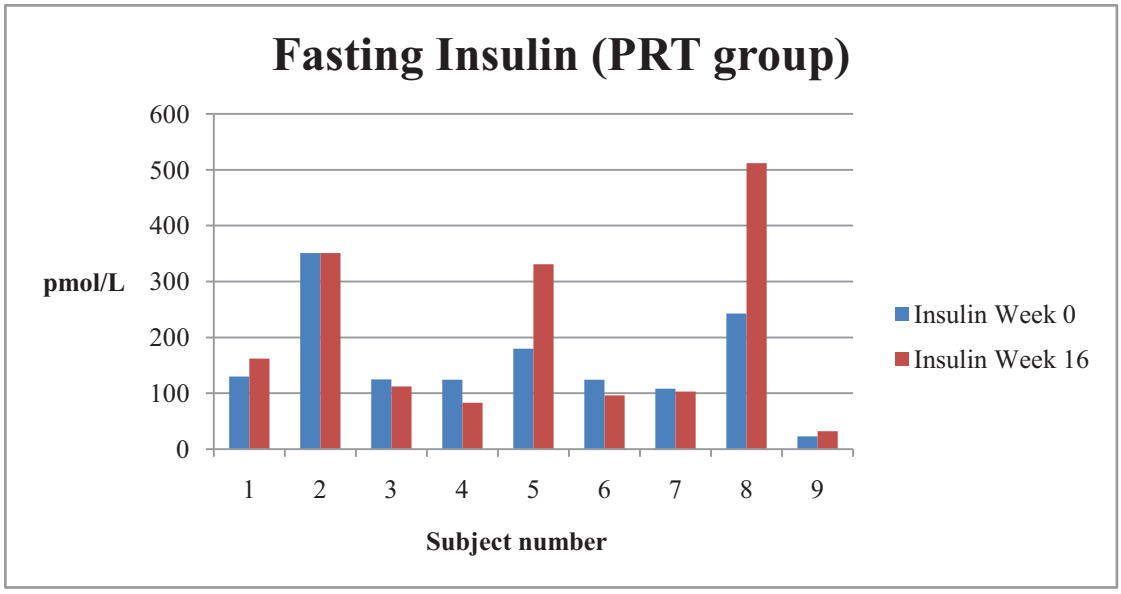
Glucose Week 16


Fasting Insulin (PRT group)
600
500
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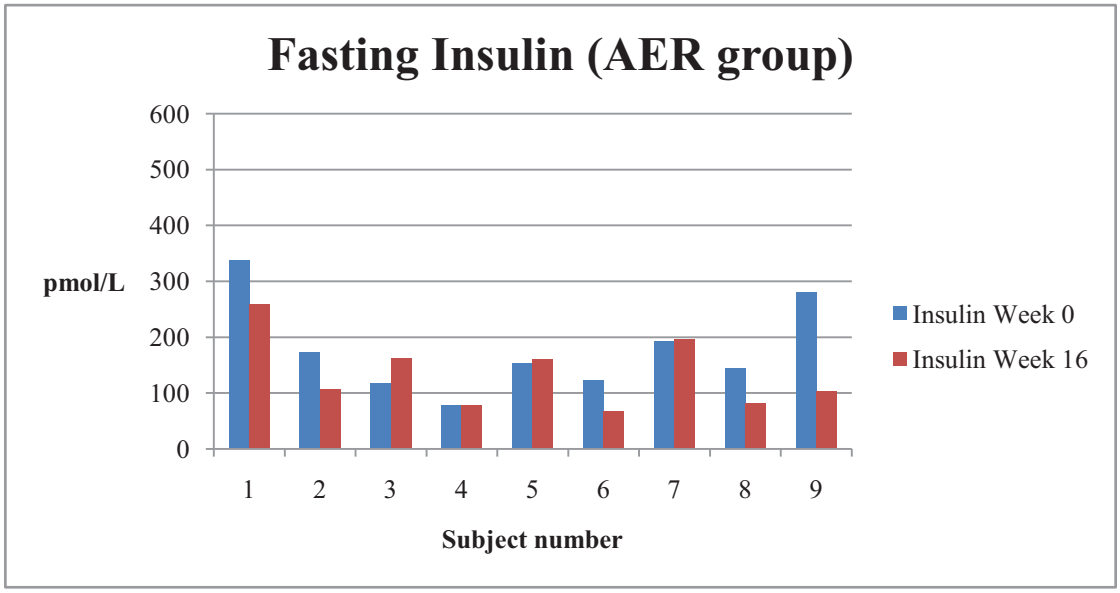
Subject number
Insulin Week 0
Insulin Week 16


Fasting Insulin (AER group)
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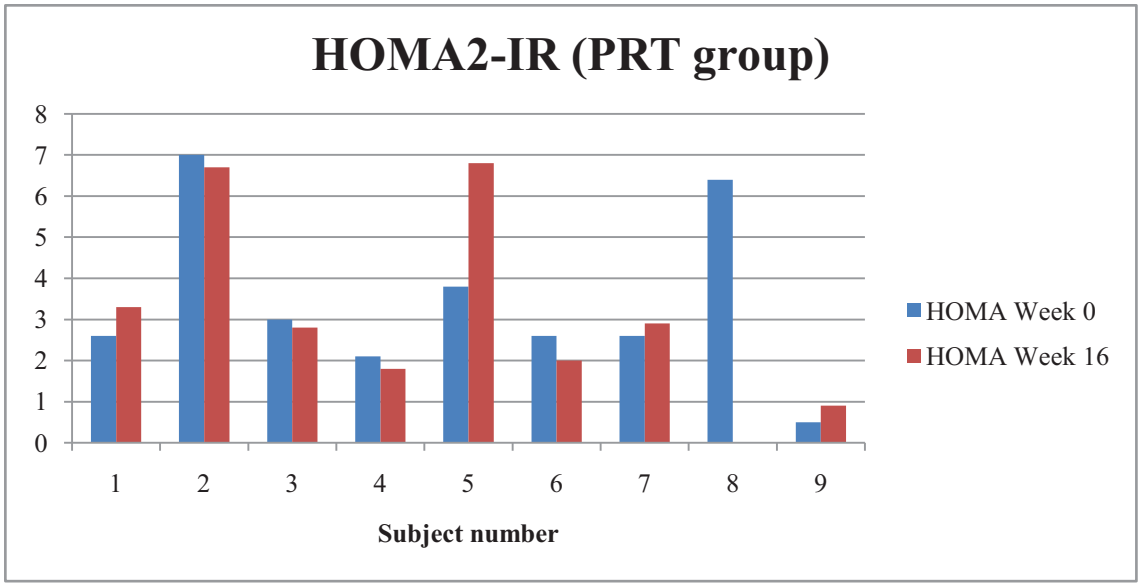
Insulin Week 16


HOMA2-IR (PRT group)
8
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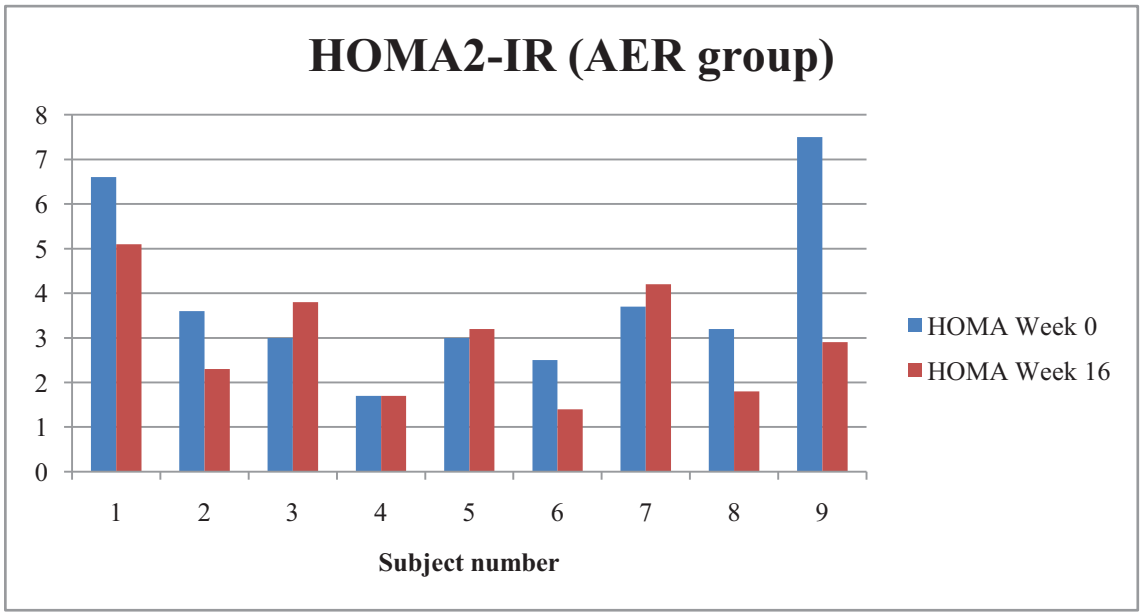
HOMA Week 0
HOMA Week 16


HOMA2-IR (AER group)
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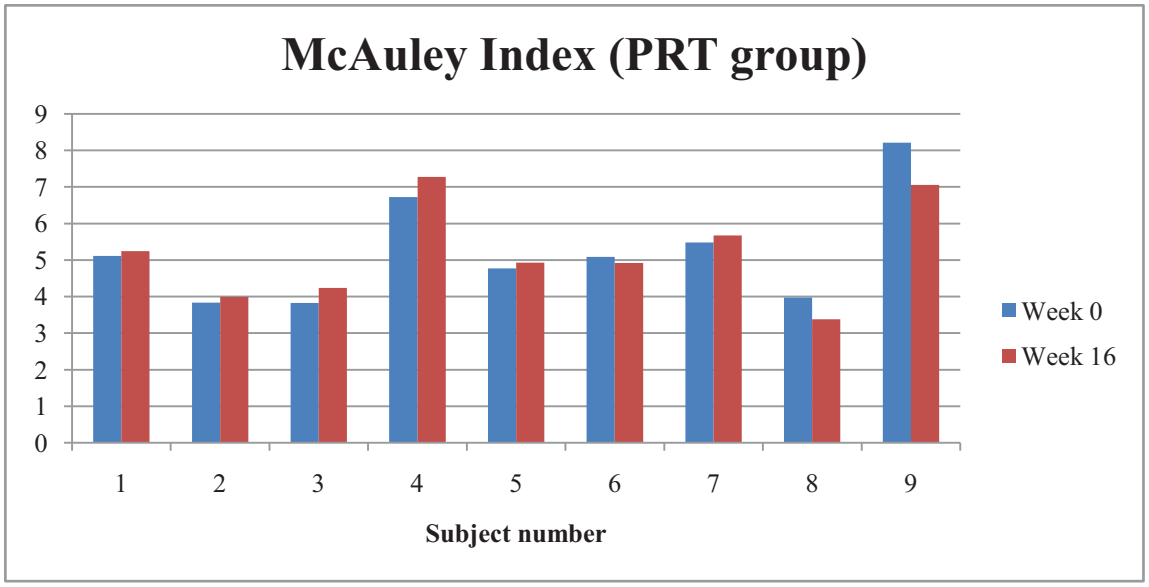
Subject number
HOMA Week 0
HOMA Week 16


McAuley Index (PRT group)
9
8
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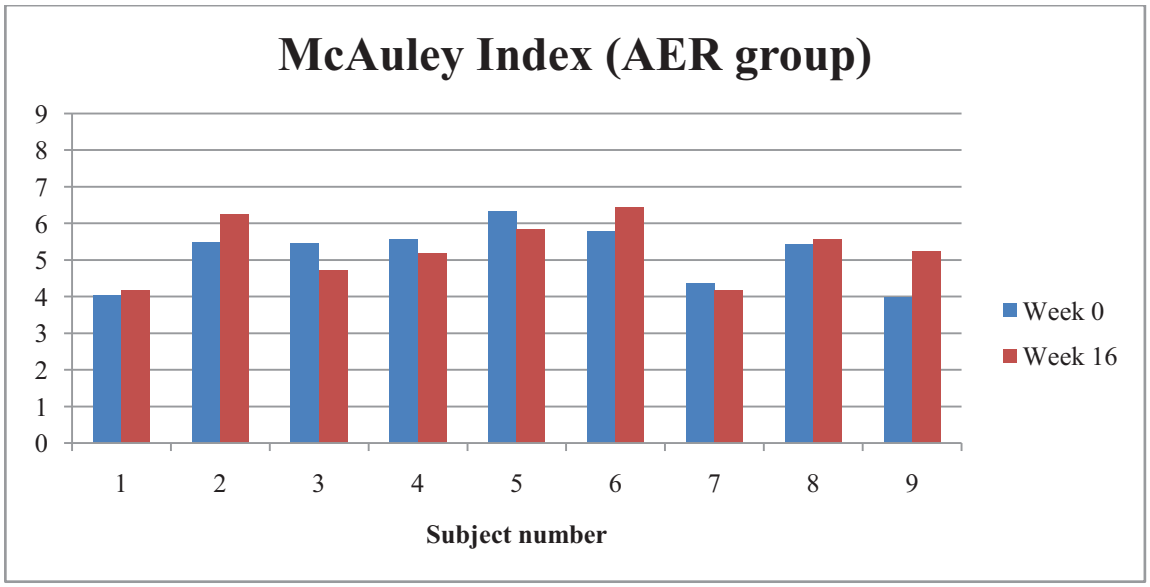
Subject number
Week 0
Week 16


McAuley Index (AER group)
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Week 0
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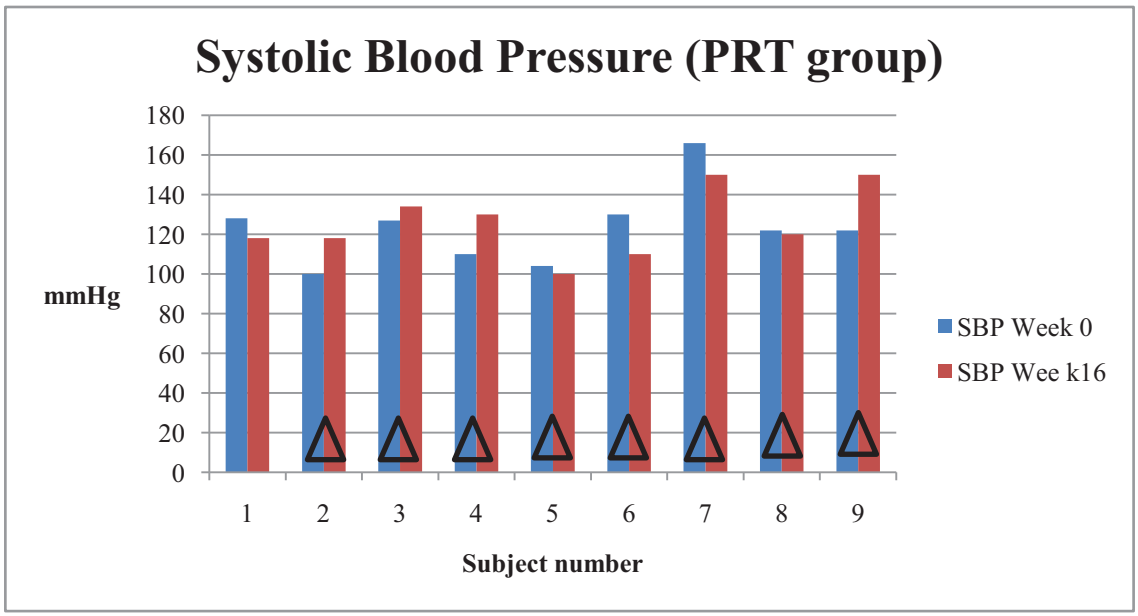
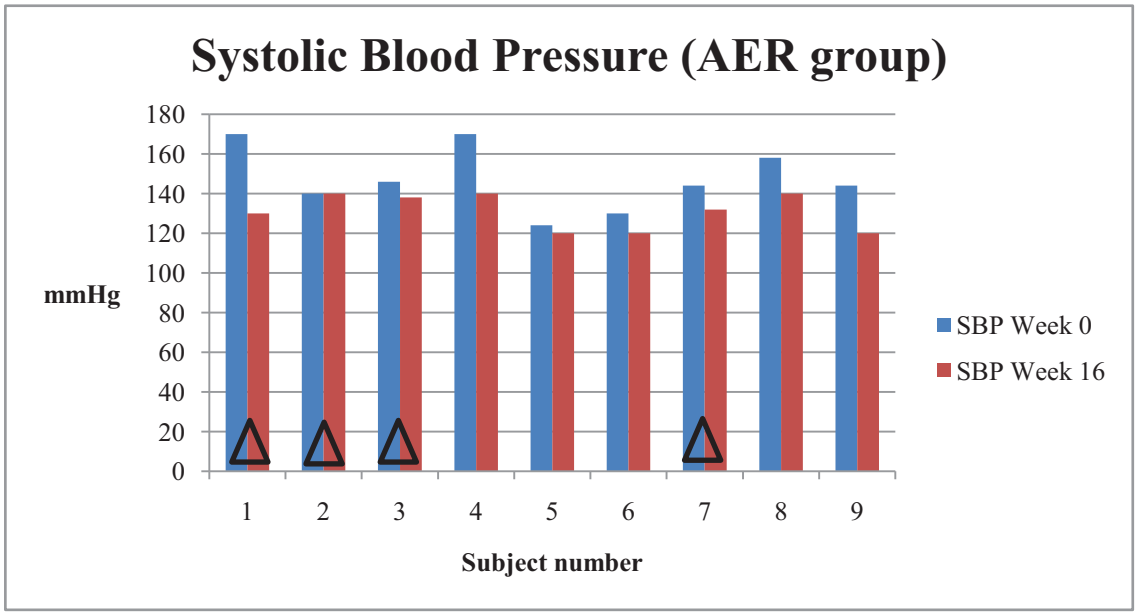
Δ = taking prescribed hypertension medications





