Physical Activity and Exercise in people with Type 2 Diabetes and Peripheral Neuropathy

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List of Abbreviations

ABS	Australian Bureau of Statistics
ACSM	American College of Sports Medicine
ADA	American Diabetes Association
ADDQOL	Audit of Diabetes Dependent Quality of Life
ADL	Activities of Daily Living
AHA	American Heart Association
AIHW	Australian Institute of Health and Welfare
AusDiab	Australian Diabetes and Obesity Lifestyle Study
BPS	Biopsychosocial
BRFSS	Behavioural Risk Factor Surveillance Survey
CTCAE	Common Terminology Criteria for Adverse Events
DFS-SF	Diabetic Foot Ulcer Scale
D-QoL	Diabetes Quality of Life
ESSA	Exercise and Sports Science Australia
HADS	Hospital Anxiety and Depression Scale
HbA1c	Glycated Haemoglobin
HDL	High Density Lipoprotein
HRR	Heart Rate Reserve
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance

IPAQ	International Physical Activity Questionnaire
IWGDF	International Working Group for the Diabetic Foot
LTPA	Leisure Time Physical Activity
METs	Metabolic Equivalents
MFI-20	Multidimensional Fatigue Inventory
MNSI	Michigan Neuropathy Screening Instrument
NAPA	Nerve Action Potential Amplitude
NCV	Nerve Conduction Velocity
NDS	Neuropathy Disability Score
NDSS	National Diabetes Service Scheme
NeuroQol	Neuropathy Specific Quality of Life
NHP	Nottingham Health Profile
NHS	National Health Survey
NIS	Neuropathy Impairment Score
NSP	Neuropathy Symptom Profile
NSS	Neuropathy Symptom Score
PAID	Problem Areas in Diabetes
PN	Peripheral Neuropathy
PPT	Physical Performance Test
QoL-DN	Quality of Life in Diabetes Neuropathy
QOLI	Quality Of Life Inventory

QST	Quantitative Sensory Tests
RPE	Rate of Perceived Exertion
SCED	Single Case Experimental Design
SF-12	Short Form-12
SF-36	Short Form-36
TUGT	Timed Up and Go Test
UniSA	University of South Australia
VPT	Vibration Perception Threshold
WHO	World Health Organization
WHOQOL	World Health Organization Quality of Life

Executive Summary

People with Type 2 diabetes and peripheral neuropathy have a decreased quality of life and greater functional deficits than those with Type 2 diabetes alone. Despite physical activity and exercise being reported as beneficial in the management of people with Type 2 diabetes, there is limited literature investigating the role of physical activity and exercise in people with Type 2 diabetes and peripheral neuropathy. With the loss of sensation and increased risk of ulceration in the feet of people with peripheral neuropathy, further investigation into the safety of physical activity and exercise is indicated. In this thesis, a biopsychosocial model was used across three studies to investigate the role of physical activity and exercise in people with Type 2 diabetes and peripheral neuropathy.

The first study investigated self-reported physical activity in a sample of people with Type 2 diabetes (n = 481) and Type 2 diabetes and peripheral neuropathy (n = 55) using the International Physical Activity Questionnaire. The results indicated that people with Type 2 diabetes and peripheral neuropathy were significantly less active than those with Type 2 diabetes alone ($p = 0.04$). Despite the results indicating that people with Type 2 diabetes and peripheral neuropathy were engaging in the recommended 150 minutes of physical activity per week, according to the American College of Sports Medicine (ACSM) (2010) (*Mdn* = 480, *IQR* = 210-1080 minutes/week), it was not necessarily at a moderate intensity, and therefore only 49% met physical activity recommendations. The findings of this study suggest greater attention to the intensity of physical activity is required.

In keeping with the biopsychosocial model, it was important to gain an understanding of how Type 2 diabetes and peripheral neuropathy impacts quality of life, and also how physical activity participation impacts quality of life. The second study assessed the quality of life in people with Type 2 diabetes and peripheral neuropathy (n=77) using a neuropathic specific quality of life questionnaire (NeuroQol), and its relationship with self-reported physical activity. People with Type 2 diabetes and peripheral neuropathy who met physical activity recommendations (ACSM, 2010), had a significantly better quality of life compared to those who did not meet physical activity recommendations. This is an important result that helps communicate the value of exercise in people with Type 2 diabetes and peripheral neuropathy.

The third study used a single case experimental design (n=8) to assess the effects of a 12-week combined aerobic and resistance exercise program on safety, quality of life, sensation and function. The results indicated that a prescribed exercise intervention was safe and did not cause any adverse reactions in any participants. In the majority of participants, outcomes measures of quality of life, sensation and function either remained stable or improved. These preliminary findings show a prescribed exercise program should not be contra-indicated for people with Type 2 diabetes and peripheral neuropathy.

This research highlighted a high proportion of people with Type 2 diabetes and peripheral neuropathy did not meet current physical activity recommendations, despite finding a positive relationship between physical activity and improved quality of life in this population. The results of the final study in this thesis supports the use of a prescribed and supervised exercise program to help mediate the negative effects of Type 2 diabetes and peripheral neuropathy, through biological, psychological and social constructs. This thesis helps to build the body of knowledge that physical activity and exercise can be done safely in people with Type 2 diabetes and peripheral neuropathy. Large scale trials are indicated to further test this conclusion.

Declaration

I declare that:

This thesis presents work carried out by myself and does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; to the best of my knowledge it does not contain any materials previously published or written by another person except where due reference is made in the text; and all substantive contributions by others to the work presented, including jointly authored publications, is clearly acknowledged.

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CHAPTER 1: Introduction

Introduction

This chapter introduces the key concepts within this thesis including Type 2 diabetes, peripheral neuropathy, physical activity and exercise. The aim of the chapter is to provide definitions and information relevant to help set the scene and rationale for the three studies undertaken as a part of this thesis.

There are various types of diabetes including Type 1, Type 2 and gestational diabetes. Whilst many researchers refer to those with 'diabetes' encompassing all forms of diabetes, Type 2 diabetes is estimated to represent 90% of those with 'diabetes' (AIHW, 2010). Throughout this thesis reference is made to those with 'diabetes' (may include Type 1, Type 2 and gestational diabetes) and those with 'Type 2 diabetes' with the latter being the focus of this research.

Type 2 Diabetes

Definitions of Type 2 diabetes

Diabetes is characterised by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism. The disturbed metabolism is a result of either defects in insulin secretion, insulin resistance, or both (Shaw and Tanamas, 2012). Symptoms of diabetes include thirst, polyuria, blurring of vision and weight loss, however, these symptoms are often not severe enough to warrant attention and subsequently, hyperglycemia sufficient enough to cause pathological harm, may be present long before a diagnosis of diabetes is made (WHO, 1999, ADA, 2010). Type 2 diabetes is the most common form of diabetes and is characterised by a defect in insulin secretion and resistance (WHO, 1999, Nolan et al., 2011).

Traditionally, diabetes has been diagnosed through fasting venous plasma glucose concentrations, (WHO, 2006a). Recently however, the World Health Organization (WHO) (2011) have recommended that diabetes may also be diagnosed using a HbA1c (glycosylated haemoglobin) test. The targets for effective blood glucose control is a HbA1c of less than 7.0% (WHO, 2006a).

The onset of Type 2 diabetes is influenced by both genetic and lifestyle factors, such as physical inactivity and obesity (Giorgino et al., 2005, Jenkins and Campbell, 2004, LeRoith, 2002, Stumvoll et al., 2005, Shaw and Tanamas, 2012). Risk factors for developing Type 2 diabetes include, among others, impaired glucose regulation, physical inactivity, being overweight, high blood pressure, high blood cholesterol and high triglyceride levels (AIHW, 2008, Stumvoll et al., 2005).

Prevalence of diabetes and Type 2 diabetes

It has been reported that there are currently over 1.5 million Australians with diabetes including those who are undiagnosed (Shaw and Tanamas, 2012). Magliano et al. (2009) have suggested that unless current trends in diabetes incidence are reversed, there will be at least two million Australian adults with diabetes by 2025, which may increase to three million if current diabetes, obesity and mortality trends continue. As Type 2 diabetes often has no definitive beginning, it has been considered difficult to accurately estimate the prevalence each year (AIHW, 2010).

There are several sources of diabetes prevalence data in Australia including the National Health Surveys (NHS) conducted by the Australian Bureau of Statistics (ABS), the National Diabetes Service Scheme (NDSS), the Medicare Benefits Scheme and the Pharmaceutical Benefits Scheme (AIHW, 2009). Most recently, the Australian Institute of Health and Welfare (AIHW) (2010) and the ABS (2009) used data from the NDSS and the NHS to estimate that 812, 200 Australians were diagnosed with diabetes in 2007-08, a prevalence of 4%. This prevalence had increased from a reported 3.6% in 2004-05. However, it is suggested that there are a large number of people with undiagnosed diabetes (Zimmet, 2003).