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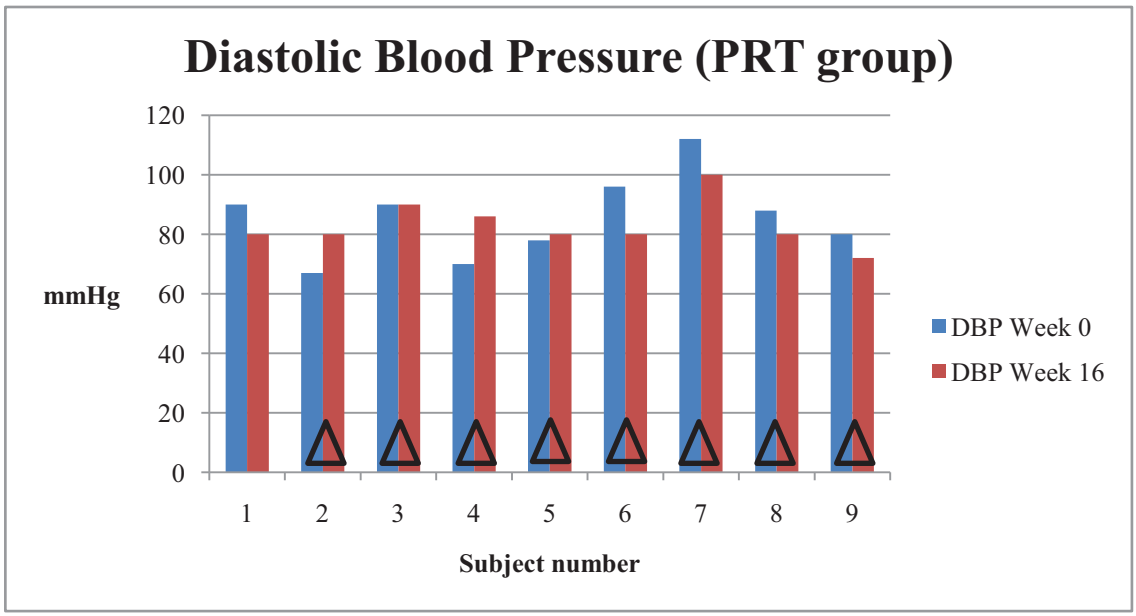
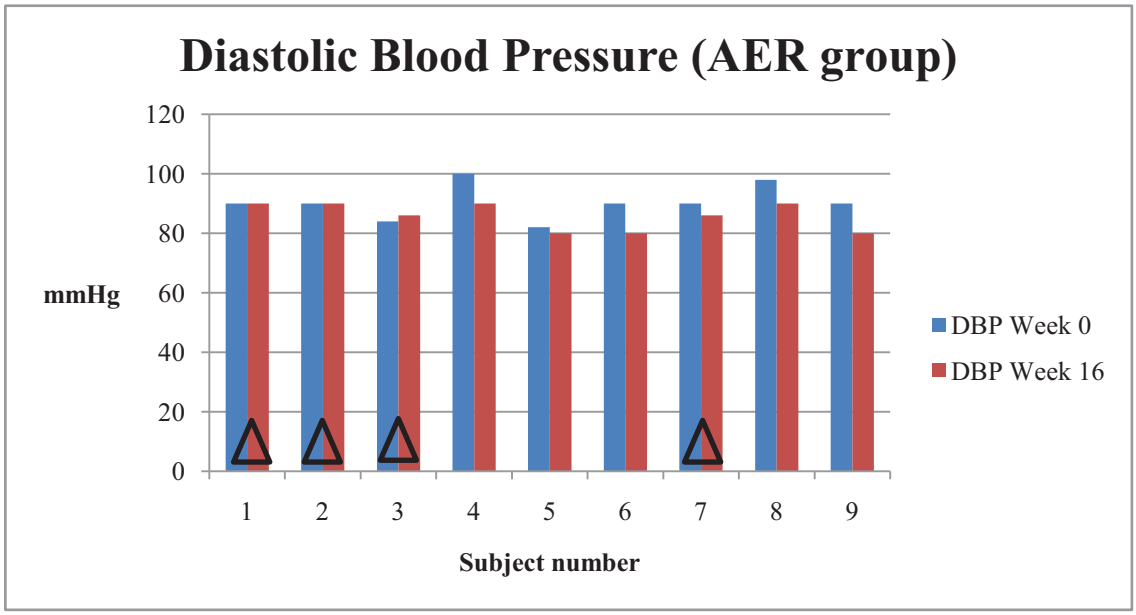
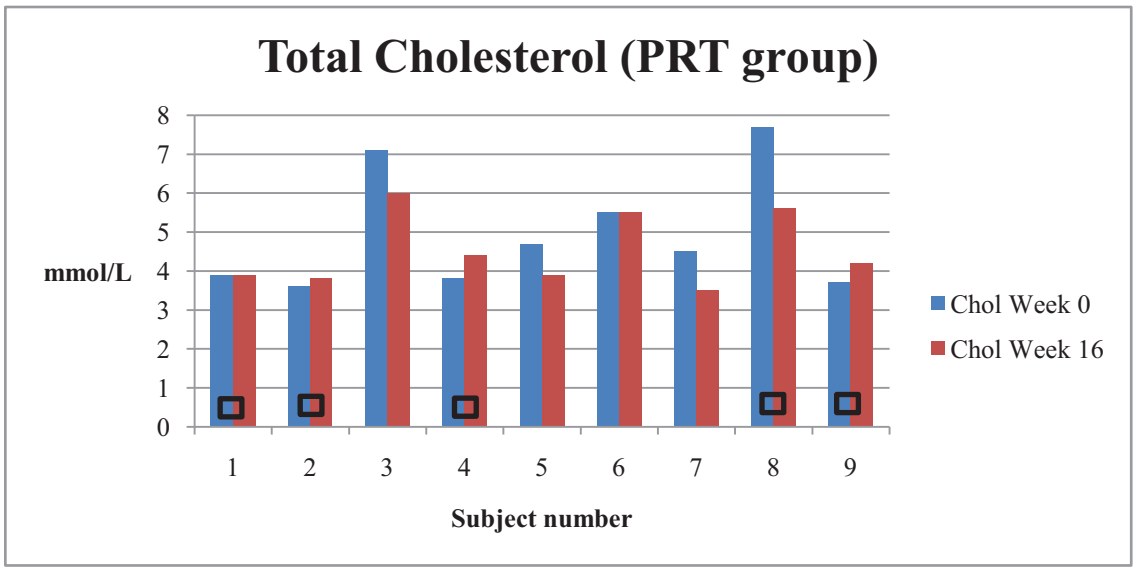
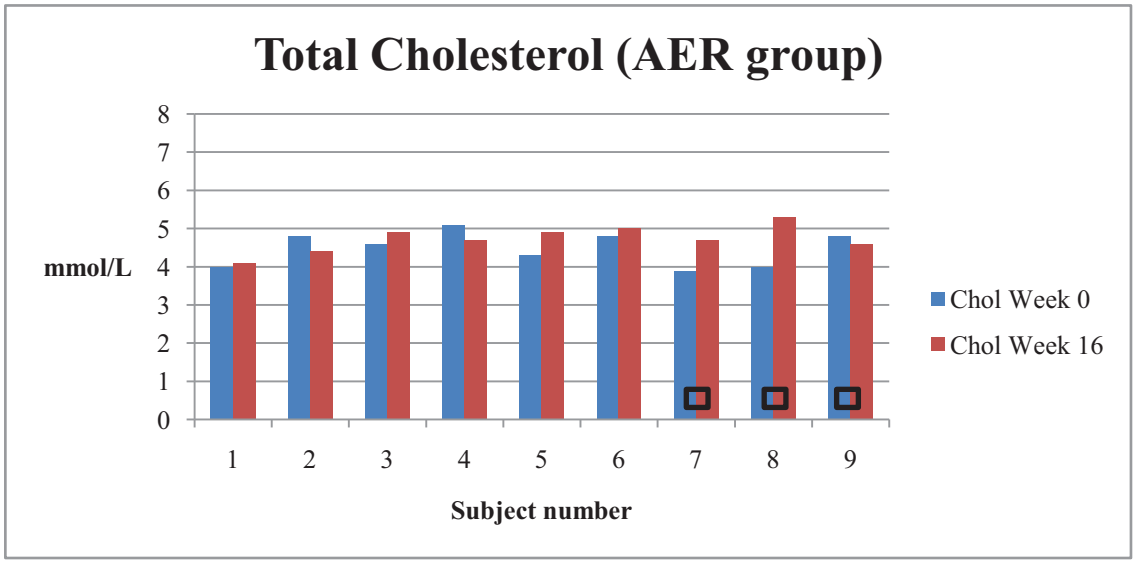




□ = taking prescribed lipid-lowering medication





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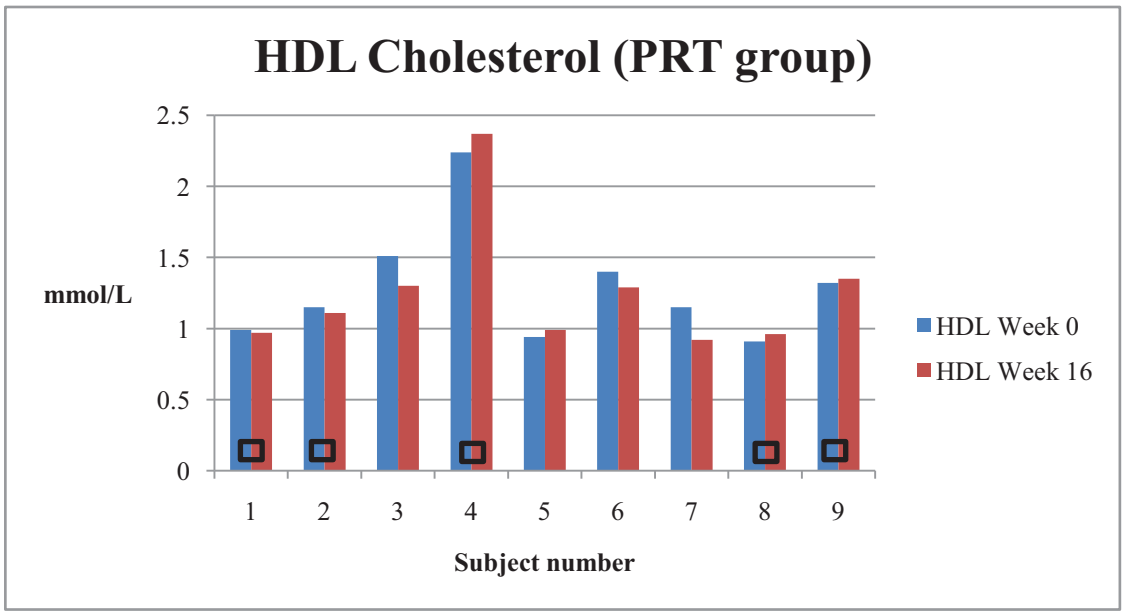

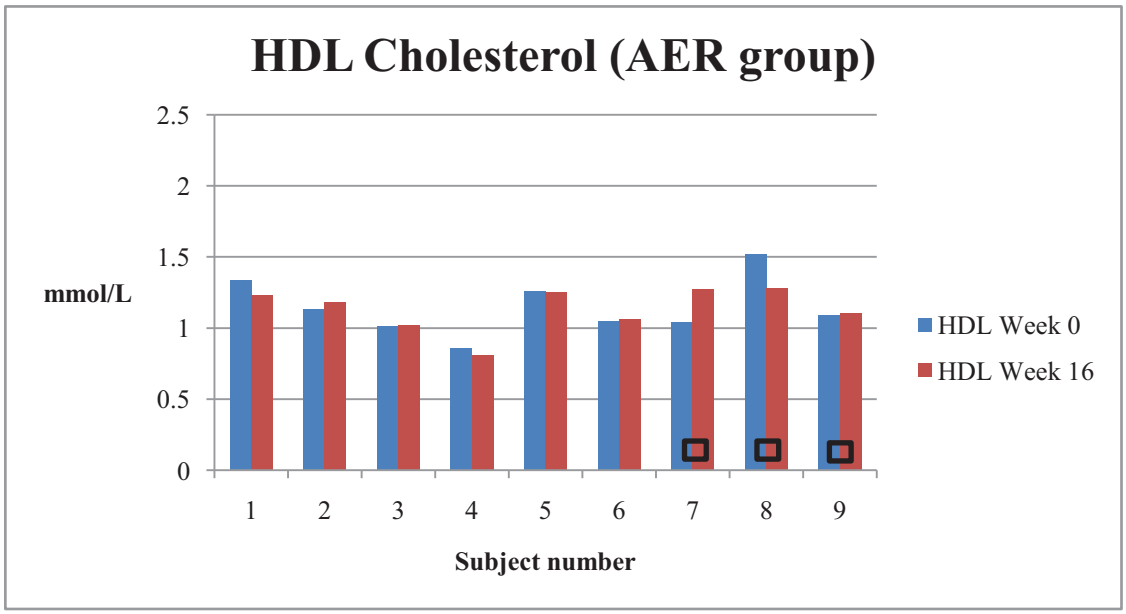

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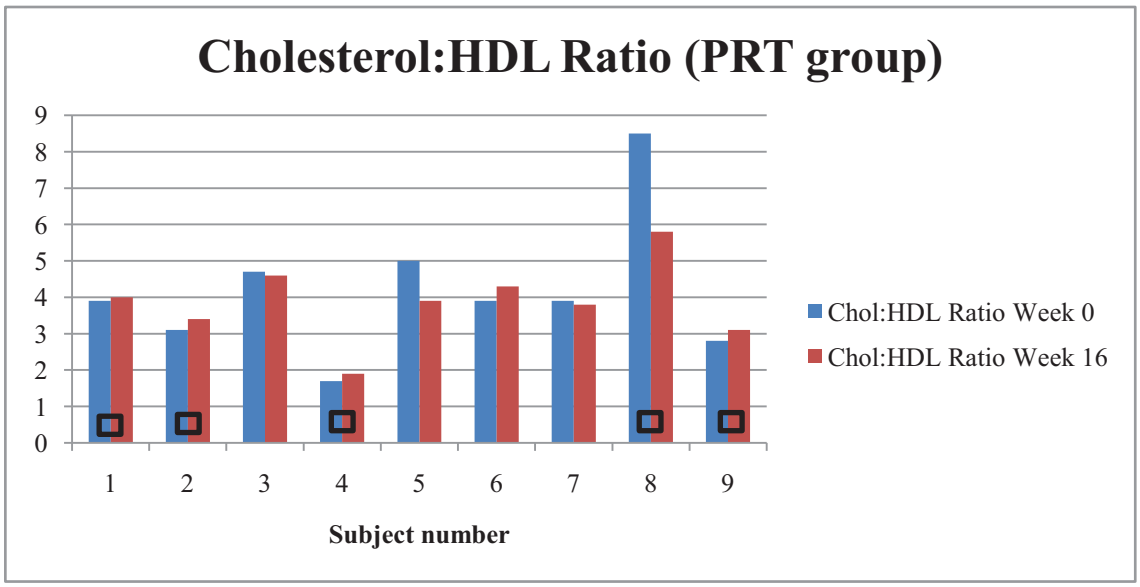

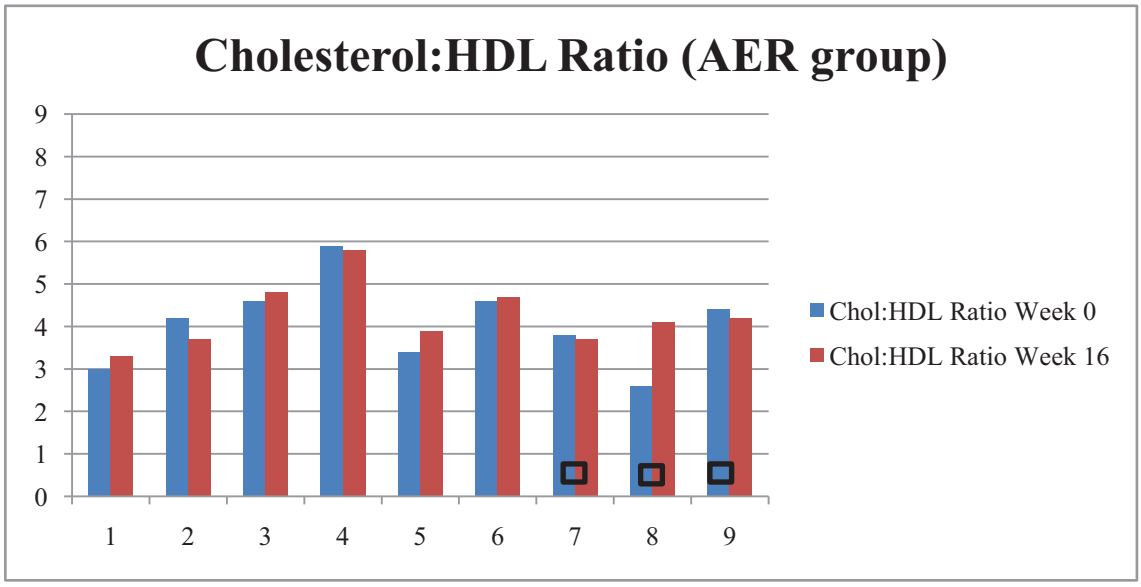

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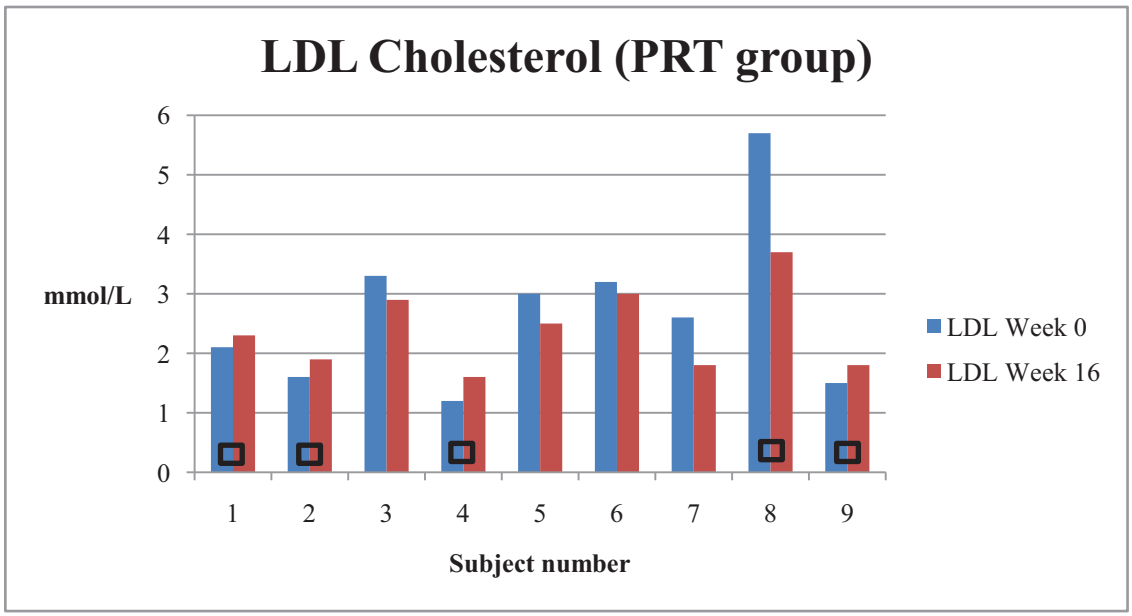

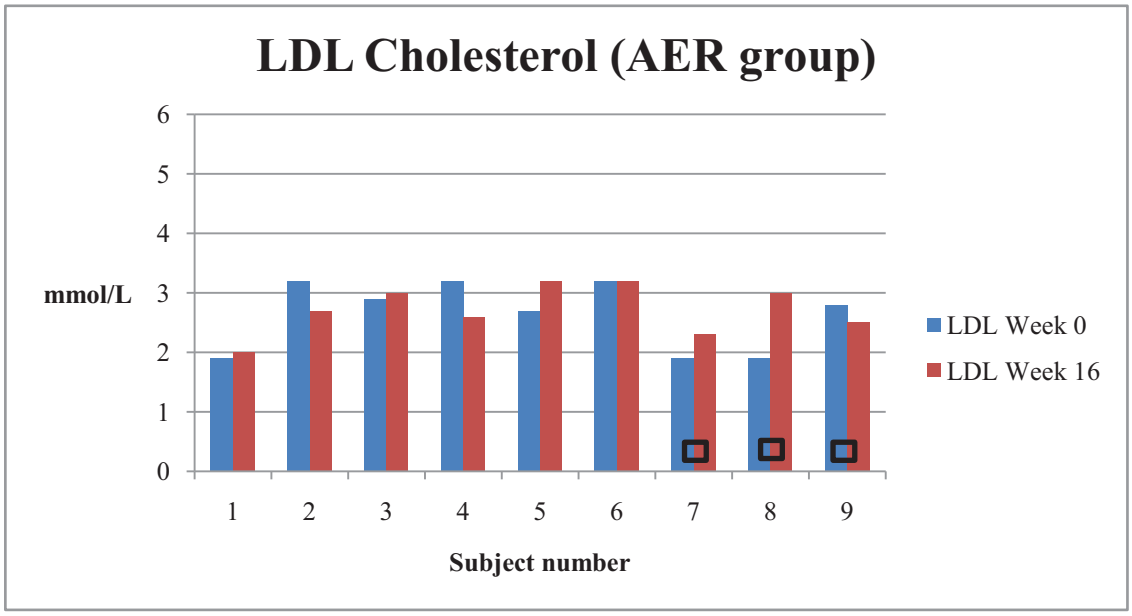

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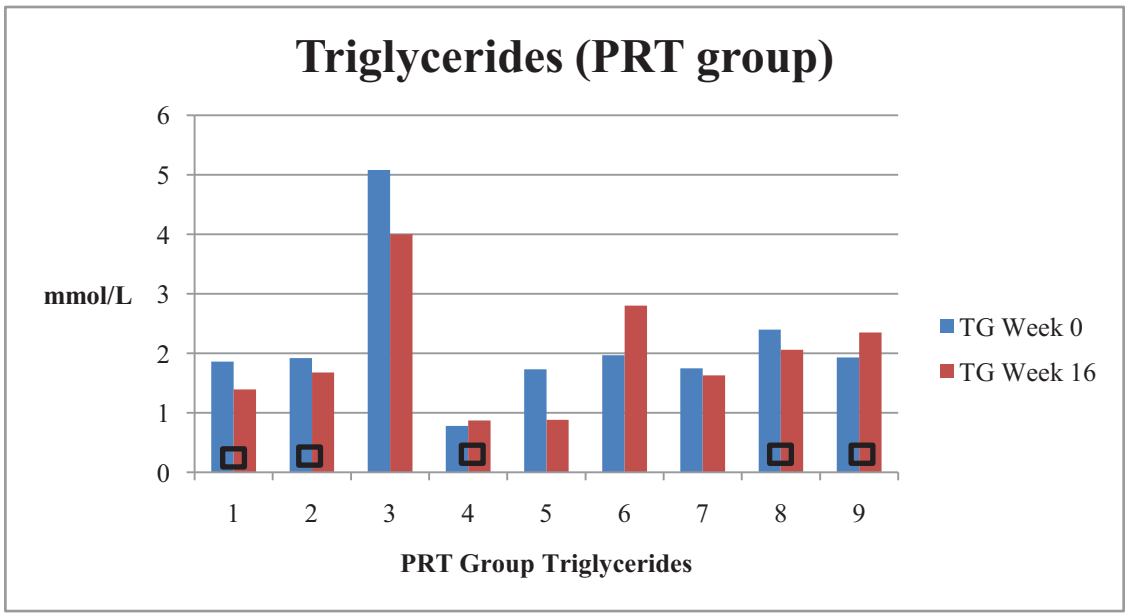

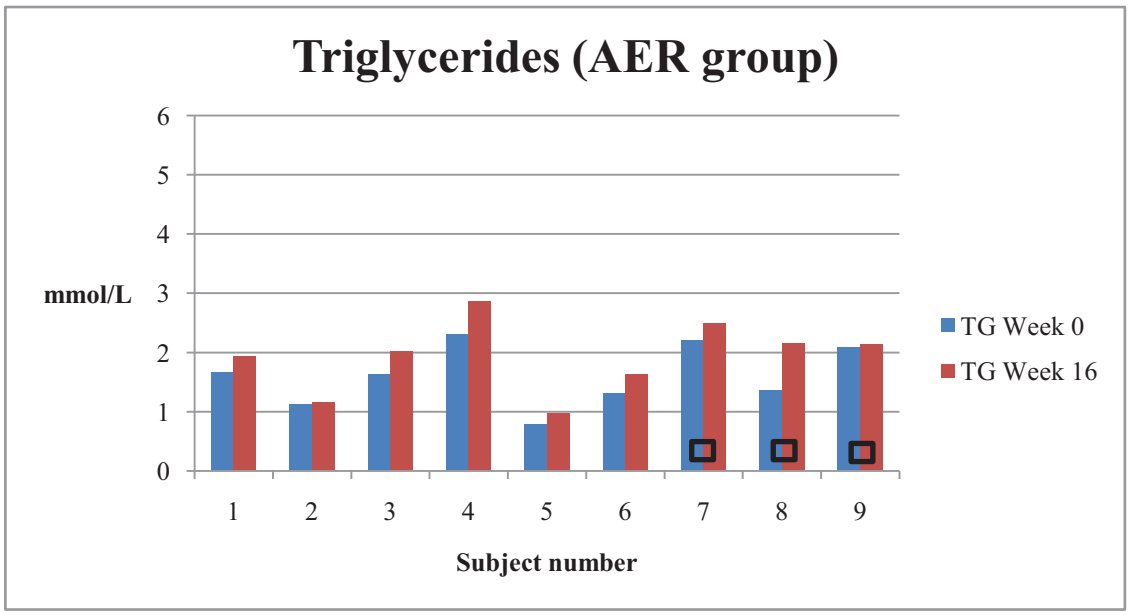

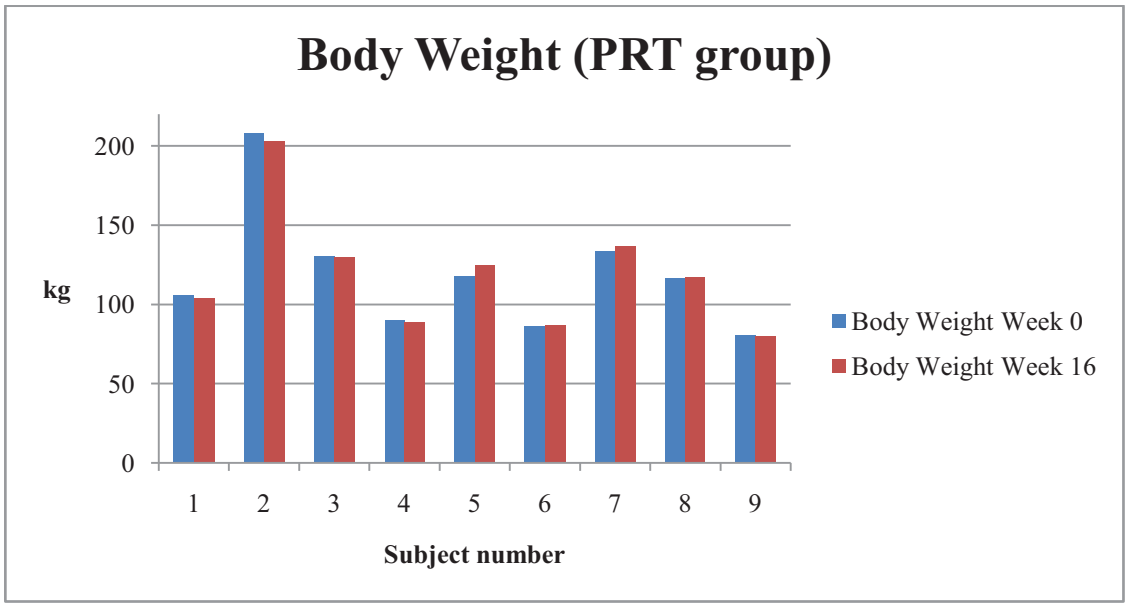
Body Weight (PRT group)
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150
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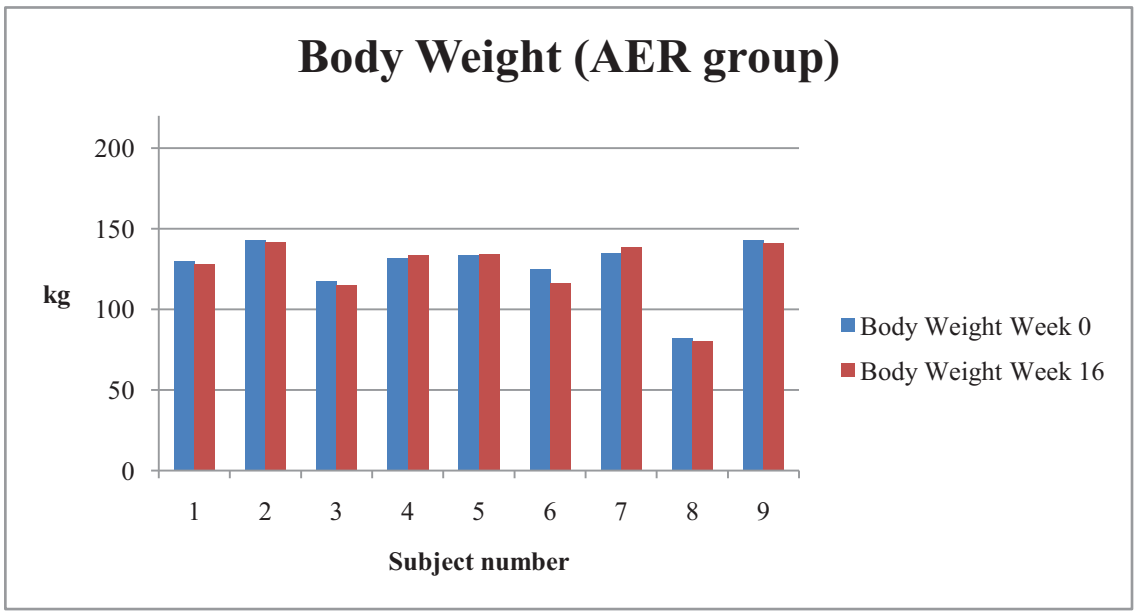
Body Weight Week 0
Body Weight Week 16


Body Weight (AER group)
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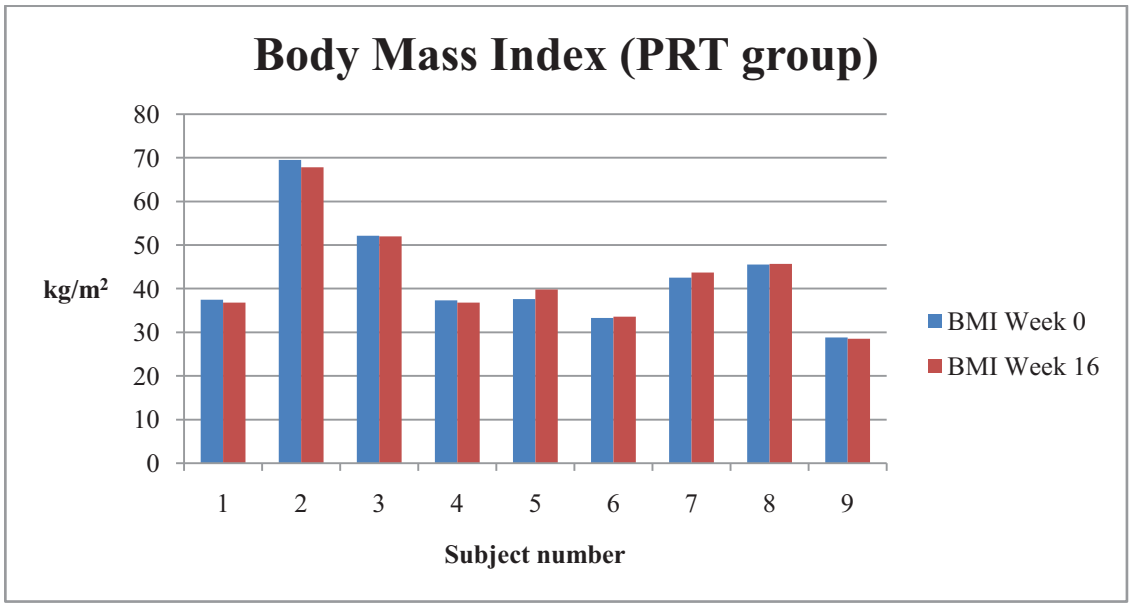
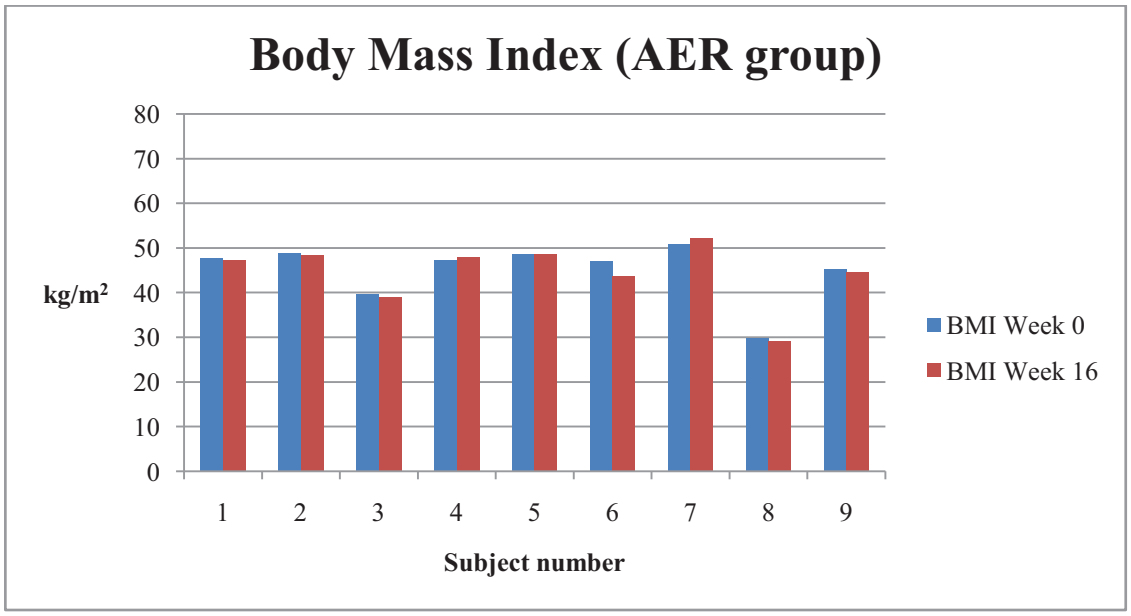
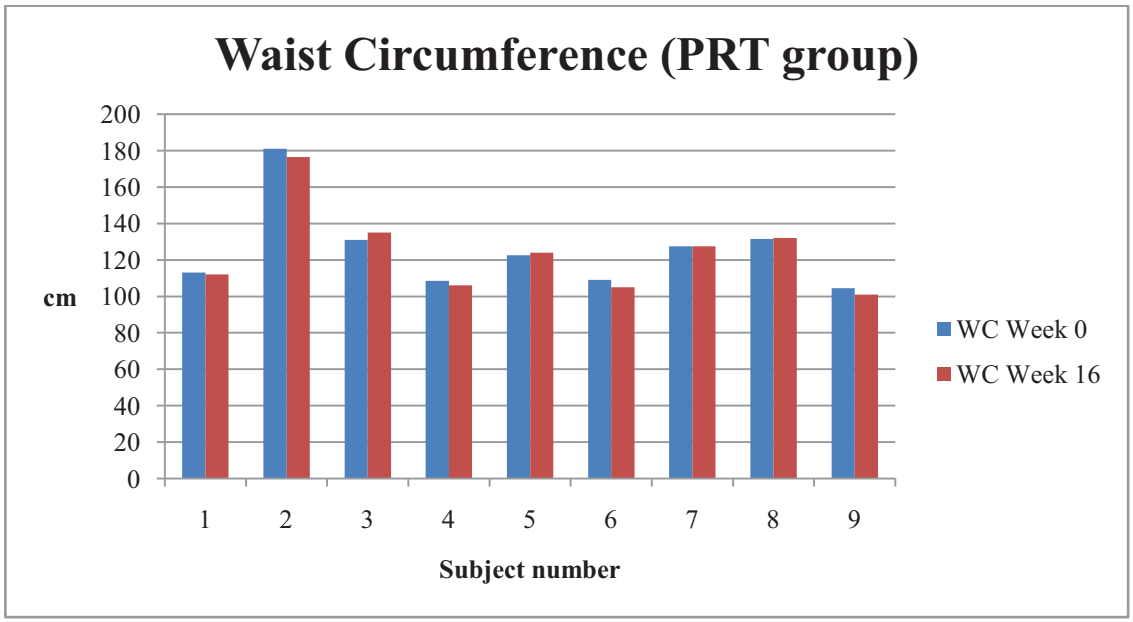
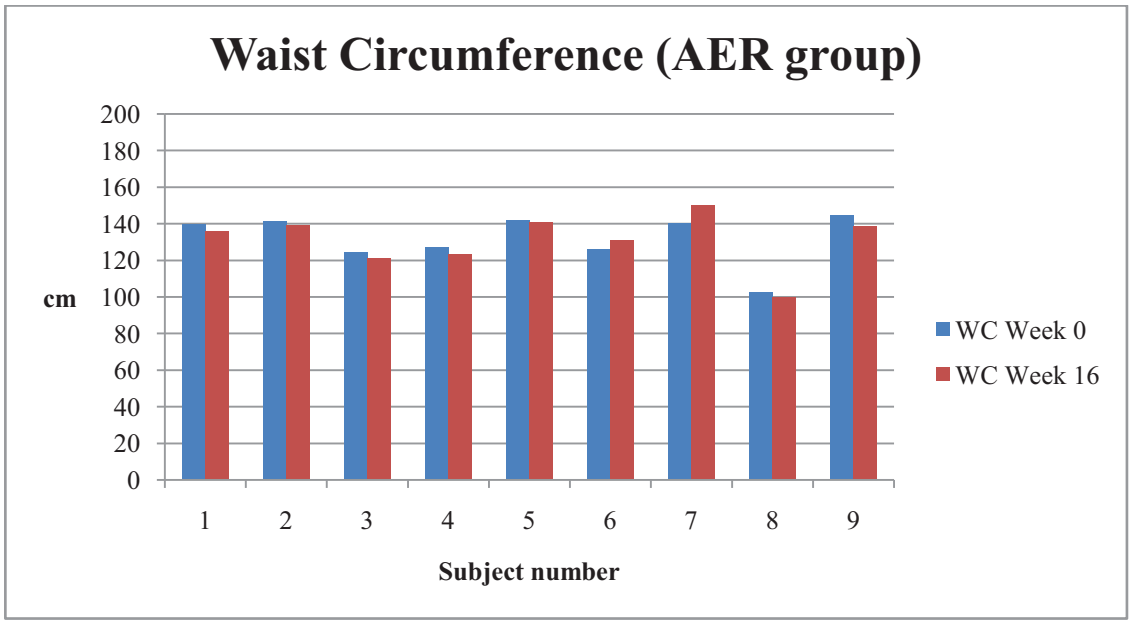
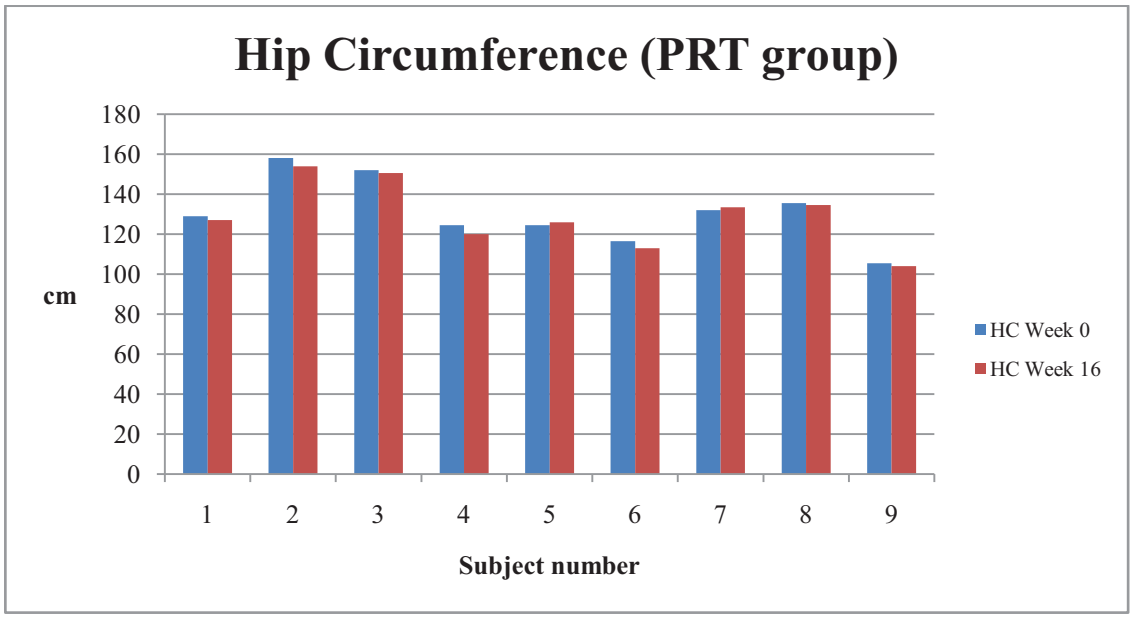
Body Weight Week 0
Body Weight Week 16