The onset of Type 2 diabetes is often asymptomatic and therefore, can be undiagnosed for many years making it difficult to accurately estimate prevalence. Dunstan et al. (2002b) provided an example of undiagnosed diabetes incidence whereby, through the use of fasting blood tests, found 50% of those with Type 2 diabetes were undiagnosed. This is supported by the AIHW (2008) who used national data to suggest that there is one undiagnosed case of diabetes for every diagnosed case. Furthermore Valentine et al. (2011) used Australian hospital admission data to report that for every five diagnosed cases of diabetes, there were approximately four undiagnosed cases.

Management of Type 2 diabetes

Type 2 diabetes is managed in three primary ways combining immediate and long-term treatment priorities, and using medical and non-medical approaches. The first and most immediate management priority is to stabilise blood glucose levels. This sometimes is achieved through diet and lifestyle changes, but often requires the use of glucose lowering medication (AIHW, 2008, WHO, 2006a). The therapy targets for effective blood glucose control is a HbA1c of less than 7.0%, with a marker greater than 8.0% requiring attention (WHO, 2006a). The second management priority is to prevent, if possible, any long term microvascular (i.e. peripheral neuropathy) and macrovascular (i.e. peripheral vascular disease) complications, and to treat any complications if and when they arise (AIHW, 2006, AIHW, 2008, AIHW, 2010, WHO, 2006a). The maintenance of normal blood glucose levels along with the early detection of sensory, circulatory and neurological changes is important and requires frequent and regular screening. The third priority of treatment is to maintain quality of life through a healthy lifestyle and support for the self-management of diabetes. This can be a demanding task due to the attention and monitoring required by the patient and other health professionals, however management plans aimed at supporting glucose control, such as prescribed exercise, self-monitoring and early detection of complications aid in the treatment of diabetes (AIHW, 2006, WHO, 2006a).

Complications of Type 2 diabetes – Peripheral Neuropathy

Diabetic neuropathy

Diabetic neuropathy is a descriptive term which includes a range of clinical and sub-clinical syndromes with differing anatomical locations, clinical progressions and possible differing underlying pathogenic mechanisms often dependent on the nerve fibres involved (Edwards et al., 2008, Vinik et al., 2000). It is widely regarded that the presence of Type 2 diabetes increases the risk of associated microvascular and macrovascular complications which may affect various systems involving the heart, eyes, kidneys and feet (Shaw and Tanamas, 2012). Diabetic neuropathy can exist in three main categories being sensory, such as the inability to feel pressure or pain, motor which is characterised by a loss of strength and inability to control movement, and autonomic which is the ability to control heart rate or digestion (Donnan and Ledger, 2006). Diabetic neuropathy can affect all categories and hence nearly every type of nerve fibre is at risk

of being damaged (Duby et al., 2004). The type of diabetic neuropathy which is the focus of this thesis is diabetic peripheral neuropathy which occurs within the peripheral nervous system (WHO, 2006a). From this point forward 'diabetic peripheral neuropathy' will be referred to as simply, 'peripheral neuropathy.'

Peripheral neuropathy

Peripheral neuropathy may affect sensory nerves which carry information to the central nervous system about sensations and motor nerves which carry signals to the muscles allowing movement (AIHW, 2008). Symmetrical polyneuropathy is the most common type of peripheral neuropathy accounting for 75% of those diagnosed with peripheral neuropathy (Bansal et al., 2006, Hughes, 1995, Vinik and Mehrabyan, 2004, WHO, 2006a). Symmetrical polyneuropathy typically affects the most distal extremities, targeting the nerves with the longest axons, in a symmetrical pattern described as a glove (hands and arms) and stocking (toes, feet and legs) distribution (Baloh, 2008, Chun-Liang et al., 2001, Donnan and Ledger, 2006, Duby et al., 2004, Edwards et al., 2008). Symptoms of peripheral neuropathy may include pain which is often described as burning, deep aching, constricting and throbbing along with non-painful symptoms such as numbness, tingling, extreme sensitivity, or feelings of deadness within the lower limb (AIHW, 2008, Boulton, 2005, Boulton et al., 2005b, Donnan and Ledger, 2006, Head, 2006, Petit and Upender, 2003). The presence of pain and sensory changes in the feet has obvious effects on the comfort, motivation and ability to engage in physical activity that involves the lower body.

Pathogenesis of peripheral neuropathy – the role of hyperglycemia

Prolonged hyperglycemia, with the associated changes in metabolism of the nerve cells, has been associated with the development of peripheral neuropathy (Cole, 2007, Donnan and Ledger, 2006, Head, 2006). Hyperglycemia results in elevated glucose levels that drive secondary pathologies such as increased activation of the polyol pathway and the accumulation of sorbitol and fructose in the nerve tissue, oxidative stress, and the formation of advanced glycation end products (Dejgaard, 1998, Duby et al., 2004, Head, 2006, Petit and Upender, 2003, Vinik, 1999, WHO, 2006a). The severity and duration of hyperglycemia affects the severity of peripheral neuropathy, with longer and more severe hyperglycemia resulting in more severe symptoms of

peripheral neuropathy (Cole, 2007). It is reported that peripheral neuropathy is progressive and irreversible, and as such much research has investigated reducing or delaying the onset of peripheral neuropathy by intensive glycemic control (Dejgaard, 1998, Donnan and Ledger, 2006, Duby et al., 2004, Leonard et al., 2004). One of the interventions known to have beneficial effects on glycemic control in people with Type 2 diabetes is physical activity and in particular prescribed exercise. This positive effect of exercise provides the rationale for this thesis which investigates the physical activity levels in people with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy.

The impact and management of peripheral neuropathy

Long standing or poorly managed peripheral neuropathy can lead to ulceration and non-traumatic amputation of the feet or legs, functional impairment of mobility, and a decreased quality of life (Bansal et al., 2006, Duby et al., 2004, Vinik and Mehrabyan, 2004, Eberhardt et al., 2006). The sensory loss associated with peripheral neuropathy leaves patients vulnerable to foot ulceration, the main precursor to amputation (Bansal et al., 2006, Duby et al., 2004, Vinik and Mehrabyan, 2004). It has been suggested that the lifetime risk of ulceration in those with diabetes is 15% (Reiber, 1996). Ulceration is caused by repetitive and excessive or prolonged pressure to the insensitive skin on the plantar surface of the foot which leads to tissue damage (van Schie, 2005). The prevention of ulcers is important given the high recurrence rate and the subsequent risk of amputation (Kastenbauer et al., 2001, Mantey et al., 1999, van Schie, 2005). Diabetes is estimated to account for approximately half of all non-traumatic amputations in Australia (AIHW, 2008) with the risk of amputation increased 15 fold for those individuals with diabetes compared to those without (Payne, 2000).

Studies have shown that those with diabetes were more likely to have impairment of mobility and function than those without diabetes, through a loss of strength and range of motion in the lower limbs (Andreassen et al., 2006, Eberhardt et al., 2006). A 40% increase in impairment of mobility in activities such as walking and climbing stairs have been reported (Bruce et al., 2005, Eberhardt et al., 2006). The disruption of the sensory nerves and subsequent loss of sensation in the feet associated with peripheral neuropathy has also been associated with limitations of function such as balance (De Rekeneire et al., 2003, Resnick et al., 2000, Ryerson et al., 2003, Sinclair et al., 2008).

It is well established that Type 2 diabetes may negatively influence the physical, social and psychological well-being of individuals (Sundaram et al., 2009). It addition it has been found that quality of life is further diminished in those with Type 2 diabetes and peripheral neuropathy (Chyun et al., 2006, Currie et al., 2006, Olaleye et al., 2001, Vileikyte et al., 2005, Lloyd et al., 2001, Mold et al., 2004, Ovayolu et al., 2008). This decrease in quality of life may be due to the loss of sensation in the extremities, painful or disruptive symptoms such as restless legs, and difficulties with functional tasks which impact on the ability to perform activities of daily living independently (Mold et al., 2004).

The World Health Organization (2006a) states that the aim of treatment for people with diabetes and peripheral neuropathy is to try and halt disease progression, minimise deterioration, and in the severe stage of peripheral neuropathy, overcome any disability and reduction of function, whilst preventing further deterioration and ulceration. Given the relationship between hyperglycemia in those with Type 2 diabetes and the incidence of peripheral neuropathy, glycemic control remains the most important step in treating those with peripheral neuropathy (Edwards et al., 2008). Preventative foot care is also critical in the management of people with peripheral neuropathy to reduce the risk of lower limb ulceration and subsequent amputation (Edwards et al., 2008, Vinik et al., 2000, Dellon, 2007).