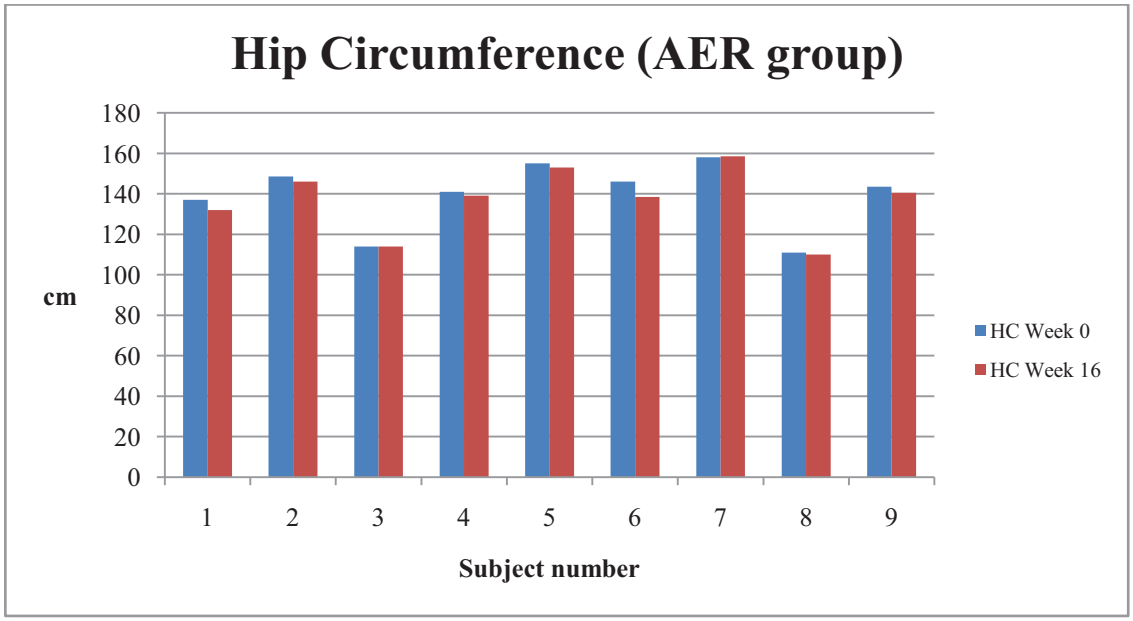

Body Mass Index (PRT group)
80
70
60
50
40
30
20
10
0
kg/m²
1
2
3
4
5
6
7
8
9
Subject number
BMI Week 0
BMI Week 16

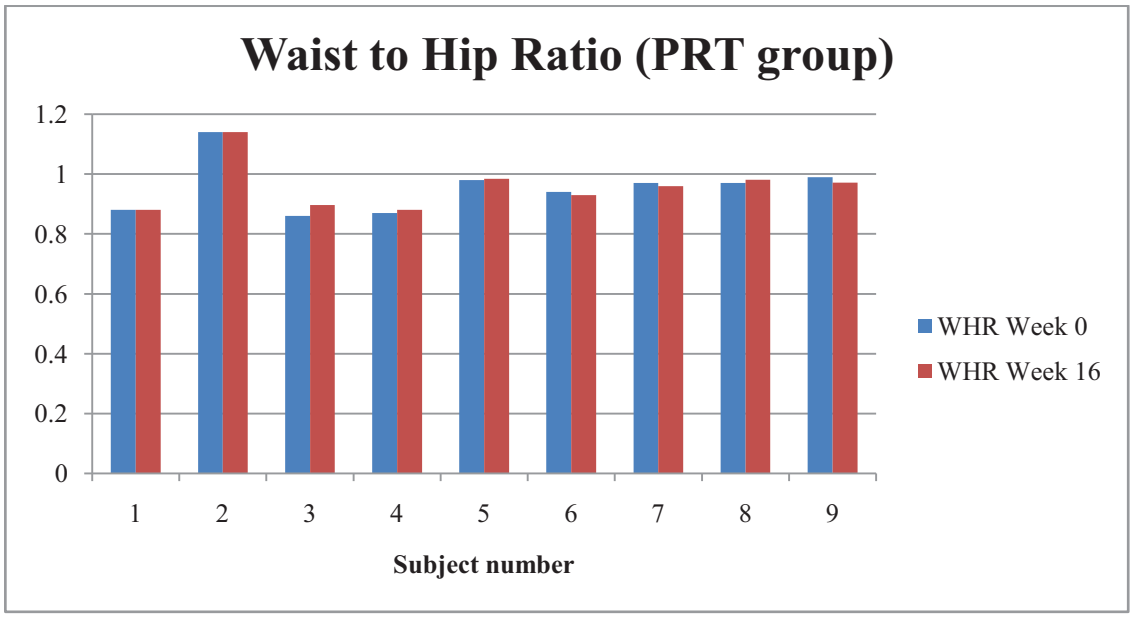

Body Mass Index (AER group)
80
70
60
50
40
30
20
10
0
kg/m²
1
2
3
4
5
6
7
8
9
Subject number
BMI Week 0
BMI Week 16

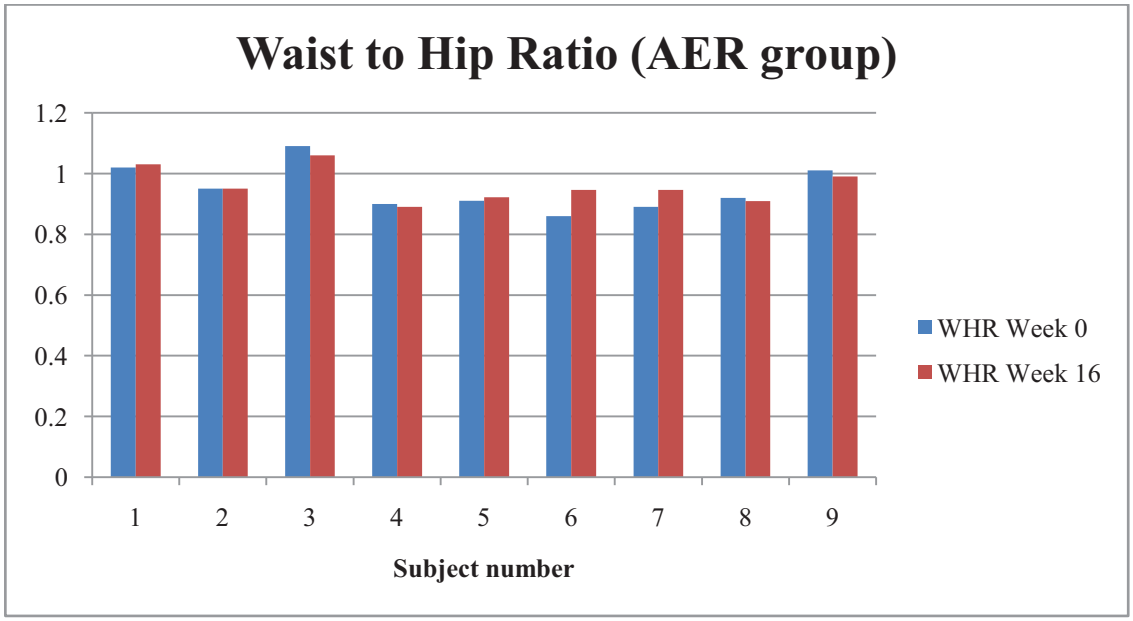

Waist Circumference (PRT group)
200
180
160
140
120
100
80
60
40
20
0
cm
1
2
3
4
5
6
7
8
9
Subject number
WC Week 0
WC Week 16

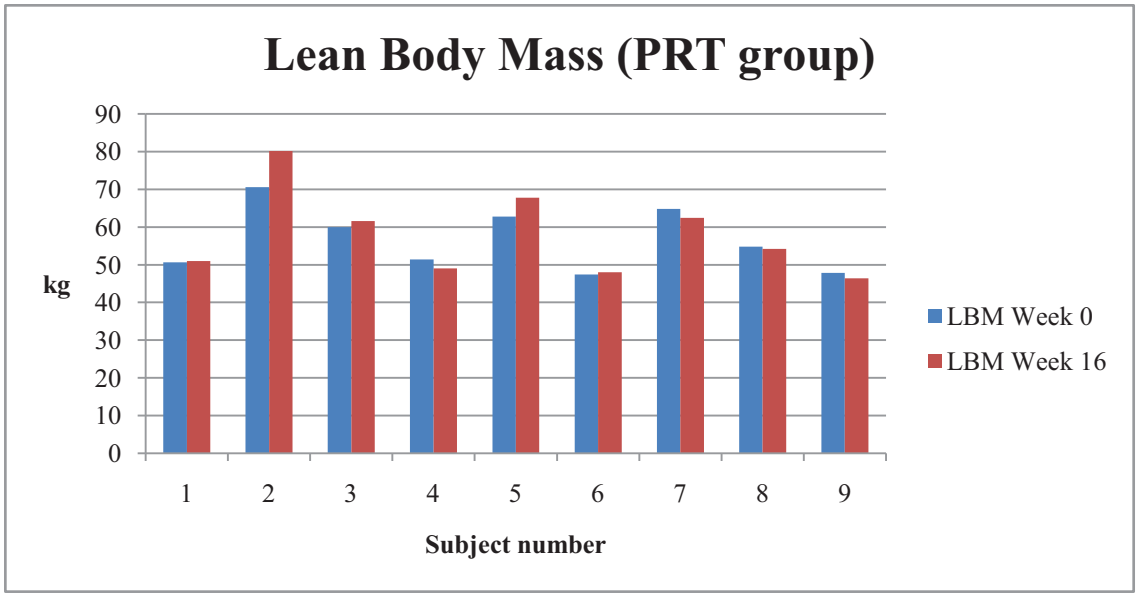

Waist Circumference (AER group)
200
180
160
140
120
100
80
60
40
20
0
cm
1
2
3
4
5
6
7
8
9
Subject number
WC Week 0
WC Week 16

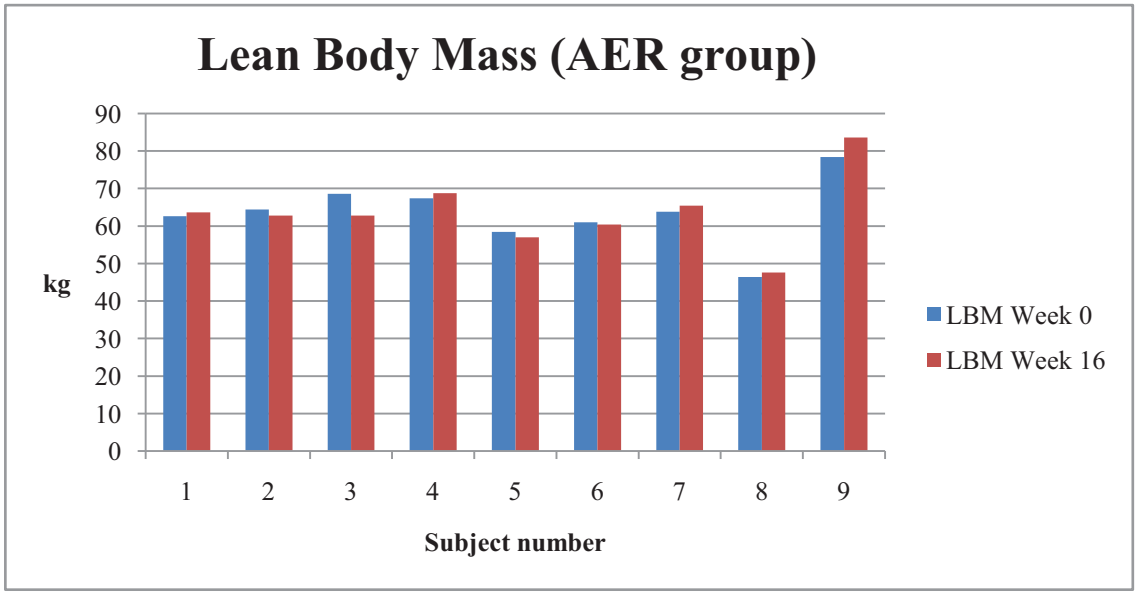

Hip Circumference (PRT group)
cm
180
160
140
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
HC Week 0
HC Week 16

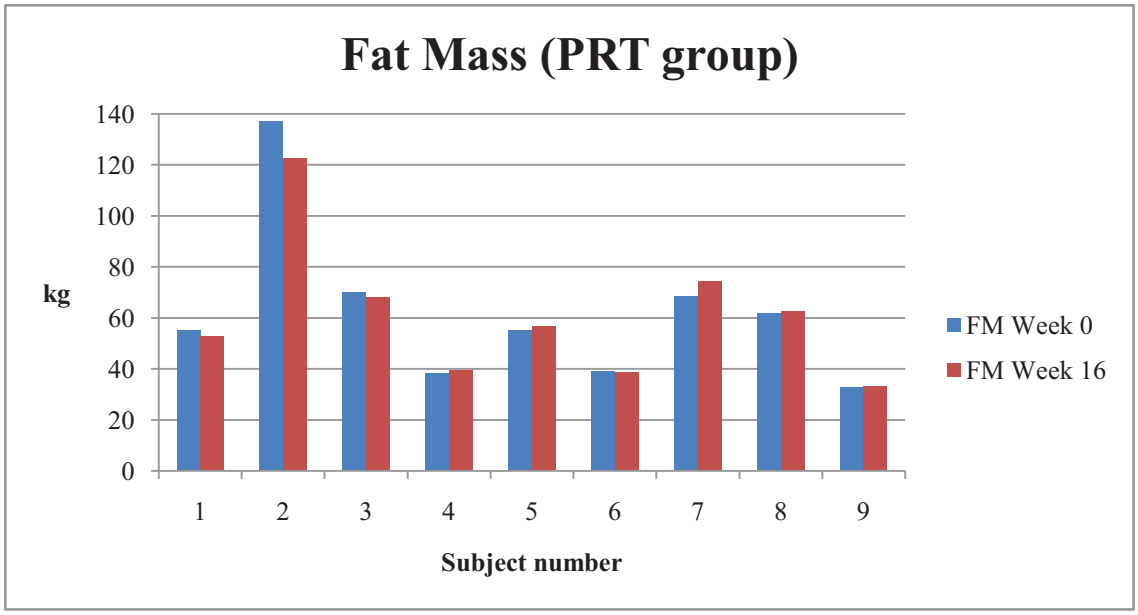

Hip Circumference (AER group)
cm
180
160
140
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
HC Week 0
HC Week 16

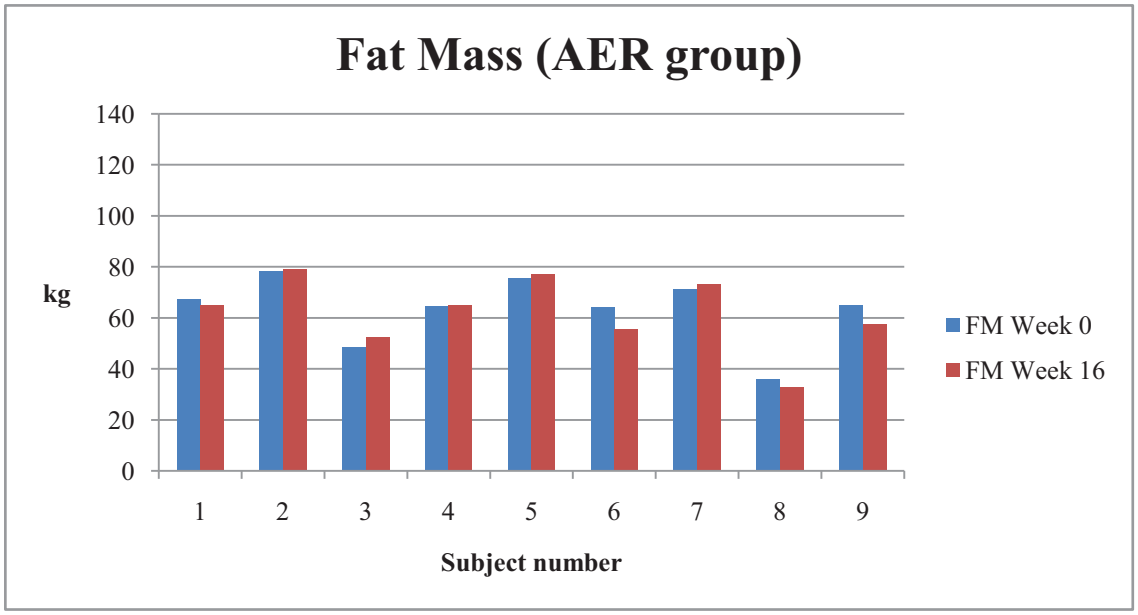

Waist to Hip Ratio (PRT group)
1.2
1
0.8
0.6
0.4
0.2
0
1
2
3
4
5
6
7
8
9
Subject number
WHR Week 0
WHR Week 16

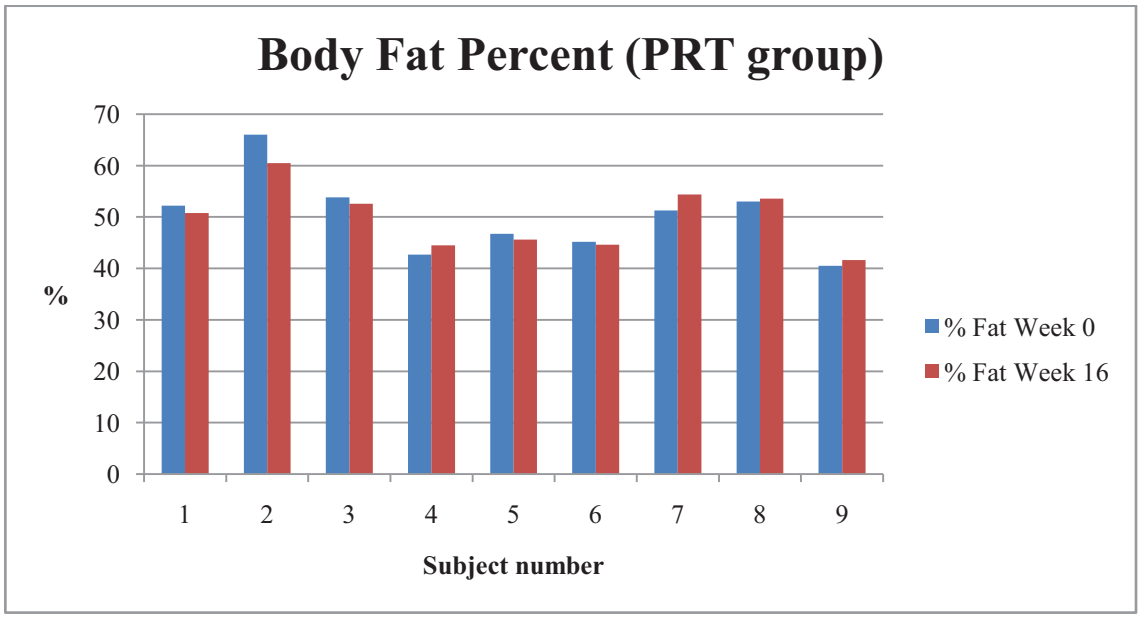

Waist to Hip Ratio (AER group)
1.2
1
0.8
0.6
0.4
0.2
0
1
2
3
4
5
6
7
8
9
Subject number
WHR Week 0
WHR Week 16

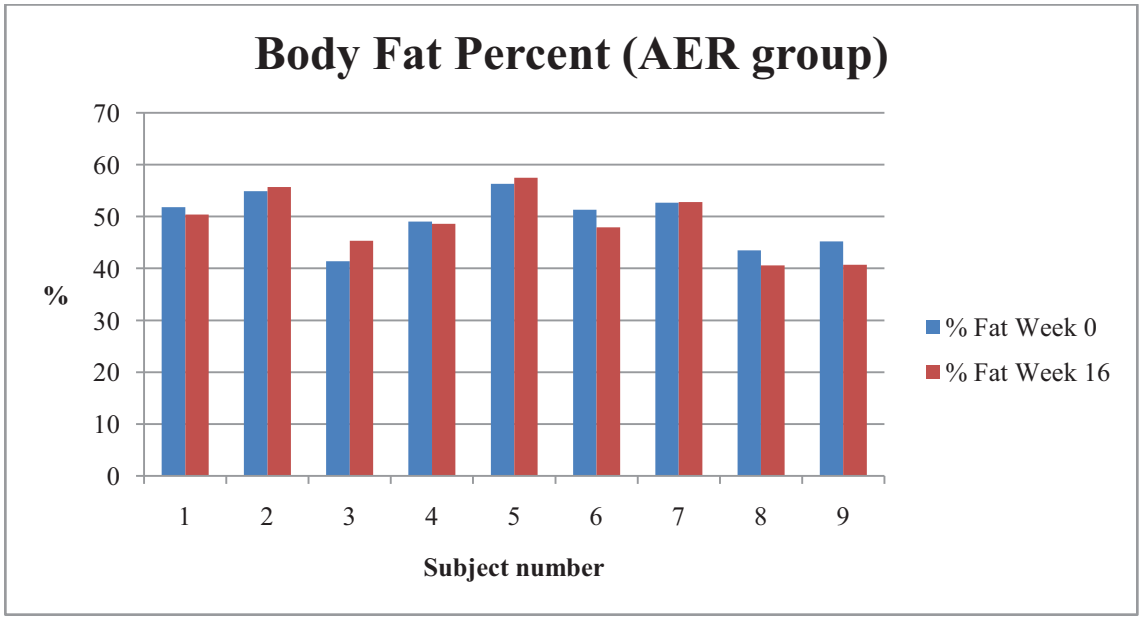

Lean Body Mass (PRT group)
kg
90
80
70
60
50
40
30
20
10
0
1
2
3
4
5
6
7
8
9
Subject number
LBM Week 0
LBM Week 16

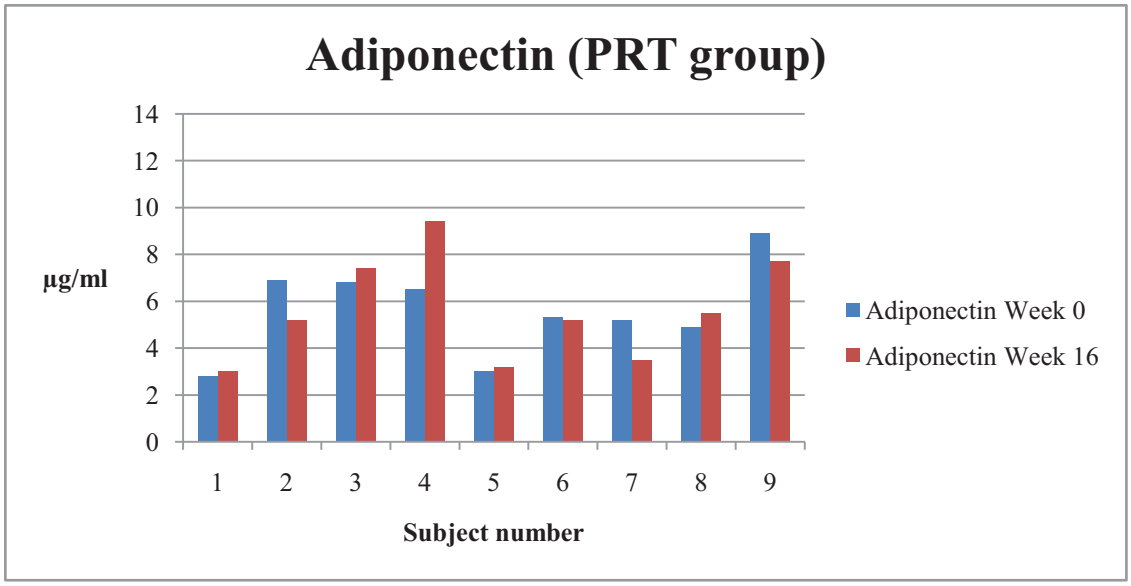

Lean Body Mass (AER group)
kg
90
80
70
60
50
40
30
20
10
0
1
2
3
4
5
6
7
8
9
Subject number
LBM Week 0
LBM Week 16

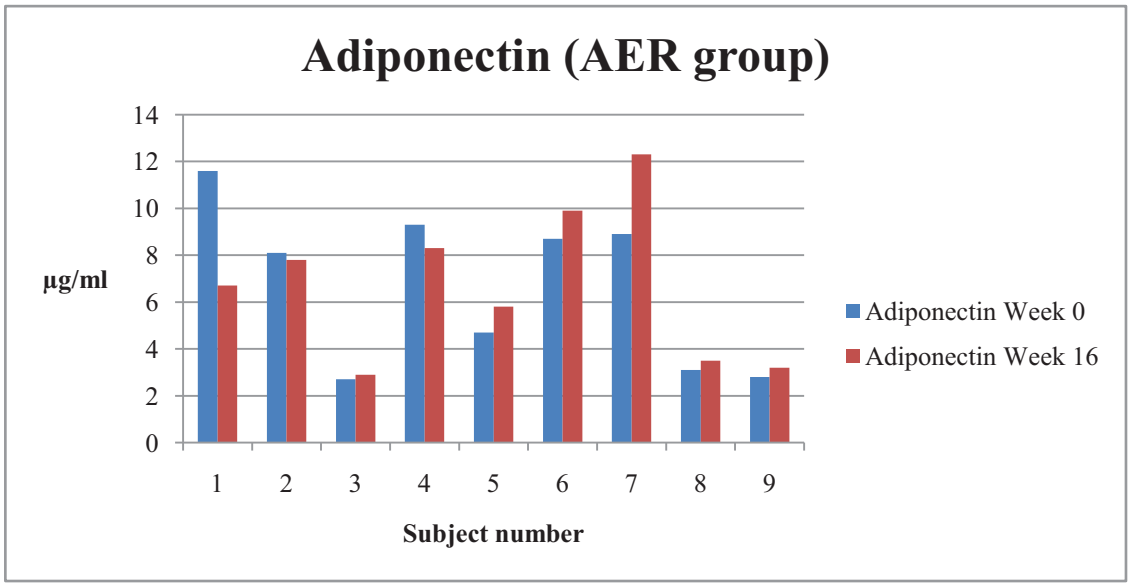

Fat Mass (PRT group)
140
120
100
80
60
40
20
0
kg
1
2
3
4
5
6
7
8
9
Subject number
FM Week 0
FM Week 16

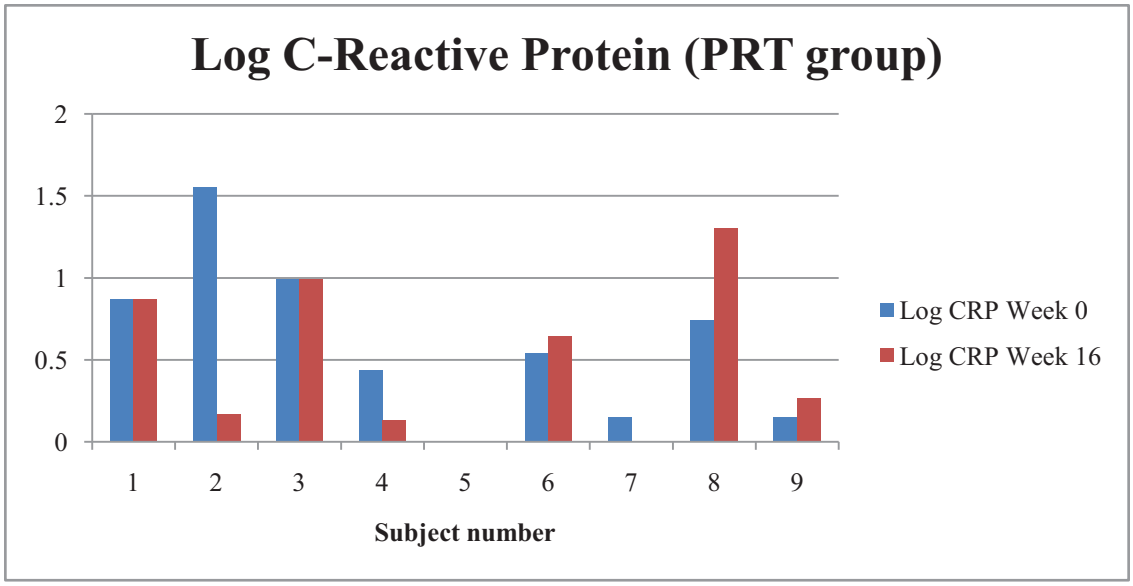

Fat Mass (AER group)
140
120
100
80
60
40
20
0
kg
1
2
3
4
5
6
7
8
9
Subject number
FM Week 0
FM Week 16

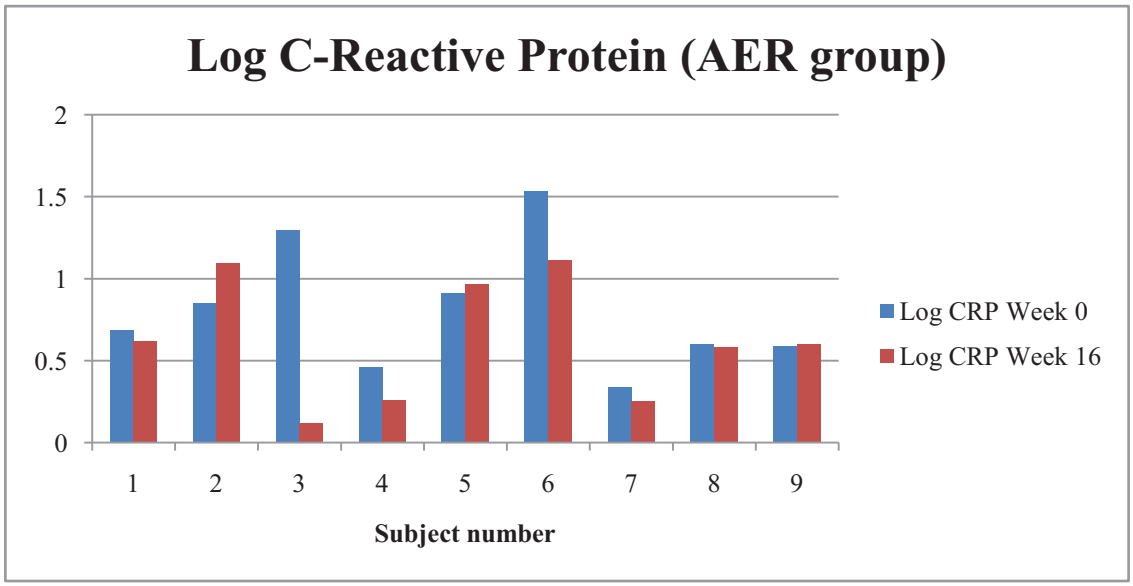

Body Fat Percent (PRT group)
70
60
50
40
30
20
10
0
%
1
2
3
4
5
6
7
8
9
Subject number
% Fat Week 0
% Fat Week 16

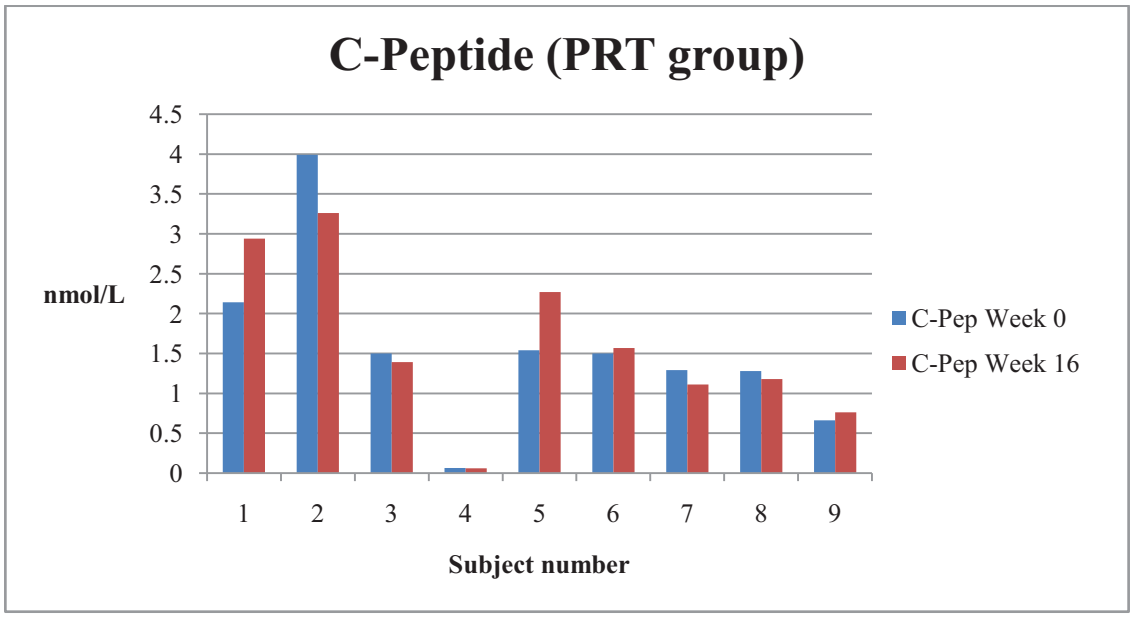

Body Fat Percent (AER group)
70
60
50
40
30
20
10
0
%
1
2
3
4
5
6
7
8
9
Subject number
% Fat Week 0
% Fat Week 16

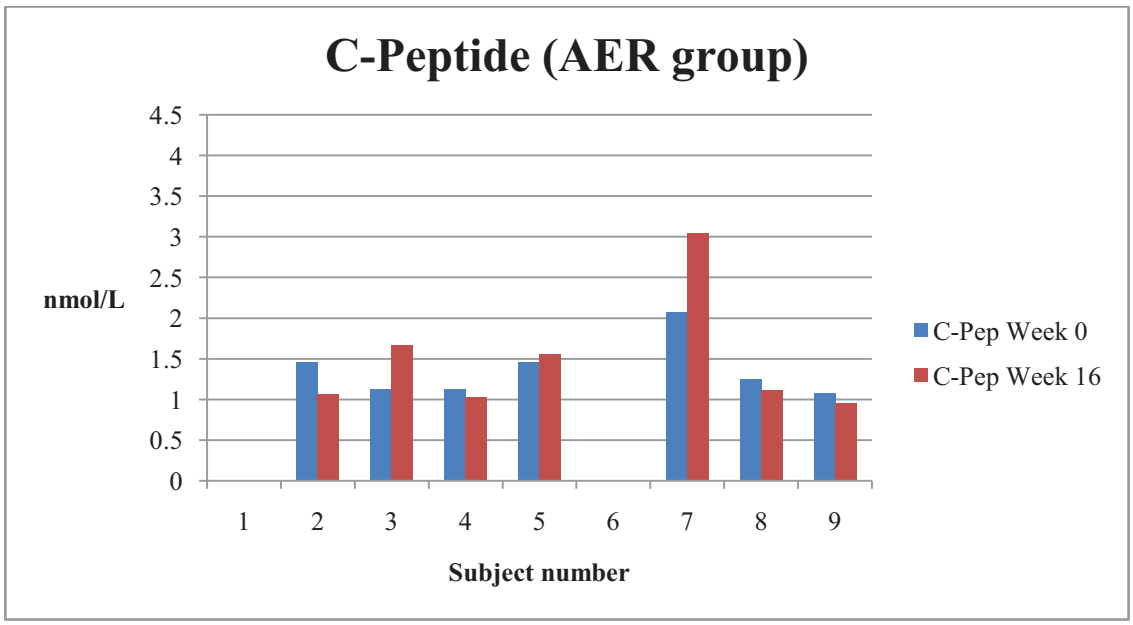

Adiponectin (PRT group)
µg/ml
14
12
10
8
6
4
2
0
1
2
3
4
5
6
7
8
9
Subject number
Adiponectin Week 0
Adiponectin Week 16

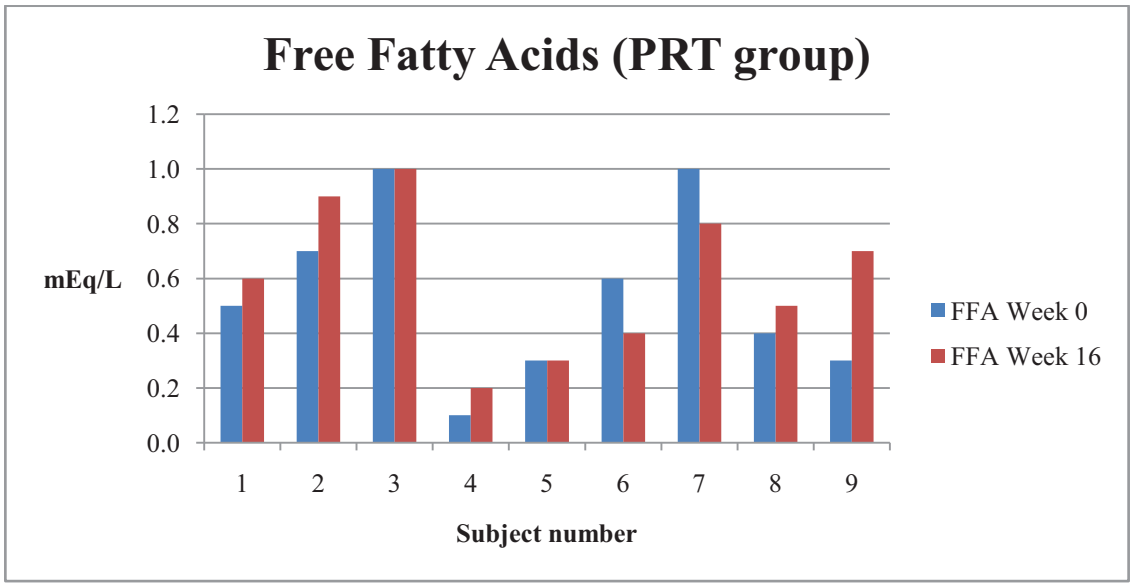

Adiponectin (AER group)
µg/ml
14
12
10
8
6
4
2
0
1
2
3
4
5
6
7
8
9
Subject number
Adiponectin Week 0
Adiponectin Week 16

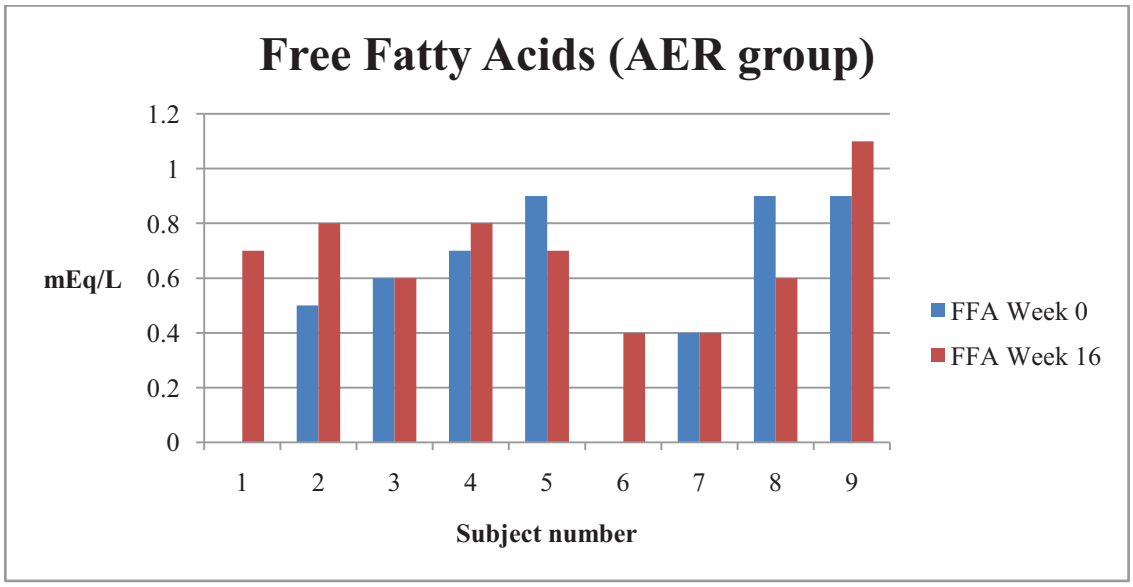

Log C-Reactive Protein (PRT group)
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Subject number
Log CRP Week 0
Log CRP Week 16