Physical Activity and Exercise

Physical activity versus exercise

Although the terms physical activity and exercise are often used interchangeably and contain common themes, it is important to note that they are different concepts. Physical activity has been defined as any bodily movement produced by skeletal muscles that results in energy expenditure and may include work, leisure, and household activities (Caspersen et al., 1985). Exercise is considered a sub-category of physical activity and has been defined as physical activity which is planned, structured and repetitive done to improve or maintain one or more components of physical fitness (Caspersen et al., 1985). The American College of Sports Medicine (ACSM, 2010) has identified people with Type 2 diabetes and peripheral neuropathy as high risk in relation to the prescription of and participation in physical activity and exercise. This is due to the increased risk of cardiovascular and hypoglycemic events, the increased risk of

injury and ulceration of the feet, and the subsequent potential for amputation. Accordingly, exercise should be carefully prescribed to those with Type 2 diabetes, but especially in those with the complication of peripheral neuropathy.

The role of physical activity and exercise in the management of peripheral neuropathy

Physical activity and exercise is a well-established treatment option for people with Type 2 diabetes, but is less well established for those with Type 2 diabetes and peripheral neuropathy. Physical activity and exercise provide a beneficial effect on blood glucose levels due to the effects on carbohydrate metabolism and insulin sensitivity (ADA, 2003a, WHO, 2006, Warren, 2010). However, it has been suggested that these favourable changes deteriorate within 72 hours of an exercise session. Therefore, regular physical activity and exercise is indicated to sustain the glucose-lowering effects and increased insulin sensitivity (ACSM, 2000a). Accordingly, the American Diabetes Association (ADA) has recommended that physical activity should be performed on a regular basis, with no more than two consecutive days without exercise (Sigal et al., 2006).

Other biological benefits of regular physical activity and exercise for all people, and those with Type 2 diabetes and peripheral neuropathy includes improved cardiovascular fitness, cholesterol levels, blood pressure and circulation (ACSM, 2000a, Dunstan and Daly, 2007, WHO, 2006, Warren, 2010). It has been reported that regular physical activity and exercise also results in psychosocial benefits and an improved quality of life, a common problem in those with Type 2 diabetes and peripheral neuropathy (ACSM, 2010). Bize et al. (2007) found positive associations between increased levels of physical activity and increased quality of life in the general adult population. However, it is unclear if this same association applies to those with Type 2 diabetes and peripheral neuropathy as no literature could be found reporting this association.

In a report by the Australian Institute of Health and Welfare (2008) two out of three people with diabetes surveyed during 2004 to 2005 reported insufficient physical activity (less than 150min/week of at least moderate physical activity). Warren (2010) found similarly, that many people with diabetes reported not doing regular physical activity. Despite the clear benefits of physical activity and exercise in the management of people with Type 2 diabetes, the motivation to commence and sustain exercise and physical activity remains a challenge (Dunstan and Daly, 2007). More recently attention has been drawn to the benefits of physical activity and exercise in those with Type 2 diabetes and peripheral neuropathy (Kluding et al., 2012, Otterman et al., 2011). Despite this increase in attention, there remains a lack of information on whether prescribed exercise is safe and beneficial for people with Type 2 diabetes and peripheral neuropathy.

In order to reduce the risk of foot or limb injury, it has been suggested that people with severe peripheral neuropathy should avoid weight-bearing and high-impact activities (Dunstan and Daly, 2007). Whilst there have been few studies investigating the effect of weight bearing exercise in people with Type 2 diabetes and peripheral neuropathy, more recently a study by Le Master et al. (2008) found that moderate walking did not increase the risk of foot ulceration or re-ulceration. Therefore, weight bearing exercise may be appropriate depending on the severity of the peripheral neuropathy. None the less, it is widely accepted that individuals with peripheral neuropathy undertaking an exercise program must regularly check their feet for the early detection and prevention of sores and ulcers should they arise (Dunstan and Daly, 2007, ACSM/ADA, 2010). Whilst the Le Master et al. (2008) study is promising, there remains a lack of information on the safety of using a prescribed exercise program in people with Type 2 diabetes and peripheral neuropathy.

Focus of this Thesis

So far, it has been established that physical activity is important in the management of Type 2 diabetes, with and without peripheral neuropathy. Currently there is minimal evidence supporting any link between physical activity and quality of life, as well as the level of physical activity in those with Type 2 diabetes and peripheral neuropathy. Therefore, it is of interest to investigate the role of physical activity in people with Type 2 diabetes and peripheral neuropathy, and whether exercise is safe and beneficial.

Therefore, the three aims of this research are to investigate the role of self-reported physical activity in people with Type 2 diabetes with and without peripheral neuropathy, the quality of life and physical activity levels in those with peripheral neuropathy and the safety and impact of a prescribed exercise program on function in those with peripheral neuropathy.

Structure of thesis

The structure of this thesis is such that these three aims will be addressed as separate studies in Chapters 4, 5 and 6. Included within each study chapter are the methods, results, and a discussion designed to answer the specific research questions. The primary research themes are outlined below.

Study 1 – Chapter 4

- Investigate the self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy and determine whether or not they are meeting current physical activity recommendations.

Study 2 – Chapter 5

- Explore the quality of life in people with Type 2 diabetes and peripheral neuropathy, and determine whether or not there is a relationship between quality of life and self-reported physical activity.

Study 3 – Chapter 6

- Evaluate an exercise intervention and its effects on self-reported quality of life, sensation and functional capacity in people with Type 2 diabetes and peripheral neuropathy, and determine whether or not it is considered safe.

The surrounding chapters present the literature (Chapter 2), theoretical framework and common methodology (Chapter 3) and the key findings, conclusions and the contribution of this thesis to the field (Chapter 7).

CHAPTER 2: Review of the Literature

This chapter reviews the relevant literature relating to peripheral neuropathy including its diagnosis, prevalence and functional implications. The quality of life for people with Type 2 diabetes and peripheral neuropathy is discussed, along with the roles of physical activity and exercise. This literature review aims to provide a platform for the theoretical framework of this thesis discussed in Chapter 3, and provide justification for the studies discussed in Chapters 4, 5 and 6.

As discussed in Chapter 1, this thesis refers to those with 'diabetes' (may include Type 1, Type 2 and gestational diabetes) and those with 'Type 2 diabetes'. Within this review of the literature, various studies have referred to those with 'diabetes' and may not have made any distinction to those with Type 2 diabetes. Due to the lack of literature in those with Type 2 diabetes and peripheral neuropathy throughout this review, some of these studies have been reported here, whilst noting that Type 2 diabetes is estimated to represent 90% of those with 'diabetes' (AIHW, 2010).

Prevalence of Peripheral Neuropathy

How peripheral neuropathy is diagnosed

As peripheral neuropathy can be a serious complication of Type 2 diabetes, it is important that it is detected in a timely manner. However, the majority of diagnoses are made well after the onset of the disease due to the unrecognised chronic hyperglycemia associated with Type 2 diabetes, which in itself is difficult to diagnose in a timely manner (Petit and Upender, 2003). This difficultly in diagnosing peripheral neuropathy has been reported by Rota et al. (2005) who found that 82% of newly diagnosed people with Type 2 diabetes presented with signs of peripheral neuropathy as identified by electrophysiological abnormalities. As there are no distinguishing features solely attributable to peripheral neuropathy, all other possible causes of the observed neuropathy must be investigated through the patient's history, and physical and clinical examination before a diagnosis is confirmed (Edwards et al., 2008, Kalish and Pomposelli, 2009, Dyck et al., 2011).

The Toronto Expert Panel on Diabetic Neuropathy (Dyck et al., 2011) recently provided updated guidelines for the minimal criteria for the diagnosis of peripheral neuropathy which is described in Table 1.

Table 1 Definitions of minimal diagnostic criteria for Peripheral Neuropathy (PN)

Possible Clinical PN	Symptoms *or* signs of PN. Symptoms may include decreased sensation, positive neuropathic sensory symptoms predominantly in the toes, feet or legs. Signs may include symmetric decrease of distal sensation or unequivocally decreased or absent ankle reflexes
Probable Clinical PN	A combination of symptoms *and* signs of distal sensorimotor polyneuropathy with any two or more of the following: neuropathic symptoms, decreased distal sensation, or unequivocally decreased or absent ankle reflexes
Confirmed Clinical PN	An abnormal nerve conduction study and a symptom or symptoms or a sign or signs of sensorimotor polyneuropathy
Subclinical PN	No signs *or* symptoms of polyneuropathy. Abnormal nerve conduction is present

(Dyck et al. 2011)

Many tests and tools have been developed for the diagnosis of peripheral neuropathy, however, there are varying opinions as to which test, or combination of tests are most appropriate for detecting peripheral neuropathy. Electrophysiology testing is a sophisticated and commonly used method of testing where a decreased nerve conduction velocity or amplitudes indicates an abnormality (Vinik et al., 2000). This process involves the stimulation of a nerve at a proximal site whilst recording the activity at the distal nerve branches, and is considered the most objective measure of distal sensory polyneuropathy (Arezzo, 1997, Dyck, 1988, Petit and Upender, 2003). Despite electrophysiology testing being considered sensitive, specific and reproducible, it is also expensive, difficult to administer in a non-clinical setting and is uncomfortable for the patient (Cornblath, 2004).