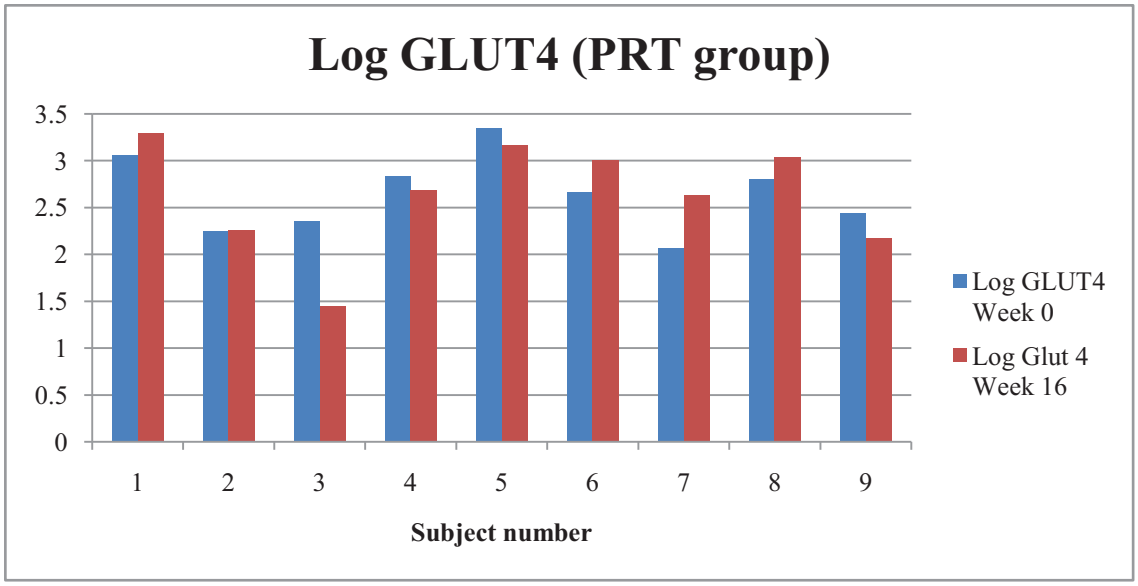

Log C-Reactive Protein (AER group)
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Subject number
Log CRP Week 0
Log CRP Week 16

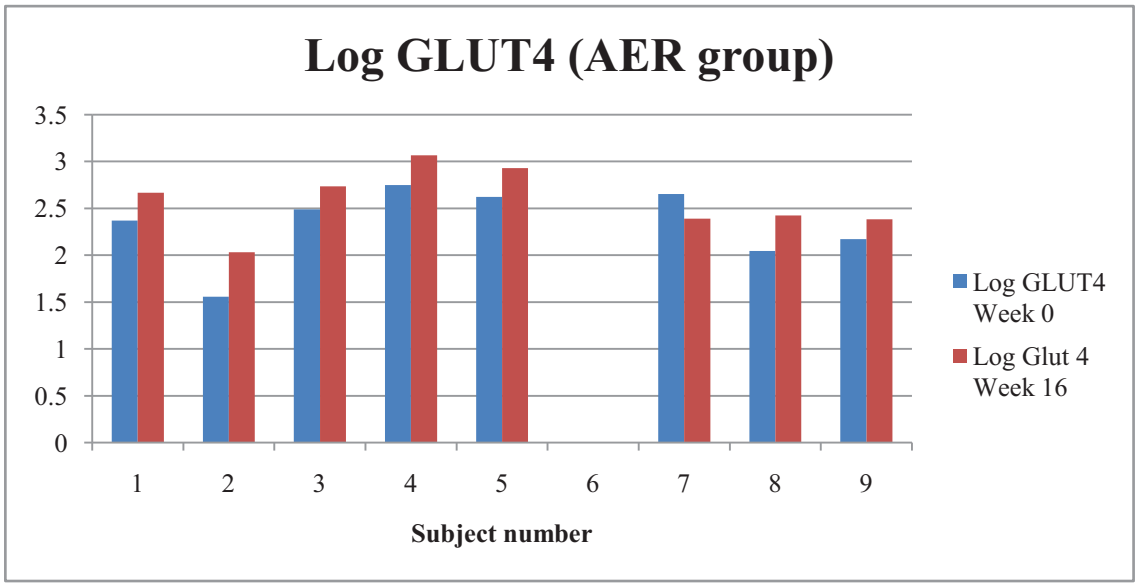

C-Peptide (PRT group)
nmol/L
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Subject number
C-Pep Week 0
C-Pep Week 16

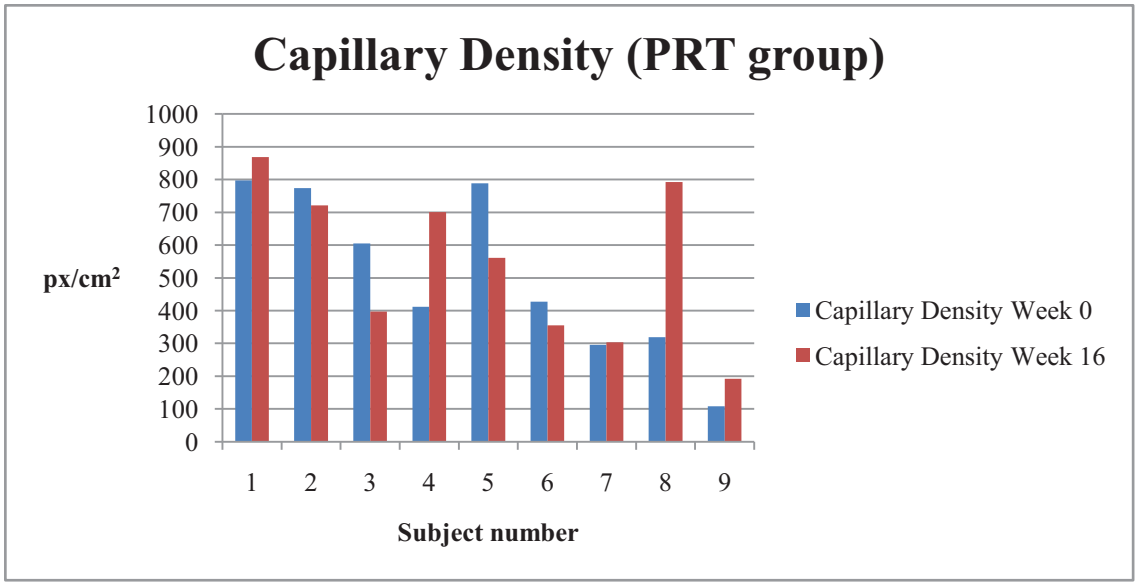

C-Peptide (AER group)
nmol/L
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Subject number
C-Pep Week 0
C-Pep Week 16

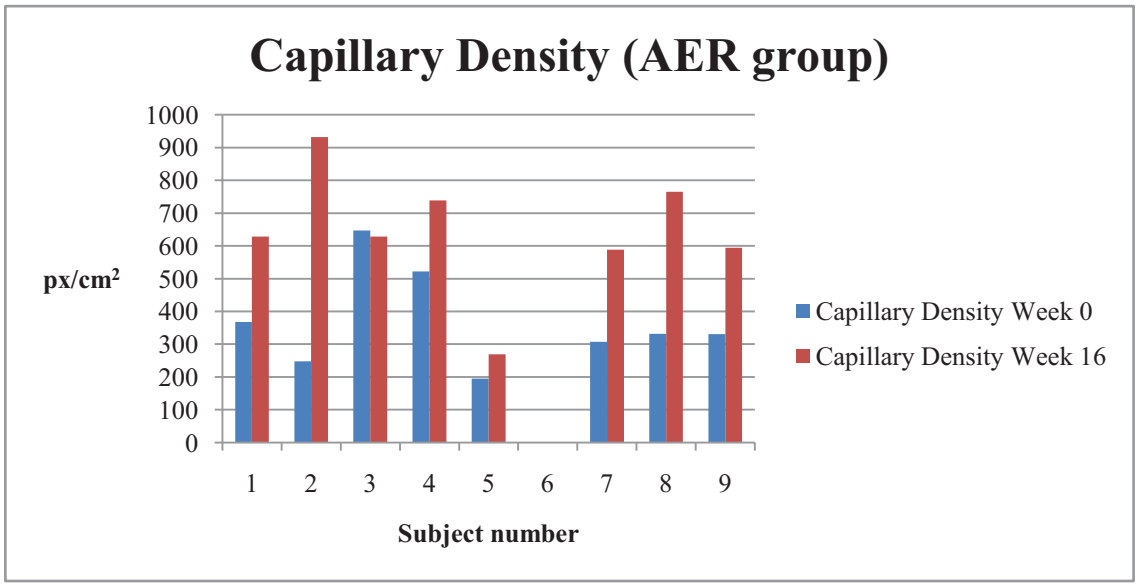

Free Fatty Acids (PRT group)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
mEq/L
1
2
3
4
5
6
7
8
9
Subject number
FFA Week 0
FFA Week 16

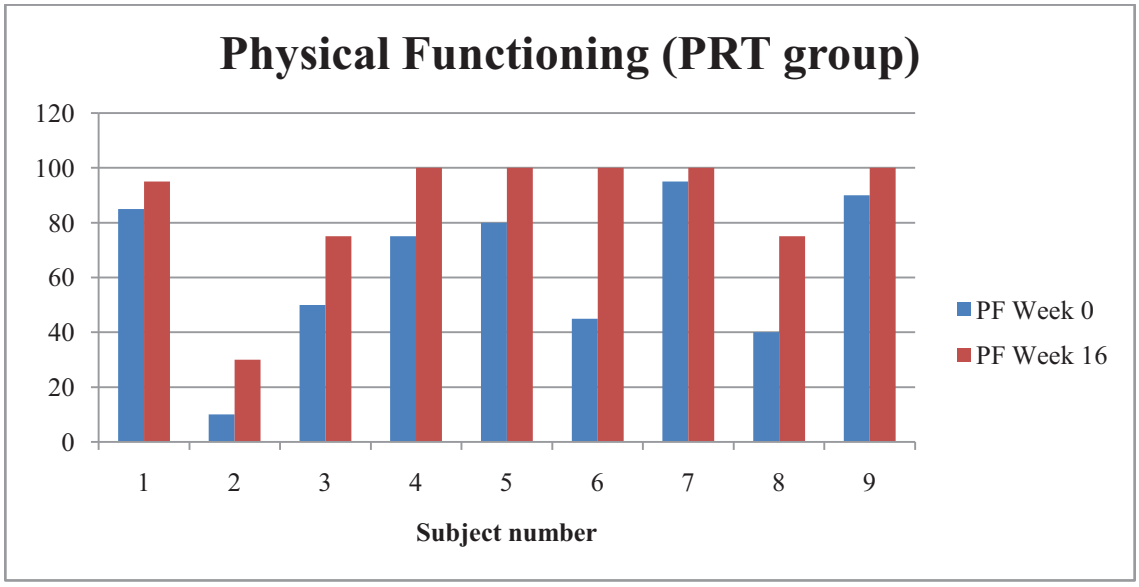

Free Fatty Acids (AER group)
1.2
1
0.8
0.6
0.4
0.2
0
mEq/L
1
2
3
4
5
6
7
8
9
Subject number
FFA Week 0
FFA Week 16

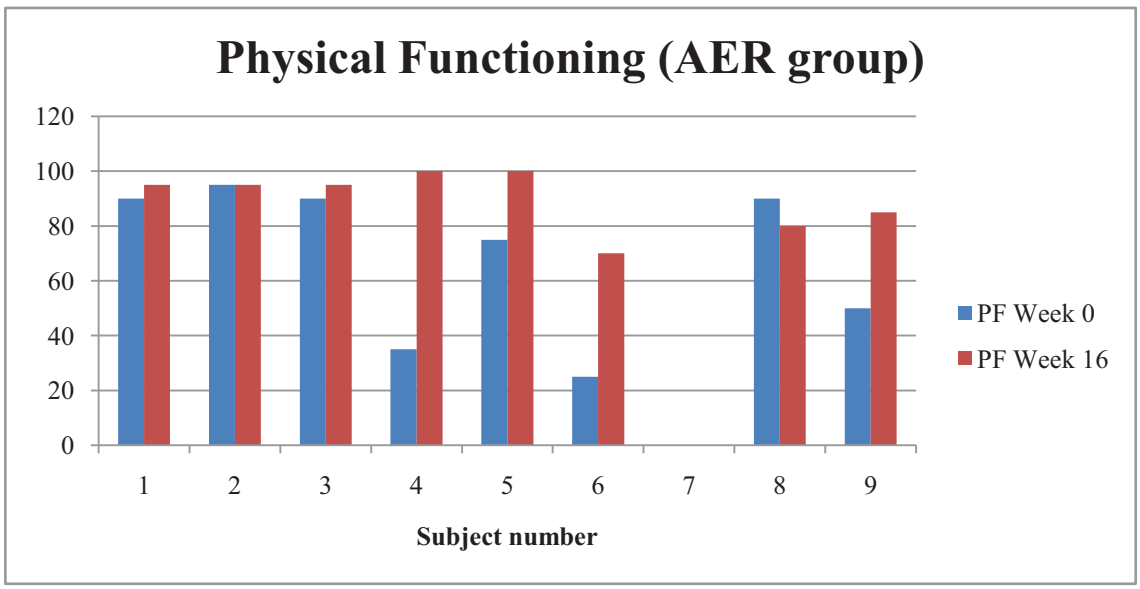

Log GLUT4 (PRT group)
3.5
3
2.5
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Subject number
Log GLUT4 Week 0
Log Glut 4 Week 16

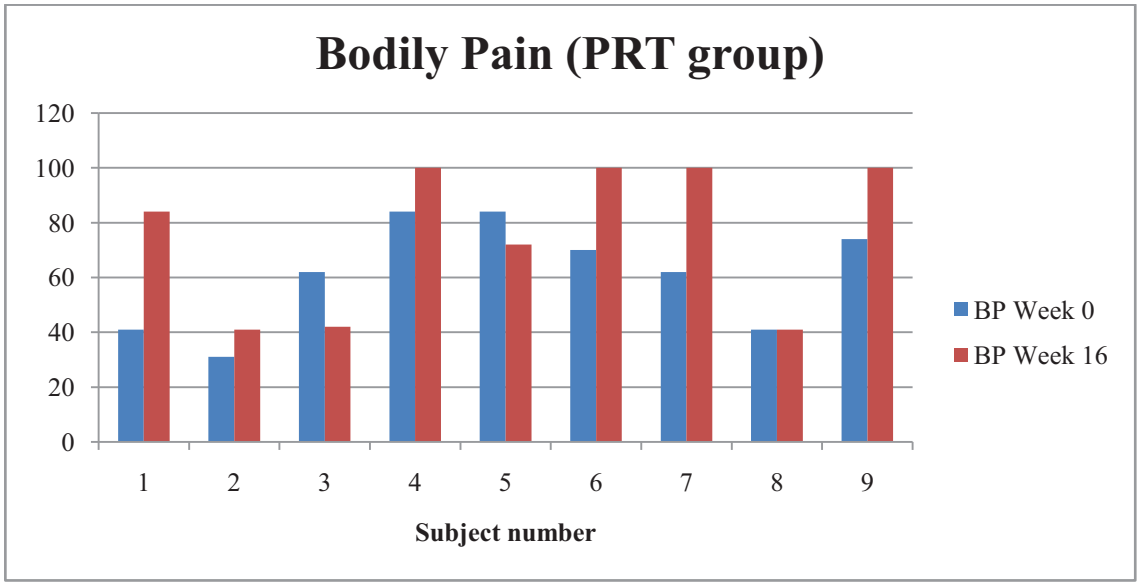

Log GLUT4 (AER group)
3.5
3
2.5
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Subject number
Log GLUT4 Week 0
Log Glut 4 Week 16

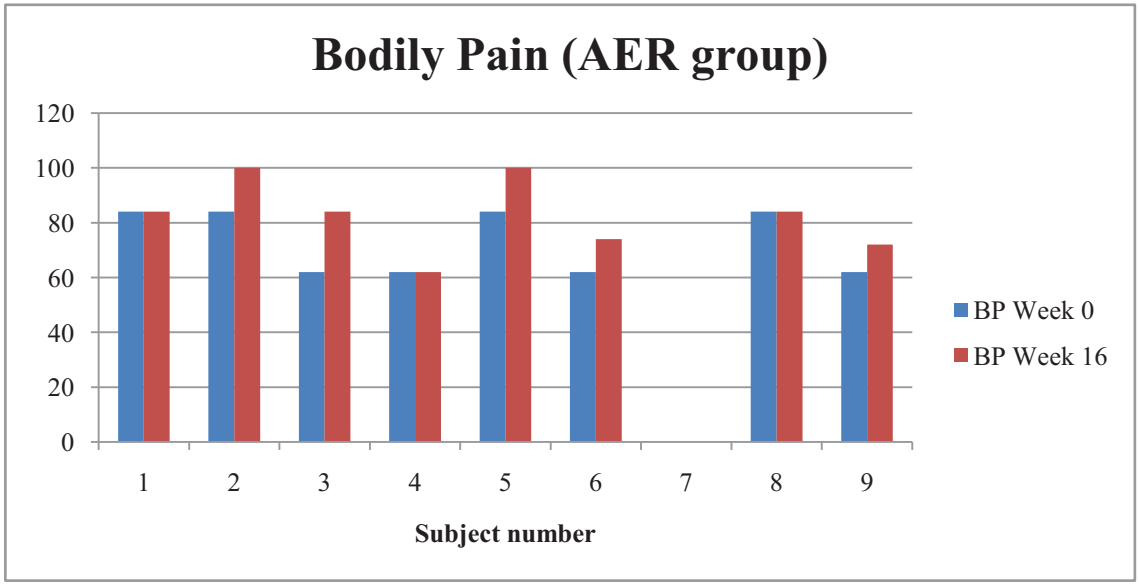

Capillary Density (PRT group)
1000
900
800
700
600
500
400
300
200
100
0
px/cm²
1
2
3
4
5
6
7
8
9
Subject number
Capillary Density Week 0
Capillary Density Week 16