Quantitative Sensory Tests (QST) are also used to test for peripheral neuropathy and include monofilament testing and vibration perception threshold testing (Dyck et al., 1991, Petit and Upender, 2003, Vinik et al., 2000). The comparison of thresholds with normative data provides evidence of sensory loss which can be assessed over time, allowing a more complete assessment of the functional integrity of the peripheral nervous system (Petit and Upender, 2003). Monofilament testing is a simple, quick and inexpensive test commonly used to help diagnose peripheral neuropathy and screen those at risk of developing foot ulcers (Kalish and Pomposelli, 2009, Petit and Upender, 2003, Perkins et al., 2010). Vibration perception threshold testing may involve the use of a tuning fork, however a biothesiometer has been reported as the preferred tool of assessment for vibration perception threshold (Kalish and Pomposelli, 2009). It has been

previously suggested that vibration is the most sensitive test in the detection of peripheral neuropathy (Dyck et al., 1985). These two QST methods of diagnosis are inexpensive and easy to use, making them feasible for use in both clinical and non-clinical settings (Cornblath, 2004).

Due to the insidious onset and development of peripheral neuropathy it has also been suggested that symptom profiles in the form of questionnaires may be helpful for diagnosis (Dyck, 1988). The nature of the symptoms, their chronology and the assessment of influencing factors can help to determine the severity of the neuropathy (Dyck, 1988, Dyck et al., 1985). These questionnaires are quick and easy to use, provide good sensitivity and specificity, and are commonly used in research settings (Petit and Upender, 2003). Examples of these questionnaires include the Neuropathy Symptom Score (NSS), the Neuropathy Impairment Score (NIS), the Neuropathy Symptom Profile (NSP) and the Neuropathy Disability Score (NDS) (Dyck, 1988, Dyck et al., 1985).

Prevalence of peripheral neuropathy

The prevalence of peripheral neuropathy in people with diabetes has been reported as difficult to accurately estimate due to the clinically silent dysfunction of nerve-fibre loss over time which often remains unidentified and the fact that diabetes itself is largely under diagnosed (Duby et al., 2004, Vinik and Mehrabyan, 2004). The prevalence of peripheral neuropathy also varies greatly depending on the criteria and measurement tools used to define its presence (Vinik and Mehrabyan, 2004). Studies conducted across various countries have reported the prevalence of peripheral neuropathy in people with diabetes as low as 3.6% in Mauritius to as high as 75.1% in Iran (Janghorbani et al., 2006, Shaw et al., 1998). Table 2 shows the range of estimated prevalence statistics and the tools used for diagnosis in studies published from various locations around the world. The studies from within Australia which assessed the prevalence of peripheral neuropathy in adults suggest that prevalence decreased with age. Tapp et al. (2003) found a prevalence of 10% in a sample (n = 891) whose mean age was 73 years, compared to Maple-Brown et al. (2004) who noted a prevalence of 24% in a sample (n = 43) whose median age was 50 years.

Table 2 Prevalence (%) of peripheral neuropathy in those diagnosed with diabetes published in peer reviewed articles published since 1993, presented from highest prevalence to lowest.

Author (date of publication)	Origin of sample	Age* (years)	n	Tests for diagnosis	%	Notes
Janghorbani et al.(2006)	Iran	52.7 ± 9.9	810	NCV, VPT, reflexes, monofilament, muscular power	75.1	
Lu 2010 et al. (2010)	China	66.0 ±10.82	435	VPT, monofilament	61.8	
Boru et al. (2004)	Turkey	57.2 ± 10.3	866	NSS, NDS, VPT	60	
Abougalambou and Abougalambou (2012)	Malaysia	≤ 35 (1.4%) < 35-50 (18%) > 50-65 (58.1%) > 65 (22.5%)	1077	VPT, self-reported symptoms	54.7	Age presented as % in age categories
Pop-Busui et al.(2009)	USA	62.4 ± 8.9	2314	MNSI	51	
Daousi et al. (2004)	UK	62.6 ± 13.8	350	VPT, NDS, NSS, PSS	50	
Hanley et al. (2005)	Canada	46.5 ± 13.3	147	MNSI	46.3	Sample were Aboriginal
Dyck et al. (1993)	USA	63.2 ± 12.1	380	NSS, NDS, NSP, NCS, VPT, temperature threshold	45	
Gill et al. (2008)	Africa	41 ± 16	105	VPT	41	
Shera et al. (2004)	Pakistan	55.2 ± 10.6	500	Monofilament, reflexes	39.6	
Al-Mahroos and Al-Roomi (2007)	Bahrain	57.3 ± 6.32	1477	NSS, NDS, VPT	36.6	
Saadi et al. (2007)	UAE	56.0 ± 11.6	57	DNS, DNES	34.7	KDM
Manes et al. (2002)	Greece	59.5 ± 7.46	821	NSS, NDS, VPT	33.5	
Candrilli et al. (2007)	US	40-49 (12.4%) 50-59 (27.9%) 60-69 (33.8%) ≥ 70 (25.9%)	850	Interview question	32.7	Age presented as % in age categories
Fedele et al. (1997)	Italy	55.8 ± 10.4	8757	MNSI	32.3	
Gregg et al. (2004)	US	62.2	419	Self-reported symptoms monofilament	28.5	Age SD not provided
Young et al. (1993)	UK	59 (18-90)	6487	NDS, NSS, VPT	28.5	

Table 2 cont. Prevalence (%) of peripheral neuropathy in those diagnosed with diabetes from peer reviewed articles published since 1993, presented from highest prevalence to lowest.

Author (date of publication)	Origin of sample	Age * (years)	Sample size	Tests for diagnosis	%	Notes
Agbor Ndip et al. (2006)	Cameroon	56.7 ±12.3	300	Monofilament, VPT	27.3	
Pradeepa et al. (2008)	India	60 ± 9	1629	VPT	26.1	
Maple-Brown et al. (2004)	Australia	50 (31-67)	43	Monofilament, VPT, reflexes, pin prick, temperature thresholds	24	Sample were Aboriginal
Jurado et al. (2008)	Spain	59.63 ± 7.87	307	VPT, reflexes, NSS	23.1	
Cabezas-Cerrato (1998)	Spain	57.2 ± 0.3	2644	NSS, NDS, VPT, monofilament	22.7	
Abbott et al. (2002)	UK	61.3 ± 14.1	9710	NSS, NDS, VPT, thermal thresholds, monofilament	22.4	
Tres et al. (2007)	Brazil	57.8 ± 11	340	MNSI	22.1	
Eppens et al. (2006)	Australia	15.3 (13.6-16.4)	24	Thermal threshold, VPT	21	
Nielsen (1998)	Saudi Arabia	50 (11.3)	375	VPT, pin prick	20	
NADC (2009)	Australia	56.8 ± 17.3	8563	VPT, monofilament	18.6	
Liu et al. (2010)	China	59.75 ± 11.42	1067	VPT, monofilament	18.3	KDM
Saadi et al. (2007)	UAE	49.9 ± 11.8	40	DNS, DNES	16.2	NDM
Shaw et al. (1998)	Mauritius	55 ± 11	433	VPT	12.7	KDM
Sorensen et al. (2002)	Australia	58.1 (53.2-62.0)	2610	VPT, monofilament, reflexes	11.4	
Tapp et al. (2003)	Australia	73 ± 10	891	NSS, NDS, monofilament, BP	10.0	
Bruce et al. (2008)	Canada	37.8 ± 12.3	467	monofilament	7	
Liu et al. (2010)	China	52.68 ± 13.02	126	VPT, monofilament	6.4	NDM
Shaw et al. (1998)	Mauritius	52 ± 12	414	VPT	3.6	NDM

NSS: Neuropathy Symptom Score
VPT: Vibration Perception Threshold
NDS: Neuropathy Disability Score
PSS: Pain Symptom Score
DNS: Diabetic Neuropathy Symptom Score
DNES: Diabetic Neuropathy Examination Score
SDPN: Symptoms of Diabetic Peripheral Neuropathy
MNSI: Michigan Neuropathy Screening Instrument
BP: Blood Pressure
NSP: Neuropathy Symptoms Profile
NDM – Newly diagnosed Diabetes Mellitus
KDM – Known Diabetes Mellitus
*reported as mean ± SD or median (range)

The Australian Institute of Health and Welfare (2008) reported that in the years 1999-2000, 10% of males and over 8% of females with diabetes had peripheral neuropathy. This figure was updated in 2004 whereby the prevalence of peripheral neuropathy of those attending a diabetes clinic was reported as 25.5% (AIHW, 2008). More recent Australian data reports an estimate of peripheral neuropathy in those with diabetes of 18.6% (NADC, 2009). These figures are particularly alarming when Cusick et al. (2005) found that the five year all-cause mortality rate for those with Type 2 diabetes was 18.9% and of the 585 non-survivors, 70% of them had varying levels of peripheral neuropathy. This preceding point again illustrates the insidious nature of peripheral neuropathy in people with Type 2 diabetes, and the varying prevalence rates indicates that peripheral neuropathy is not uniformly reported.

Problems associated with Type 2 Diabetes and Peripheral Neuropathy

The presence of peripheral neuropathy in people with Type 2 diabetes has been associated with lower limb sensory deficiencies, painful symptoms, an increased risk of ulceration and amputation, and a decrease in lower limb strength (Andreassen et al., 2006, Bansal et al., 2006, Vinik and Mehrabyan, 2004). These factors have been linked to a reduction in functional capacity and quality of life in those with Type 2 diabetes and peripheral neuropathy.

The impact of peripheral neuropathy on the lower limb

Sensory impairments and painful symptoms

As mentioned in Chapter 1, peripheral neuropathy can affect both sensory and motor nerve fibres which may lead to both painful and non-painful symptoms (AIHW, 2008). Peripheral neuropathy can present in many forms and often be contradictory, including those who report severe pain yet upon examination may have only a minimal nerve damage, compared to those who present with insensate feet who are in fact asymptomatic (Boulton, 2005, Vinik and Mehrabyan, 2004). Peripheral neuropathy can often present with diminished or absent deep-tendon reflexes (i.e. Achilles tendon), or in more advanced cases, complications such as lower limb ulceration, Charcot's foot, weakness and gait disturbances, indicating larger sensory-motor fibre dysfunction (Edwards et al., 2008, Petit and Upender, 2003). More specifically, neuropathy involving large sensory-motor fibres in peripheral nerves impairs proprioception and light touch (Edwards et al., 2008).

Peripheral neuropathy may also present with severe pain without much motor weakness, suggesting more the involvement of small sensory fibres in the peripheral nerves (Petit and Upender, 2003). Small fibre neuropathy impairs pain and temperature perception which leads to parethesias and painful symptoms (Edwards et al., 2008) which are often exacerbated at night (Boulton et al., 2005b, Vinik et al., 2000). Painful symptoms include burning pain, deep aching, constricting and throbbing feelings, along with non-painful symptoms such as numbness, tingling, extreme sensitivity, or feelings of asleep or deadness within the lower limb (AIHW, 2008, Boulton, 2005, Boulton et al., 2005b, Donnan and Ledger, 2006, Head, 2006, Petit and Upender, 2003).

Ulcers and amputation

The sensory loss associated with peripheral neuropathy increases the risk of foot ulceration and associated amputation (Bansal et al., 2006, Duby et al., 2004, Vinik and Mehrabyan, 2004). It has been suggested that the lifetime risk of developing an ulcer in those with diabetes is 15% (Reiber, 1996). Furthermore, it has been reported that the recurrence rates of foot ulcers is greater than 50% after three years (Boulton et al., 2005a). Therefore, the prevention of ulcers is important given the high recurrence rate and the subsequent risk of amputation (Kastenbauer et al., 2001, Mantey et al., 1999, van Schie, 2005). The diagnosis of peripheral neuropathy and the presence of foot ulcers are independent risk factors for lower limb amputation in people with diabetes (Adler et al., 1999). Diabetes is estimated to account for approximately half of all non-traumatic lower-limb amputations (AIHW, 2008) while the risk of amputation is increased 15 fold for those individuals with diabetes compared to those without (Payne, 2000).

Decreased lower limb strength

The loss of lower limb strength in people with diabetes, peripheral neuropathy, and factors associated with peripheral neuropathy is also a major concern. Andersen et al. (1996) found that people with diabetes had a significant reduction (21%) in ankle strength compared to those without diabetes. There was also a decreased knee extensor (16%) and knee flexor (17%) strength between groups. A decreased muscle strength at the ankle in those with diabetes has been supported by Andreassen et al. (2006). Similarly, Hilton et al. (2008) found that the strength in the ankle plantar flexors and dorsi flexors were 79% and 41% respectively lower in people with diabetes and peripheral neuropathy compared to those who did not have these

conditions. Gutierrez et al. (2001) found that older diabetic women with mild peripheral neuropathy did not have the ability to rapidly produce ankle torque and thus have a decreased ability to recover from a lateral perturbation, increasing the risk of falls. Insensitivity to the monofilament, vibration threshold, and motor nerve conduction amplitude were associated with an 11%, 7% and 8% lower quadriceps strength in people with diabetes (Strotmeyer et al., 2009). The authors also reported that monofilament insensitivity and nerve conduction amplitude were both associated with a 17% decrease in ankle strength (Strotmeyer et al., 2009). Most recently, Ijzerman et al. (2012) found that in a sample of people with Type 2 diabetes, of which 63% were diagnosed with peripheral neuropathy, there was a 34% to 47% reduction in knee and ankle strength compared to those without diabetes.

Decreased muscle strength in people with diabetes and peripheral neuropathy is thought to be related to insufficient nerve re-innervation leading to weakness and an increased intermuscular adipose tissue in the lower limbs (Hilton et al., 2008, Andreassen et al., 2009). Furthermore, diabetes and peripheral neuropathy have been linked with atrophy in the lower limb and it has been suggested that the total volume of the foot muscle is halved in those with diabetes and peripheral neuropathy (Andersen et al., 2004a).

The impact of peripheral neuropathy on function and quality of life

It has been shown by several authors that people with Type 2 diabetes and peripheral neuropathy have functional impairments such as difficulty in walking, mobility, and maintaining balance which stems from a decreased lower limb strength and sensory awareness associated with Type 2 diabetes and peripheral neuropathy.

Studies have shown that those with diabetes are more likely to have severe functional impairment than those without diabetes (De Rekeneire et al., 2003, Ryerson et al., 2003, Sinclair et al., 2008). Recently, it has been suggested that the decline over six years in physical disability and functional limitations in people with Type 2 diabetes was 14% and 38% respectively (Sakurai et al., 2012). Many researchers have highlighted lower-extremity functions such as walking, climbing stairs, balancing and rising from a chair as being problematic (De Rekeneire et al., 2003, Gregg et al., 2000, Volpato et al., 2002). Specifically, those with diabetes reported more difficulty in walking one mile, rising from a chair, and climbing up 20 steps than those

without diabetes (De Rekeneire et al., 2003). Others have suggested that those with Type 2 diabetes have an increased risk of difficulty with instrumental activities of daily living (Bossoni et al., 2008). It has been reported that these functional issues have been linked to poor glycemic control (Bossoni et al., 2008, De Rekeneire et al., 2003).

A higher mobility impairment has also been reported in people with peripheral neuropathy (Bruce et al., 2005). Liedberg and Vrethem (2009) found that the painful symptoms associated with peripheral neuropathy had severe consequences for daily life such as walking, occupational performance, housework and leisure. However in this report, only 52% of those with painful symptoms were diagnosed with diabetes, with the remaining 48% diagnosed with peripheral neuropathy through other etiologies. Eberhardt et al. (2006) found that those with diabetes and a lower-extremity disease (peripheral neuropathy, peripheral arterial disease or a combination of both) had a higher prevalence of mobility limitation such as walking and climbing stairs.

As already discussed the decline in functional performance in those with diabetes and peripheral neuropathy may be linked to the deficits in sensory feedback and strength. People with diabetes and peripheral neuropathy tend to have a higher concentration of intermuscular adipose tissue which has a negative impact on their lower limb strength (Hilton et al., 2008). This increase in intermuscular adipose tissue in those with diabetes and peripheral neuropathy has also been associated with a lower physical function as measured using a nine item Physical Performance Test (PPT) and activity monitoring (Hilton et al., 2008, Tuttle et al., 2011). Several authors have also reported links between functional and mobility impairments in people with diabetes and those who have a reduced peripheral nerve function as assessed by sensitivity and nerve conduction tests. Strotmeyer et al. (2008) has reported that a poor peripheral nerve function explained a portion of the association between diabetes and physical disability with poor sensory function independently associated with worse physical performance in activities such as walking, chair stand and balance times. This is supported by Cordeiro et al. (2009) who found significant correlations between abnormal proprioceptive sensitivity and poor performances in the timed get-up and go and the Berg Balance Scale, two tests which encompass walking, chair stands and balance times as assessed by Strotmeyer et al. (2008). It is assumed that any type of intervention that can reduce the functional and mobility impairments in people with Type 2 diabetes and peripheral neuropathy will assist to maintain quality and independence in their lives.

Quality of life along with functional status is a primary measure of the effectiveness of health programs, as well as being used to assess the effects of a disease on an individual (O'Connor, 2004). Quality of life and health-related quality of life are two terms which are often cited in the literature. Quality of life has been defined as a subjective wellbeing which may refer to physical, emotional, self-determined, or observer measures (O'Connor, 2004). Health-related quality of life is the component of quality of life due to the individual's health state, and most commonly refers to the individual's subjective sense of well-being, functional status, or self-perceived health (O'Connor, 2004).