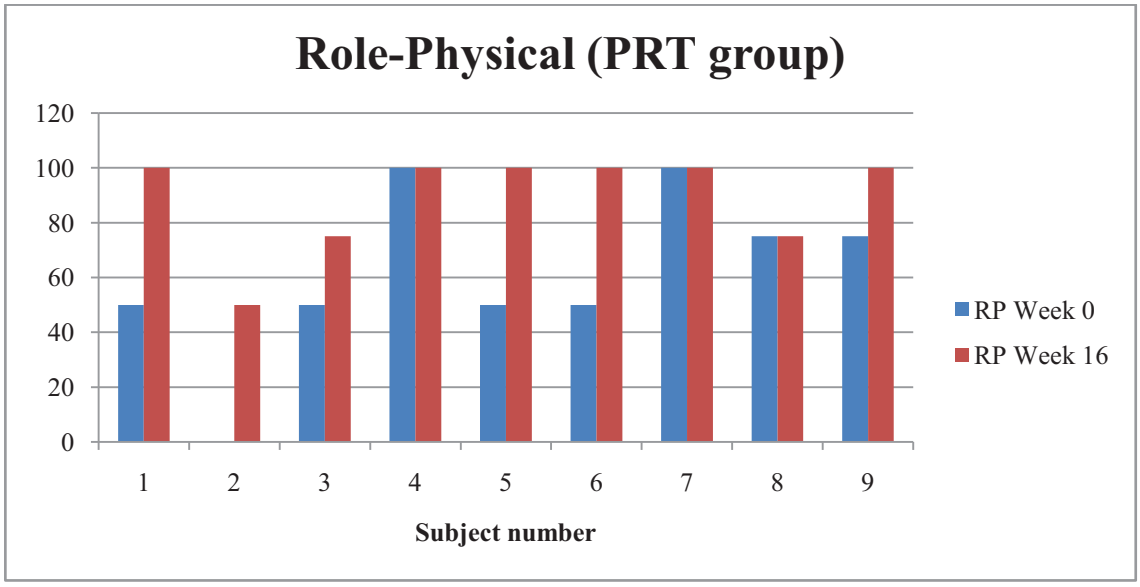

Capillary Density (AER group)
1000
900
800
700
600
500
400
300
200
100
0
px/cm²
1
2
3
4
5
6
7
8
9
Subject number
Capillary Density Week 0
Capillary Density Week 16

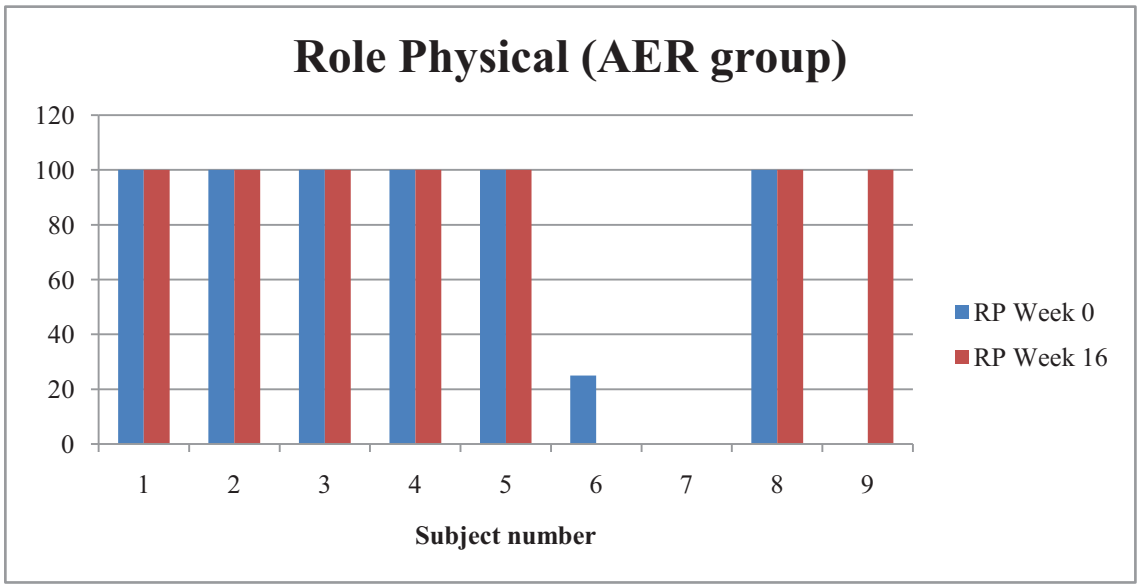

Physical Functioning (PRT group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
PF Week 0
PF Week 16

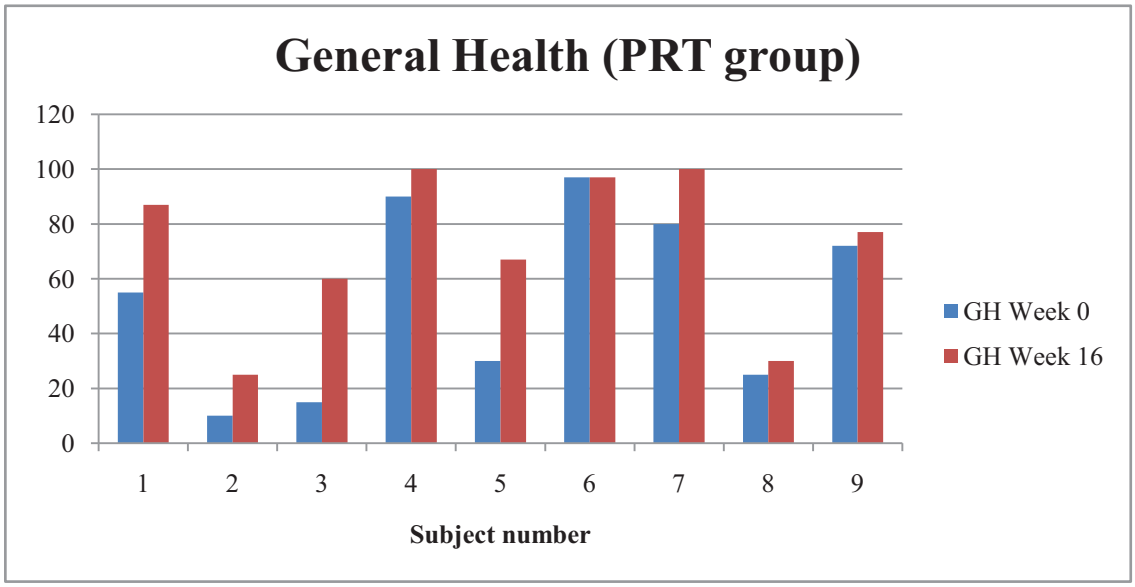

Physical Functioning (AER group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
PF Week 0
PF Week 16

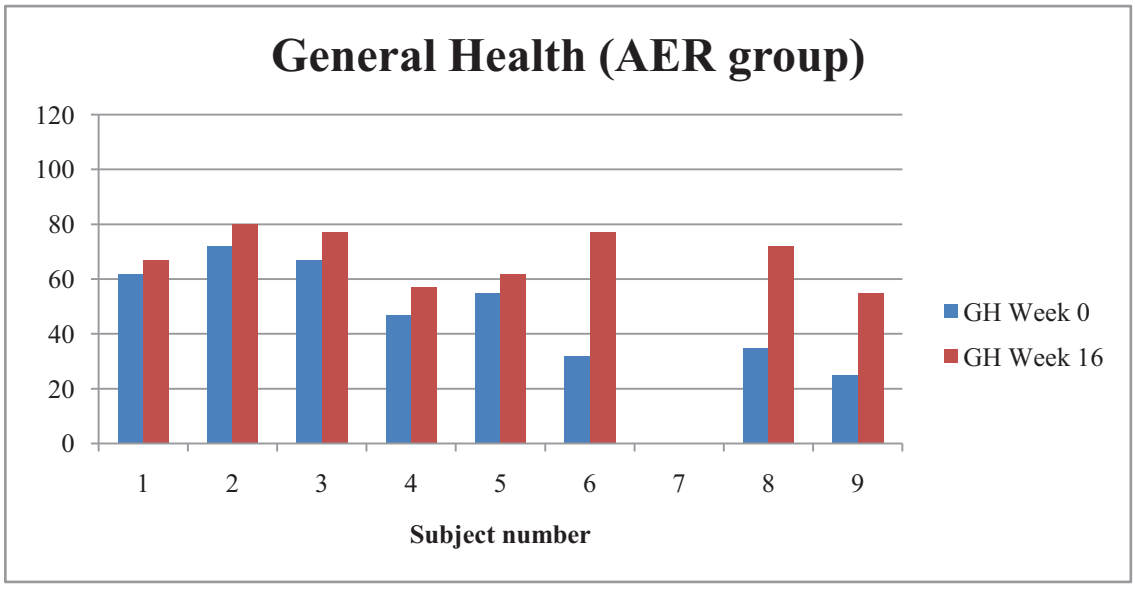

Bodily Pain (PRT group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
BP Week 0
BP Week 16

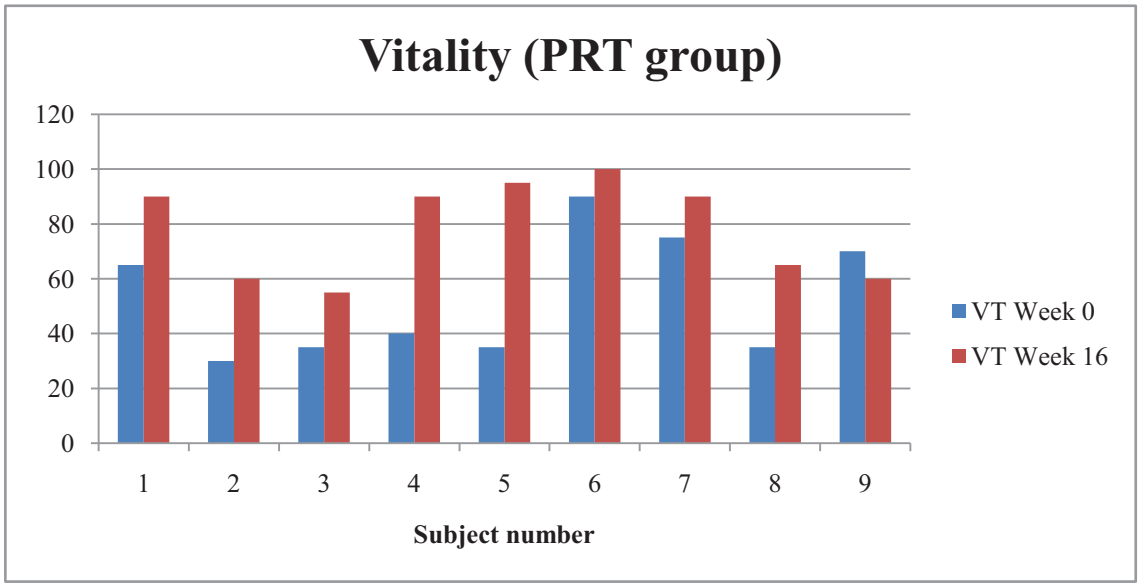

Bodily Pain (AER group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
BP Week 0
BP Week 16

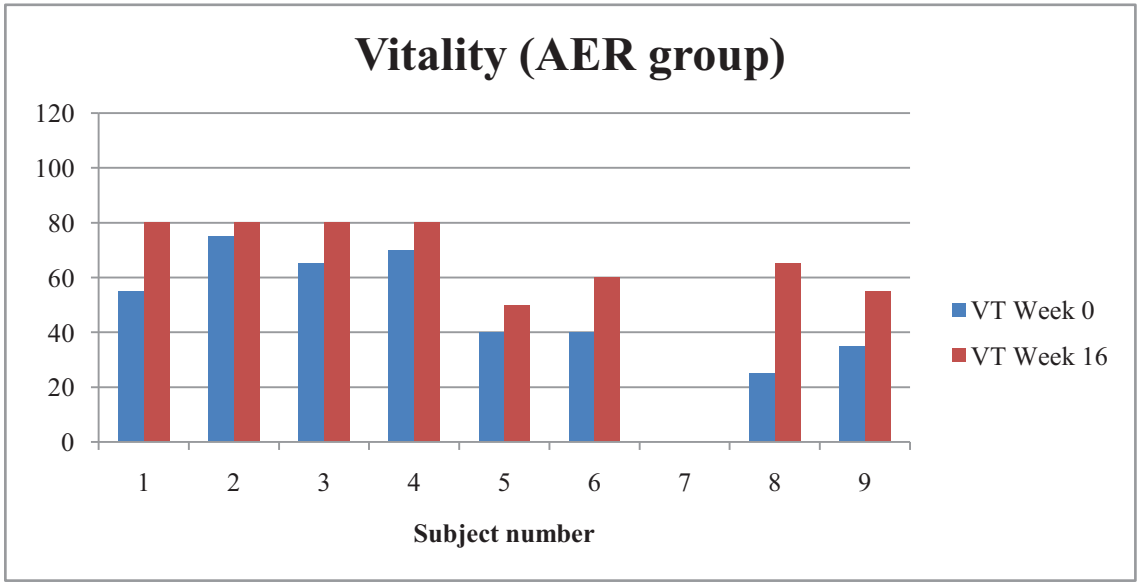

Role-Physical (PRT group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
RP Week 0
RP Week 16

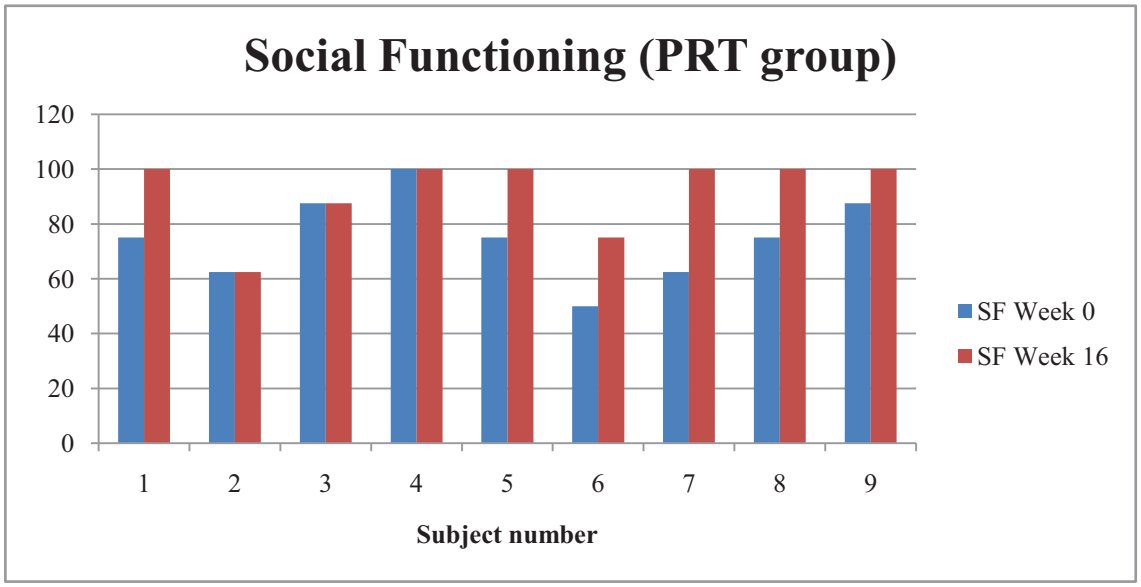

Role Physical (AER group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
RP Week 0
RP Week 16


General Health (PRT group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
GH Week 0
GH Week 16


General Health (AER group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
GH Week 0
GH Week 16


Vitality (PRT group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
VT Week 0
VT Week 16


Vitality (AER group)
120
100
80
60
40
20
0
1
2
3
4
5
6
7
8
9
Subject number
VT Week 0
VT Week 16


Social Functioning (PRT group)
120
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80
60
40
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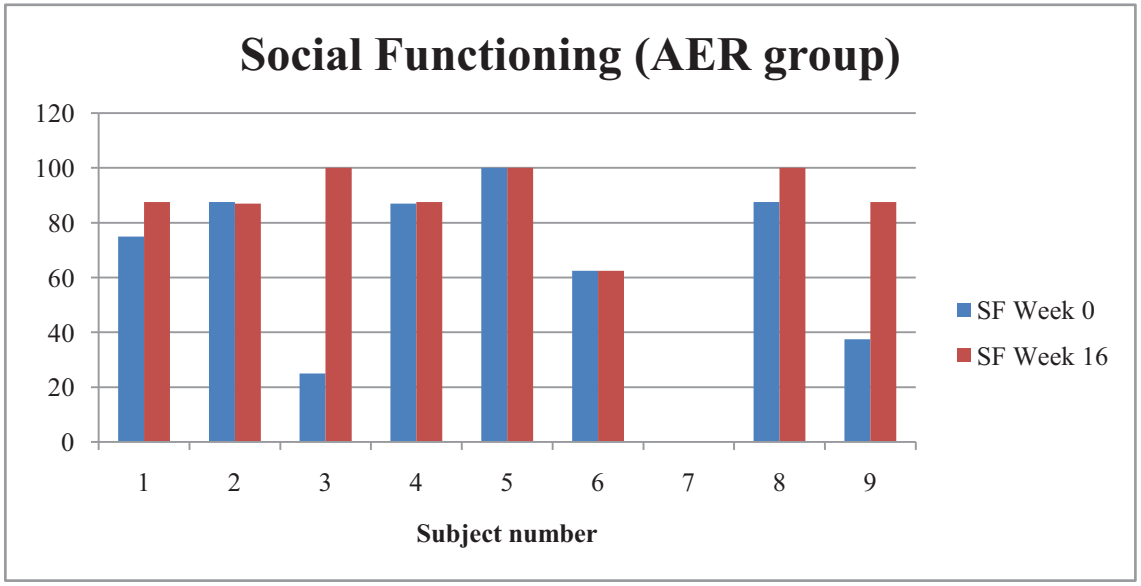
9
Subject number
SF Week 0
SF Week 16


Social Functioning (AER group)
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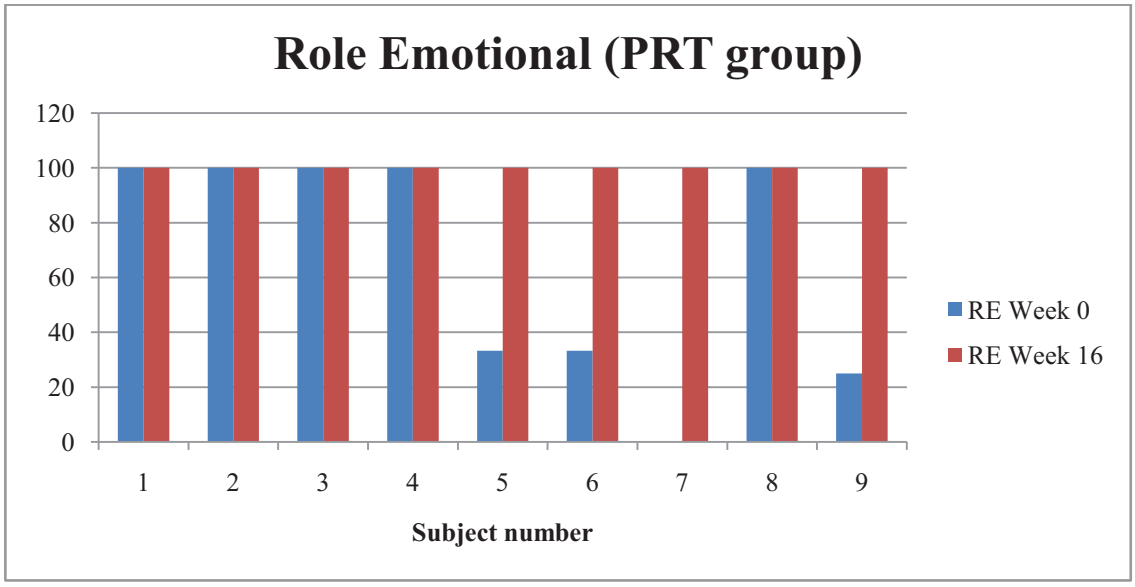
Subject number
SF Week 0
SF Week 16