The quality of life of individuals with a variety of chronic diseases such as Type 2 diabetes is known to be diminished (Sundaram et al., 2007, Vileikyte et al., 2005) and may be used to predict disease progression and response to therapy (Chyun et al., 2006). Sundaram et al. (2007) assessed the relationship between health status, quality of life and glycemic control on those with Type 2 diabetes and found that whilst diabetes negatively impacted quality of life, those with HbA1c levels within ADA guidelines had a better quality of life than those with higher HbA1c levels (Sundaram et al., 2007). An earlier study examined quality of life across varying glucose tolerance levels and found that there was a gradual decrease in quality of life across categories of glucose tolerance (Tapp et al., 2006). Sundaram et al. (2007) and Tapp et al. (2006) used quality of life instruments, the Audit of Diabetes Dependent Quality of Life (ADDQoL) and the Short Form-36 (SF-36) respectively. However in contrast, Papelbaum et al. (2010) found that quality of life in those with diabetes was not associated with levels of HbA1c. Papelbaum et al. (2010) utilised the Problem Areas In Diabetes scale (PAID) which has been described as a measure of the emotional adjustment to life with diabetes (Welch et al., 1997), and therefore may not have captured the same dimensions of quality of life compared to the studies which did find a relationship between quality of life and HbA1c.

It has been suggested that Type 2 diabetes influences the physical, social and psychological well-being of individuals because of its chronic nature and associated complications (Sundaram et al., 2009). Upon diagnosis of Type 2 diabetes people report feeling anxious, frightened and angry which impacts on their daily life, and continues throughout the disease progression (Mosnier-Pudar et al., 2009). It has been noted that people with diabetes were more likely to rate their health as 'fair' or 'poor' compared to those without diabetes (AIHW, 2008, Pena et al., 2010).

The AIHW (2008) reported that 48% of respondents with diabetes rated their health as fair or poor, compared to 15% of those without diabetes. More recently, Pena et al. (2010) found 64% of a sample of people with diabetes rated their health as fair or poor compared with 39% in those without diabetes. Furthermore, researchers have found that people with diabetes are more depressed than those without diabetes (Goldney et al., 2004) and this depression was associated with a decreased adherence to treatment, poor metabolic control and an increase in complications (Egede and Ellis, 2010).

Several Australian researchers have found that people with diabetes have a poorer quality of life compared to those without diabetes (Colagiuri et al., 2003, NWAHS, 2007), an association also noted in recent international articles (Papelbaum et al., 2010, Pena et al., 2010, Saito et al., 2006). Diabetes impacts on both mental and physical health. Smith and McFall (2005) found that people with diabetes reported 4.2 days per month impaired by mental health issues associated with their diabetes and up to 8.4 days impaired by physical health issues. Saito et al. (2006) also found that diabetes affected physical scores more than mental health scores of quality of life. Physical domains of quality of life which have been reported to be affected by diabetes include physical fitness, daily activities, pain, mobility and overall health status (Colagiuri et al., 2003, Pena et al., 2010). The extent and impact on quality of life needs to be considered as this may vary depending on how well managed the condition is.

Other factors which may predict the quality of life in those with diabetes include gender and the duration of diagnosis. Misra and Lager (2009) reported that females with Type 2 diabetes had a poorer quality of life compared to males, citing a greater burden in areas of social interactions, physical complaints and dietary restriction. Pena et al. (2010) also reported that females with diabetes reported a poorer perception of health related quality of life than males with diabetes. It has also been suggested that those people who have been diagnosed with diabetes for longer had a poorer quality of life compared with those of fewer years since diagnosis (Glasgow et al., 1997, Saito et al., 2006).

It has been cited by various authors that quality of life is further diminished in people with diabetes and peripheral neuropathy (Chyun et al., 2006, Currie et al., 2006, Olaleye et al., 2001, Vileikyte et al., 2005, Lloyd et al., 2001, Mold et al., 2004, Ovayolu et al., 2008). Chyun et al. (2006) assessed quality of life using the SF-36 and the Diabetes Quality of life (D-QOL) measure, and found that the presence of signs or symptoms of peripheral neuropathy were consistently associated with lower quality of life scores. Similarly, Ovayolu et al. (2008) used the SF-36 and the World Health Organization Quality of Life Questionnaire (WHOQoL-BREF) and found that those with diabetes and peripheral neuropathy had lower scores for functional, well-being, general, physical, psychological and social measures. Lloyd et al. (2001) found that, despite excluding those with the most severe cases of peripheral neuropathy, those with peripheral neuropathy had a significantly lower quality of life score for the mental domain of the SF-36 compared to those without peripheral neuropathy.

The studies mentioned above used generic quality of life instruments, and it may be that the use of a disease-specific instrument detects more subtle changes in health-related quality of life (Lloyd et al., 2001). Currie et al. (2006) used a neuropathy-specific quality of life instrument (QoL-DN: Quality of Life in Diabetes Neuropathy) and concluded that the severity of peripheral neuropathy was predictive of poor health and quality of life. More recently, Vileikyte et al. (2009) used somatic experiences and psychological measures of a neuropathic specific questionnaire (NeuroQol) to determine that peripheral neuropathy is a risk factor for depressive symptoms due to pain and unsteadiness.

There are views that the diminished quality of life in people with diabetes and peripheral neuropathy is more due to the peripheral neuropathy, specifically the symptoms of sensory loss, pain, ulceration and amputation, loss of strength and functional decline. It has been suggested that there is a link between the diminished quality of life in those with diabetes and peripheral neuropathy, and the functional deficits associated with the peripheral neuropathy (Mold et al., 2004). Padua et al. (2005) assessed the effect of functional disability in people with peripheral neuropathy and found a significant negative relationship between disability and quality of life indicating that as the level of disability increased, quality of life decreased. Furthermore, Padua et al. (2001) assessed the impact of peripheral nerve impairments on quality of life using the SF-36 and found that a loss of sensation as measured using the monofilament, and a loss of vibration

perception measured using a Biothesiometer, were significantly related to the loss of physical function and its effect on quality of life. Research using a neuropathy-specific tool also found that those with Type 2 diabetes and symptoms of peripheral neuropathy had higher depression scores (Vileikyte et al., 2005).

Several authors have found that painful peripheral neuropathy in people with diabetes is also associated with a decreased quality of life (Benbow et al., 1998, Davies et al., 2006, O'Connor, 2009, Van Acker et al., 2009). Specifically, Van Acker et al. (2009) found that scores for physical and mental quality of life scales were independently affected by painful peripheral neuropathy. Similar results were reported where participants with painful peripheral neuropathy were found to have significantly poorer scores in emotional reaction, energy, pain, physical mobility and sleep domains (Benbow et al., 1998). The above findings are not surprising given neuropathic pain is associated with anxiety, depression, loss of mobility and independence, which may contribute to a decreased overall quality of life (Benbow et al., 1998).

The quality of life of those with diabetic foot ulcers, which is a common complication of diabetes and peripheral neuropathy, is also said to be diminished. Although some of the participants cited below did not have peripheral neuropathy, it is known that peripheral neuropathy is one of the main etiologic factors which contribute to ulcer formation (Goodridge et al., 2005). As such it could be estimated that a large proportion of the samples below in fact included those with diabetes and peripheral neuropathy, among other complications.

A literature review conducted by Goodridge et al. (2005) concluded that complications of diabetes which included foot ulcers had a negative effect on health related quality of life. Specifically, a summary of both quantitative and qualitative studies confirmed that diabetic foot ulcers reduced quality of life through the domains of activities of daily living, physical functioning, psychological status and social situation (Goodridge et al., 2005). Valensi et al. (2005) found that the largest differences between those who had diabetic foot ulcers versus those who did not, were the physical functioning and emotional roles domains of the SF-36. Several studies have found that quality of life further declined in those who had a diabetic foot ulcer which did not heal compared to those who had an ulcer which did heal (Nabuurs-Franssen et al., 2005, Tennvall and Apelqvist, 2000, Winkley et al., 2009). Most recently, Ribu (2010) reported that those with diabetic foot ulcers reported a poor quality of life, largely due to the physical

impairment caused by the ulcer. Such is the diminished quality of life in people with diabetic foot ulcers, that it has been suggested that those with ulceration may report a poorer quality of life than those with an amputation, due to the constant fear of recurrent ulceration, repeated bouts of infection, and potential life-long disability (Price, 2004). Despite many of the above studies using generic quality of life instruments, it has been noted by Ribu (2010) that the use of disease-specific instruments such as the DFS-SF (Diabetic foot ulcer scale) and the NeuroQol may better detect functional complications specific to diabetic foot ulcers.

From the studies discussed investigating the quality of life in people with diabetes, Type 2 diabetes and peripheral neuropathy it is clear that the symptoms associated with peripheral neuropathy have a negative effect on health, wellbeing and quality of life.

Management of Peripheral Neuropathy using Physical Activity and Exercise

The role of physical activity and exercise in the management of people with Type 2 diabetes and peripheral neuropathy is important due to physiological effects such as glucose metabolism (Warren, 2010). However as outlined in this literature review so far, it has become apparent that glucose control is not the only problem associated with the presence of Type 2 diabetes and peripheral neuropathy. The decline in functional capacity and quality of life bought on by the sensory loss, painful symptoms, ulceration, amputation and loss of strength associated with peripheral neuropathy are important issues which also must be managed. It has been proposed that the use of physical activity and exercise may also have a positive therapeutic effect on these factors.

A few authors have investigated the effects of physical activity on outcomes associated with sensory loss in people with diabetes and in people with diabetes and peripheral neuropathy. (Balducci et al., 2006, Fisher et al., 2007, Kluding et al., 2012, Dixit et al., 2014). Balducci et al. (2006) conducted an randomised controlled aerobic training program, whereby participants with Type 2 diabetes without a diagnosis of peripheral neuropathy completed four hours of walking on a treadmill between 50 to 80% of their heart rate reserve each week for a period of four years. Outcomes which were measured included vibration perception thresholds (VPT), nerve distal latency, nerve conduction velocity (NCV) and nerve action potential amplitude (NAPA). The

authors found a significant change in NCV for both the peroneal and sural nerve between the exercise and control group (Balducci et al., 2006). It was also found that the percentage of people who developed sensory neuropathy during the four year period was significantly higher in the control group than the exercise group (29.8% versus 6.5%), and the percentage of participants whose VPT increased during the study were also significantly higher in the control group (Balducci et al., 2006). It was concluded that a long term aerobic training program could modify the natural history of peripheral neuropathy and even prevent its onset (Balducci et al., 2006). Despite the seemingly positive results however, this study failed to assess the effect of physical activity on those already with neuropathy, as at the commencement of the study, no participants had any form of neuropathy.

Electrophysiological change has also been seen in participants with Type 2 diabetes and peripheral neuropathy who completed a 24-week aerobic exercise program (Fisher et al., 2007). The results of this non-controlled pre-test, post-test research study showed there was a significant improvement in nearly all electrophysiological parameters post intervention including motor conduction velocities and amplitudes, sensory conduction velocities and F-wave latencies (Fisher et al., 2007). The authors concluded that exercise could be performed safely in patients with diabetes and peripheral neuropathy and could produce an improvement in nerve function (Fisher et al., 2007).

Most recently, Dixit et al. (2014) used a single blind, parallel group randomised controlled trial to investigate the effect of an eight week moderate intensity aerobic exercise program on various electrophysiological outcomes including NCV. The experimental group were asked to participate in three moderate aerobic training sessions per week using a treadmill, monitored using a combination of heart rate and rate of perceived exertion (RPE). The results indicated significant changes in distal peroneal NCV and Sural sensory NCV between the two groups, and it was concluded that moderate intensity aerobic training may disrupt the natural progression of peripheral neuropathy in people with Type 2 diabetes. The above mentioned three studies from Fisher et al. (2007), Balducci et al. (2006) and Dixit et al. (2014) only utilised aerobic training throughout the intervention. With reduced strength in the lower limbs being a consequence of peripheral neuropathy, a combined aerobic and resistance training program may be indicated.

Kluding et al. (2012) used a pilot study (non-controlled pre-test, post-test design) to assess the feasibility and effectiveness of a 10-week combined aerobic and strengthening exercise program on pain, neuropathic symptoms and electrophysiologcal parameters. Specifically, outcome measures included pain using a visual-analog scale, the Michigan Neuropathy Screening Instrument (MNSI), nerve conduction velocities, quantitative sensory testing such as vibration detection threshold and intraepidermal nerve fibre density and epidermal axon branching from skin biopsies. Following the 10-week program there were a significant reduction in pain, symptoms (MNSI) and a significant increase in intraepidermal nerve fibre branching. Despite the seemingly positive results the authors noted that this was a pilot study and that further research is warranted (Kluding et al., 2012). Further studies to explore the value of a combined aerobic and resistance training program are therefore indicated.

Many studies have investigated the effects of various exercise programs designed to improve the functional impairments associated with Type 2 diabetes and peripheral neuropathy by targeting strength and balance. A 2004 Cochrane systematic review, which was updated in 2008 and again in 2011 examined the effect of exercise on functional ability in the treatment of people with peripheral neuropathy including measures such as muscle strength, endurance and broader measures of health and well-being (White et al., 2004). The selection criteria for the systematic review of any randomised or quasi-randomised controlled trials of at least eight weeks yielded one primary study (Lindeman et al., 1995), however two other trials of less than eight weeks duration (Richardson et al., 2001, Ruhland and Shields, 1997) were also included as secondary studies. Of the above named studies, two of them did not assess anyone with diabetic peripheral neuropathy, rather hereditary motor and sensory neuropathy, chronic peripheral neuropathies and toxic neuropathies (Ruhland and Shields, 1997, Lindeman et al., 1995). The third was a controlled prospective single-blind study which incorporated a three week strengthening program for participants with diabetes and peripheral neuropathy, and resulted in an improved lower limb strength and measures of balance (Richardson et al., 2001).

Since the publication of the systematic review conducted by White et al. (2004), several authors have reported the effects of various types of exercise programs in people with diabetes and peripheral neuropathy. Song et al. (2011) found an eight week randomised pre-test, post-test balance program, in addition to health education classes, significantly improved balance and

functional measures in participants with diabetes and peripheral neuropathy when compared to participants who only received the education classes. The exercise program was conducted twice weekly for a duration of one hour.

Otterman et al. (2011) investigated the feasibility and effectiveness of a non-controlled pre-test, post-test combined aerobic and resistance training program for participants with complications from diabetes using functional outcome measures. All participants, of which 90% had Type 2 diabetes, had been diagnosed with peripheral neuropathy and foot deformities, and may have been diagnosed with other complications such as retinopathy, nephropathy and hypertension. The participants were also considered high risk as 50% had previous foot ulceration, 10% had an active foot ulcer and 20% had some form of amputation (Otterman et al., 2011). The 12-week exercise program was conducted via group sessions within a hospital setting, and included 30 minutes of aerobic exercise between 40-65% HRR (Heart Rate Reserve) and a resistance training program comprising major muscle groups starting at two sets of ten repetitions at 40%1RM (one repetition maximum), increasing to three set of 15 repetitions at 65%1RM. Outcome measures included HbA1c, maximum peak knee extension, and perceived limitations in functioning, with results concluding that the program was feasible and effective by significantly improving all of the above named outcome measures (Otterman et al., 2011).

Tuttle et al. (2012) detailed a single case report of the effects of a 12-week moderate intensity, progressive exercise program incorporating flexibility, balance, strengthening and aerobic training in a 76 year old male who had diabetes and severe peripheral neuropathy. Functional outcome measures assessed included a modified PPT, and dorsi-flexion and plantar-flexion strength. Aerobic exercise was performed on a treadmill and strengthening exercises involved the use of body weight resistance. The results showed an improvement in ankle strength and HbA1c, but no improvement in scores of the PPT (Tuttle et al., 2012).

Ahn and Song (2012) assessed the effects of a 12-week Tai Chi program considered to be a moderate intensity aerobic exercise, on glucose control, neuropathy scores and balance among others, in those with Type 2 diabetes and peripheral neuropathy. The research design was a pre-test, post-test with a non-equivalent control group. The program was conducted twice weekly. There was a significant improvement in all of the outcome measures compared to those who did not participate in the intervention.

Finally, Mueller et al. (2013) investigated the effects of a 12-week combined balance, flexibility, strengthening and aerobic program in people with diabetes and peripheral neuropathy using a randomised controlled trial with participants randomised into either the weight bearing, or non-weight bearing group. Exercise sessions were conducted three times per week, with primary outcome measures assessed before and after the intervention including the six-minute walk distance and daily step counts. Secondary outcome measures included foot and ankle ability measures, the Beck Depression Inventory, a nine item physical performance test and blood glucose control (HbA1c). There were significant differences in gains in the six-minute walk distance and daily step counts in the weight bearing group compared to the non-weight bearing group, however the non-weight bearing group demonstrated greater improvements in glucose control than the weight bearing group (Mueller et al., 2013).

In the studies outlined above where participants diagnosed with diabetes and peripheral neuropathy were included, there were variations in sample sizes, duration of the program, the mode of exercise, and the research design. Richardson et al. (2001), Song et al. (2011), Ahn and Song (2012), Mueller et al. (2013), and Dixit et al. (2014) used both an intervention and control group comprising of between ten and 40 participants in the intervention group. Alternatively, all remaining studies used only an intervention group with sample sizes ranging from one to 22 (Fisher et al., 2007, Kluding et al., 2012, Otterman et al., 2011, Tuttle et al., 2012). However, it should be noted that whilst Tuttle et al. (2012) reported a single case design, the participant was a part of an ongoing randomised controlled trial suggesting further results with more participants and a control group was to follow. The relatively small sample sizes reported in these studies highlights the difficulty of doing research with this population, and supports the notion that research is still developing. It is therefore important to fully understand the impact of various exercises and their effects on the high risk nature of peripheral neuropathy, before making exercise recommendations.