Role Emotional (PRT group)
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20
0
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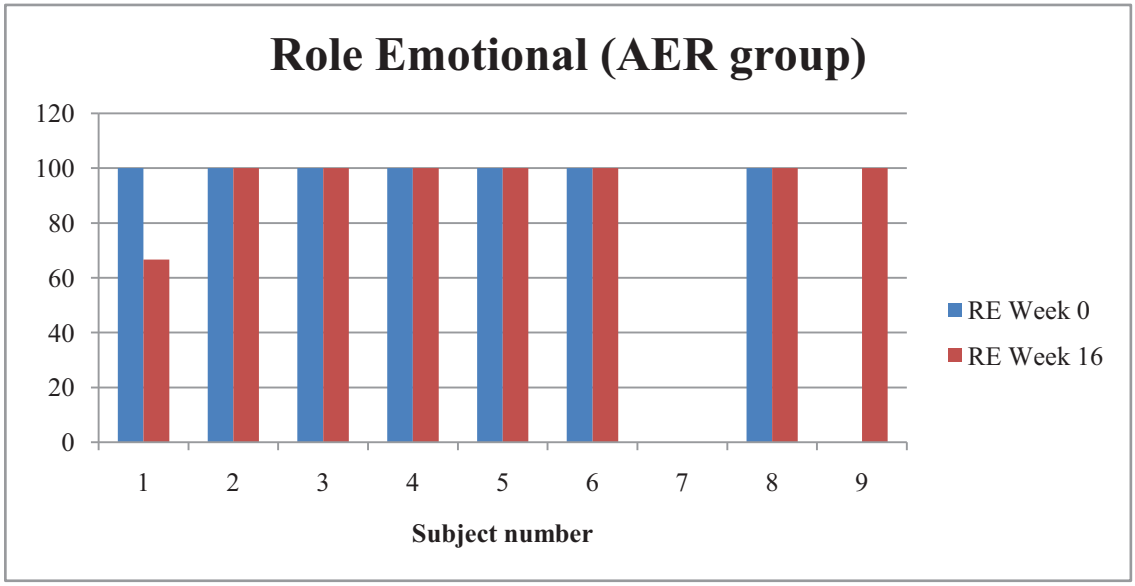
Subject number
RE Week 0
RE Week 16


Role Emotional (AER group)
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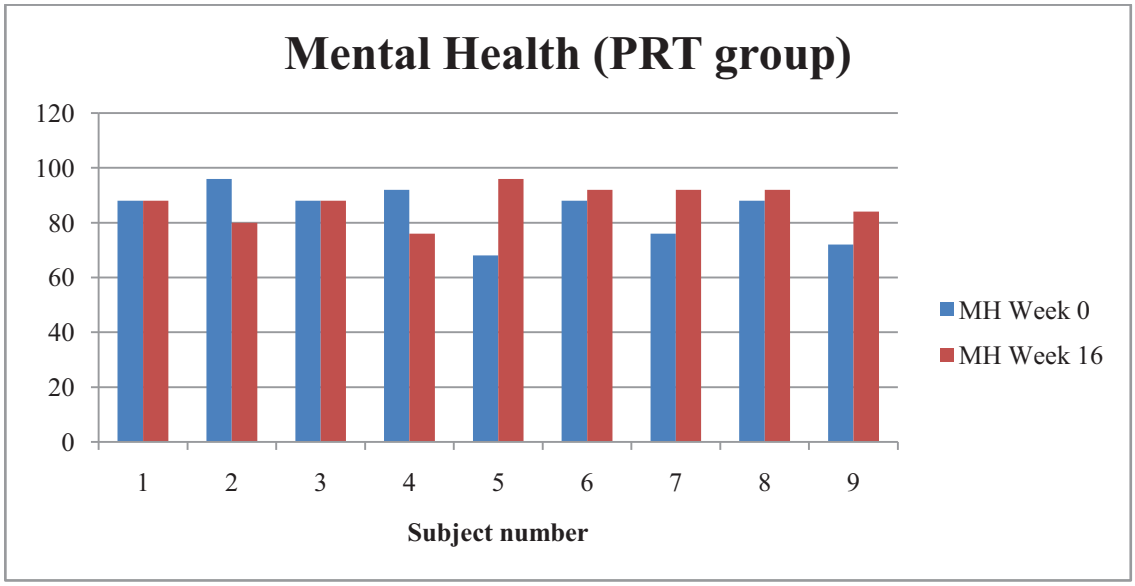
Subject number
RE Week 0
RE Week 16


Mental Health (PRT group)
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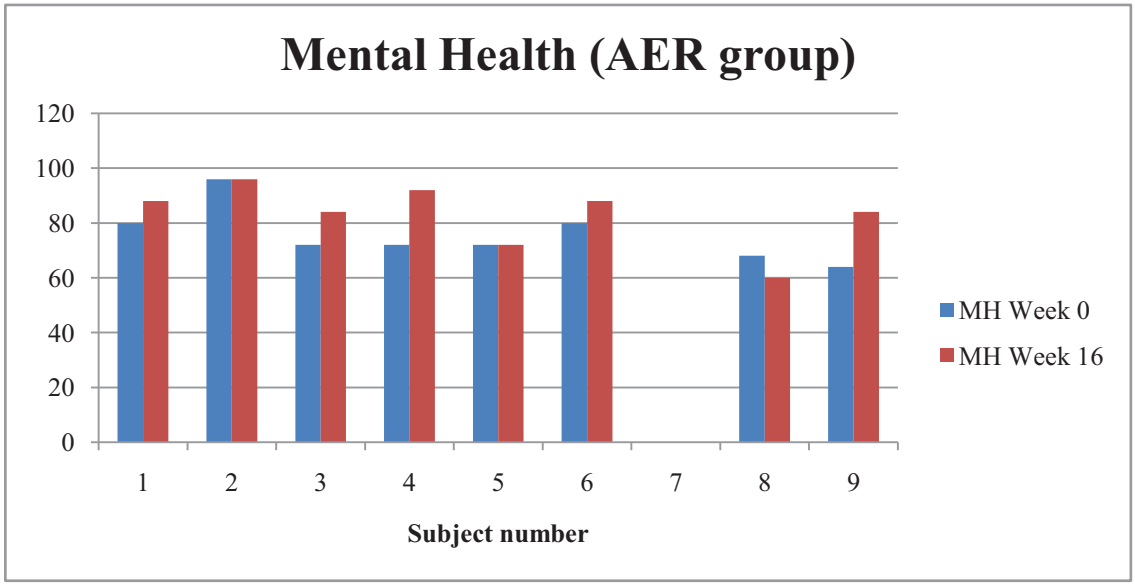
Subject number
MH Week 0
MH Week 16


Mental Health (AER group)
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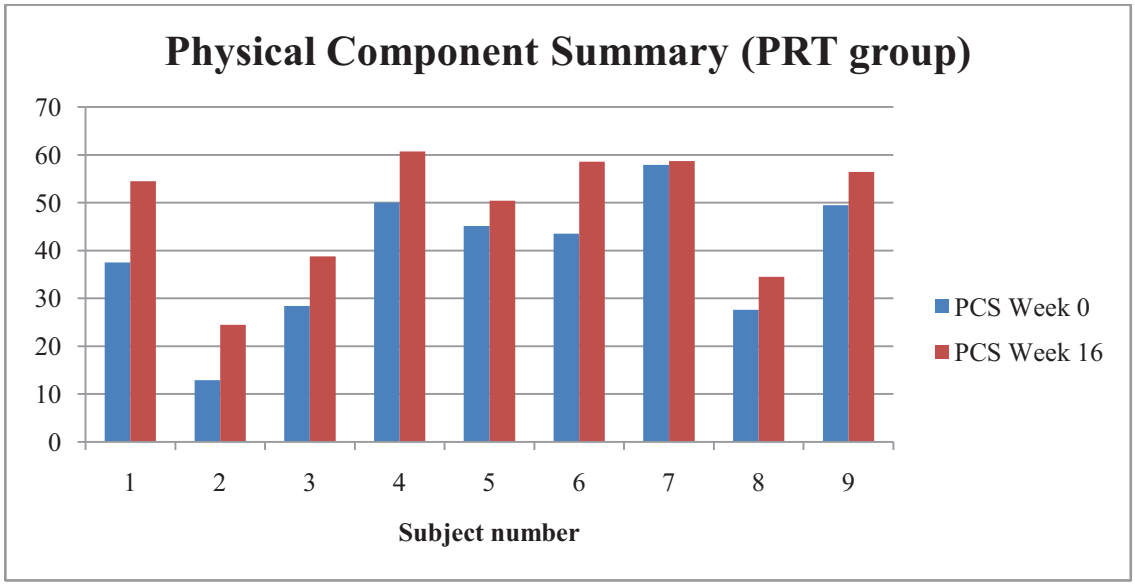
Subject number
MH Week 0
MH Week 16


Physical Component Summary (PRT group)
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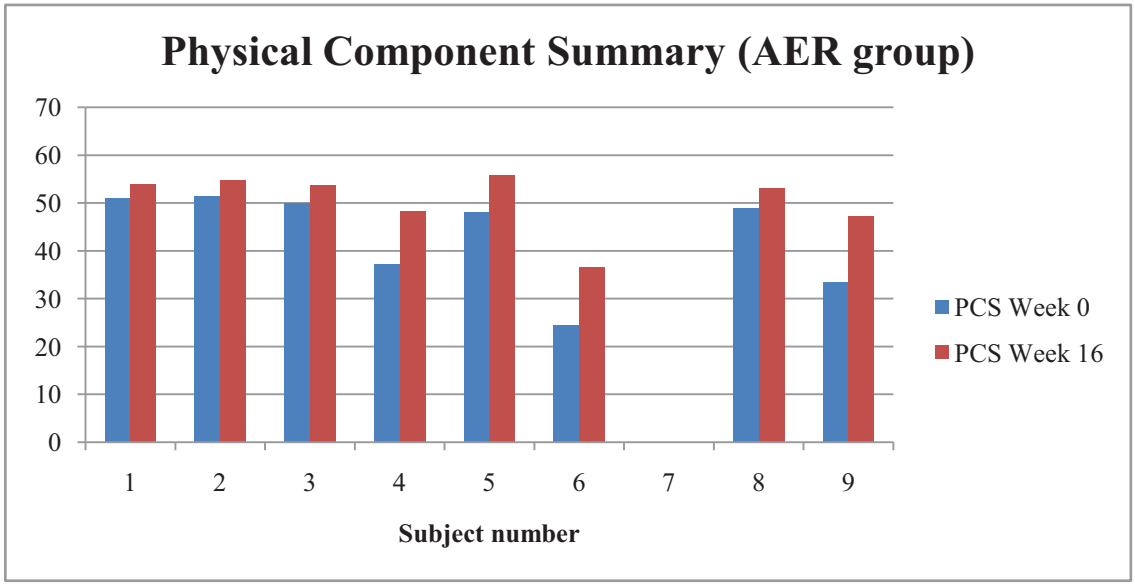
Subject number
PCS Week 0
PCS Week 16


Physical Component Summary (AER group)
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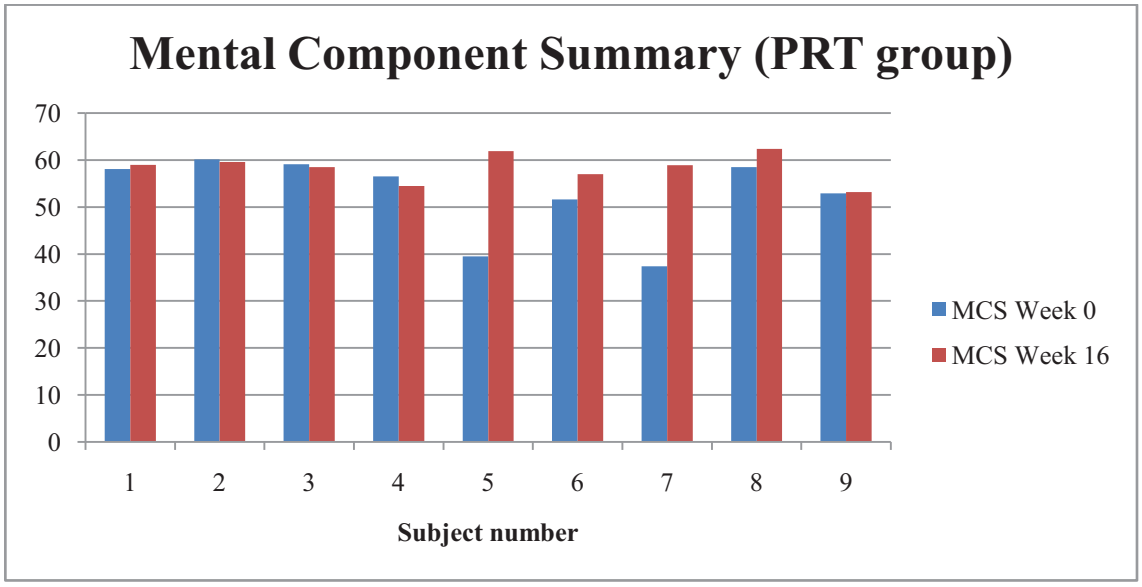
Subject number
PCS Week 0
PCS Week 16


Mental Component Summary (PRT group)
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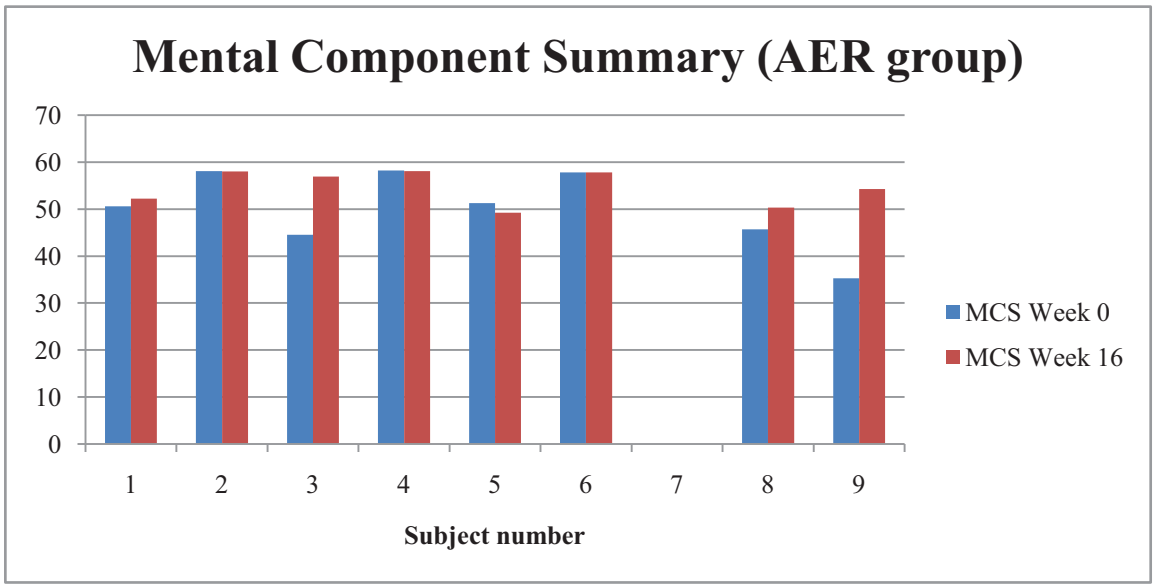
Subject number
MCS Week 0
MCS Week 16


Mental Component Summary (AER group)
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Subject number
MCS Week 0
MCS Week 16

APPENDIX F

Publications and Conference Presentations

Parts of the work presented in this thesis have been published and presented in the following forums:

PUBLISHED ABSTRACTS

Sukala W, Rowlands DS, Leikis ML, Hoong I, Page RA, Krebs, Cheema BS. (2009). Randomized trial of aerobic versus resistance training in Polynesian adults diagnosed with T2DM and visceral obesity: Metabolic outcomes. *Canadian Journal of Applied Physiology*, p. 98-9.

Sukala W, Rowlands DS, Leikis ML, Hoong I, Page RA, Krebs, Cheema BS. (2009). Can exercise improve metabolic outcomes in Polynesian with "diabesity". *Proceedings of the 33rd New Zealand Society for Study of Diabetes Annual Scientific Meeting*, p.28.

Sukala W, Rowlands DS, Leikis ML, Hoong I, Page RA, Krebs, Cheema BS. (2009). Exercise improves quality of life but not glycemic control in Polynesian adults diagnosed with type 2 diabetes and visceral obesity. *Proceedings of the 33rd New Zealand Society for Study of Diabetes Annual Scientific Meeting*, p.27.

I. Hayat, A. Hollings, R.A. Page, **W.R. Sukala**, B.S. Cheema, D.S. Rowlands, B. Breier, M. Leikis, J.D. Krebs, I. Lys. (2010). *Procedings of the 79th Scientific Meeting of the Wellington Health and Biomedical Research Society*, p.37.

Irum Hayat, Birinder S. Cheema, **William R. Sukala**, Rachel A. Page, David S. Rowlands, Bernhard Breier, Jeremy D. Krebs, Isabelle Hoong. (2009). Exercise training in Polynesians with type 2 diabetes and visceral obesity: Effects on specific obesity markers. Proceedings of the New Zealand Postgraduate Conference, p. S13.

CONFERENCE PRESENTATIONS—ORAL

William R. Sukala, David S. Rowlands, Murray J. Leikis, Isabelle Hoong, Rachel A. Page, Jeremy D. Krebs, and Birinder S. Cheema. Outcomes of the South Pacific Islands Resist Diabetes with Intense Training Study. *Capital and Coast District Health Board (In-service education for clinical staff).* 22 September 2010.

William R. Sukala, David S. Rowlands, Murray J. Leikis, Isabelle Hoong, Rachel A. Page, Jeremy D. Krebs, and Birinder S. Cheema. Can exercise improve metabolic outcomes in Polynesians with "diabesity?" A randomised trial. *New Zealand Society for the Study of Diabetes 33rd Annual Scientific Meeting.* 30 June – 3 July 2009.

William R. Sukala, David S. Rowlands, Murray J. Leikis, Isabelle Hoong, Rachel A. Page, Jeremy D. Krebs, and Birinder S. Cheema. Exercise improves quality of life but not glycemic control in Polynesian adults diagnosed with type 2 diabetes and visceral obesity. *New Zealand Society for the Study of Diabetes 33rd Annual Scientific Meeting.* 30 June – 3 July 2009.

W.R. Sukala, D.S. Rowlands, M.J. Leikis, I. Hoong, R.A. Page, J.D. Krebs, and B. Cheema. Randomised trial of aerobic versus resistance training in Polynesian adults diagnosed with T2DM and visceral obesity: Metabolic outcomes. *Canadian Society for Exercise Physiology Annual General Meeting*. 11–14 November 2009.

William R. Sukala. South Pacific Islands Resist Diabetes with Intense Training Study. *New Zealand Society for the Study of Diabetes Wellington Forum Meeting.* Lower Hutt, New Zealand. 29 November 2007.

I. Hayat, B.S. Cheema, **W.R. Sukala**, R.A. Page, D.S. Rowlands, B. Breier, J.D.Krebs, I. Lys. Exercise training in a Polynesian group with type 2 diabetes and visceral obesity in New Zealand: Effects on specific obesity markers. *Australian Diabetes Society and Australian Diabetes Educators Association Annual Scientific Meeting.* 1–3 September 2010.

Irum Hayat, Birinder S. Cheema, **William R. Sukala**, Rachel A. Page, David S. Rowlands, Bernhard Breier, Jeremy D. Krebs, Isabelle Hoong. Exercise training in Polynesians with type 2 diabetes and visceral obesity: Effects on specific obesity markers. *New Zealand Postgraduate Conference*. 20-21 November 2009.

CONFERENCE POSTER PRESENTATION

Irum Hayat, Andy Hollings, Rachel A. Page, **William, R. Sukala**, Birinder S. Cheema, David S. Rowlands, Bernhard Breier, Murray Leikis, Jeremy D. Krebs, and Isabelle Lys. Impact of 16 weeks progressive resistance training on mitochondrial activity and fat metabolism in skeletal muscle tissue of SPIRIT study cohor*t. Wellington Health and Biomedical Research Society Meeting.* 23 August 2010.