The studies which have been discussed above assessing the effect of exercise in people with Type 2 diabetes and peripheral neuropathy have used varying pre-test, post-test research designs. Several studies utilised a control group who did not partake in the intervention (Ahn and Song, 2012, Richardson et al., 2001, Song et al., 2011) while others only used an intervention group (Fisher et al., 2007, Kluding et al., 2012, Otterman et al., 2011, Tuttle et al., 2012). The exercise intervention in this thesis used a Single Case Experimental Design (SCED) which is explained in detail in Chapter 3.

The duration of the above mentioned studies ranged between three weeks to 24 weeks and used various modes of exercise including strengthening and balance, Tai Chi, aerobic, resistance and combined programs. LeMaster et al. (2008) reported that the promotion of weight-bearing activities, namely walking, did not lead to a significant increase in foot ulceration, and therefore recommended that weight-bearing activities may be considered safe for those with diabetes and peripheral neuropathy. In 2010 the ADA and the ACSM confirmed this research from LeMaster et al. (2008) by including moderate weight-bearing activities in their recommended activities for those with diabetes and peripheral neuropathy but who did not have acute foot ulceration (ACSM/ADA, 2010). Since this time, many authors have used forms of weight-bearing aerobic exercise (mostly walking), in the prescription of exercise programs, often accompanied by other non-weight bearing exercises (Kluding et al., 2012, Otterman et al., 2011, Tuttle et al., 2012, Dixit et al., 2014, Mueller et al., 2013).

In contrast to the above mentioned studies Kruse et al. (2010) found a 12-month exercise program designed to improve lower-extremity strength and balance in those with diabetes and peripheral neuropathy was not beneficial, as there was no reduction in falls or improvement of balance or strength. It should, however, be noted that Kruse et al. (2010) used mostly a home-based program and that only 45% of the intervention group completed more than half of the required study protocol. The results of this study indicate that exercise programs for people with diabetes and peripheral neuropathy should be supervised and monitored closely to encourage adherence, to maximise any functional benefits of the program.

During the development phase of this thesis, the systematic review conducted by White et al. (2004) was the only study assessing the effects of exercise on the functional outcomes in people with peripheral neuropathy. The lack of literature at that time helped provide justification for further research and was the motivation for this thesis. Furthermore, of the three studies identified in the systematic review, only one used participants with diabetes and peripheral neuropathy (Richardson et al., 2001). It appears this gap has not escaped the attention of other researchers, as recently more studies have been published assessing the effect of exercise on functional outcomes in people with diabetes and peripheral neuropathy with varying methodologies and outcomes (Ahn and Song, 2012, Otterman et al., 2011, Song et al., 2011, Tuttle et al., 2012, Mueller et al., 2013). The above mentioned studies investigating the effect of various type of exercise training on electrophysiological and function outcomes in people with diabetes and peripheral neuropathy are summarised in Table 3.

Table 3 Summary of studies evaluating exercise training in people with diabetes and diabetes and peripheral neuropathy

Reference	Participants	Research Design	Intervention			Outcome Measures	Conclusions
			Mode	Duration	Frequency		
Electrophysiological Outcomes							
Dixit et al. (2014)	T2D + PN	RCT	Aerobic	8-wk	3 days/wk	• NCV	Moderate intensity aerobic exercises can play a valuable role to disrupt the normal progression of peripheral neuropathy.
Kluding et al. (2012)	Diabetes + PN	Non-controlled Pre-test, post-test	Aerobic and strengthening	10-wk	3-4 days/wk	• Pain • MNSI • NCV • VPT • Skin biopsies	The program resulted in a significant reduction in pain, symptoms and intraepidermal nerve fibre branching.
Fisher et al. (2007)	T2D + PN	Non-controlled Pre-test, post-test	Aerobic	24-wk	3 days/wk	• Motor NCV • F-Wave latencies	Exercise could be performed safely and could produce an improvement in nerve function.
Balducci et al. (2006)	T2D	RCT	Aerobic	4-y	4 hours/wk	• VPT • NCV • Nerve distal latency • NAPA	A long term aerobic training program could modify the natural history of peripheral neuropathy and even prevent its onset.

T2D: Type 2 Diabetes, PN: Peripheral Neuropathy, RCT: Randomised Controlled Trial, NCV: Nerve Conduction Studies, 6MWD: 6-Minute Walk Distance, PPT: Physical Performance Test, MNSI: Michigan Neuropathy Screening Instrument, VPT: Vibration Perception Threshold, NAPA: Nerve Action Potential Amplitude, SWMF: Semmes-Weinstein Monofilament, wk: week, y: years, m: month

Table 3 cont. Summary of studies evaluating exercise training in people with diabetes and diabetes and peripheral neuropathy

Reference	Participants	Research Design	Intervention			Outcome Measures	Conclusions
			Mode	Duration	Frequency		
Functional Outcomes							
Mueller et al. (2013)	T2D + PN	RCT	Balance, flexibility, strengthening and aerobic	12-wk	3 days/wk	• 6MWD • Daily step counts • Foot and Ankle Ability Measure • Beck Depression Inventory • PPT • Haemoglobin A1c • Ankle strength • Skin lesions	The ability of this population to increase measures of 6MWD and daily step counts with a weight bearing exercise program compared with a non-weight bearing exercise program.
Ahn and Song (2012)	T2D + PN	Pre-test post-test with non-equivalent control	Tai Chi	12-wk	2 days/wk	• Haemoglobin A1c • SWMF • Symptom scores • Single-leg stance • Quality of Life	The program improved glucose control, balance, neuropathic symptoms and some dimensions of quality of life.
Tuttle et al. (2012)	T2D + PN	Single-case	Balance, flexibility, strengthening and aerobic	12-wk	3 days/wk	• 6MWD • Daily step counts • Foot and Ankle Ability Measure • PPT • Haemoglobin A1c • Ankle strength	The program was successful in increasing some measures of muscle strength, physical function and activity without causing injury in the participant.
Otterman et al. (2011)	Diabetes + PN	Non-controlled Pre-test, post-test	Aerobic & resistance	12-wk	3 days/wk	• Haemoglobin A1c • Knee strength • Patient-Specific Functional Scale	The program was feasible and effective by significantly improving all outcome measures.

T2D: Type 2 Diabetes, PN: Peripheral Neuropathy, RCT: Randomised Controlled Trial, NCV: Nerve Conduction Studies, 6MWD: 6-Minute Walk Distance, PPT: Physical Performance Test, MNSI: Michigan Neuropathy Screening Instrument, VPT: Vibration Perception Threshold, NAPA: Nerve Action Potential Amplitude, SWMF: Semmes-Weinstein Monofilament, wk: week, y: years, m: month

Table 3 cont. Summary of studies evaluating exercise training in people with diabetes and diabetes and peripheral neuropathy

Reference	Participants	Research Design	Intervention			Outcome Measures	Conclusions
			Mode	Duration	Frequency		
Song et al. (2011)	Diabetes + PN	RCT	Balance	8-wk	2 days/wk	• Postural sway • Single-leg stance • Berg Balance Scale • Functional reach test • Timed-up-and-go • 10m walk	The program improved balance and trunk proprioception and suggests that a balance exercise program is suitable for people with diabetes peripheral neuropathy.
Kruse et al. (2010)	Diabetes + PN	RCT	Strength & balance	12-m	3 days/wk	• Berg Balance Scale • Timed-up-and-go • Single-leg stance • Ankle strength • Falls efficacy scale • Foot function index disability scale	The program had a minimal effect on participants' balance and lower extremity strength. Increasing weight bearing activity did not alter the rate of falls.
LeMaster et al. (2008)	Diabetes + PN	RCT	Aerobic and strengthening	12-m	3 days/wk	• Daily step counts • Foot lesions and ulcers	Promoting weight-bearing activity did not lead to significant increases in foot ulcers.
Richardson et al. (2001)	Diabetes + PN	Prospective controlled single blind	Strengthening	3-wk	not specified	• Tandem stance time • Single-leg stance • Functional reach test • Activities-specific Balance and Confidence Scale	The brief program improved clinical measures of balance.

T2D: Type 2 Diabetes, PN: Peripheral Neuropathy, RCT: Randomised Controlled Trial, NCV: Nerve Conduction Studies, 6MWD: 6-Minute Walk Distance, PPT: Physical Performance Test, MNSI: Michigan Neuropathy Screening Instrument, VPT: Vibration Perception Threshold, NAPA: Nerve Action Potential Amplitude, SWMF: Semmes-Weinstein Monofilament, wk: week, y: years, m: month

Aside from the various biological benefits of exercise and physical activity in people with diabetes mentioned above, there are also many social and psychological benefits of exercise and physical activity which positively influence morbidity and quality of life (ACSM, 2000a, Dunstan and Daly, 2007). Glasgow et al. (1997) found that self-reported physical activity was the only significant self-management behaviour able to predict the quality of life in people with diabetes. Similarly, Smith and McFall (2005) found that exercise was associated with a reduction of impaired quality of life days per month. Those who exercised reported several domains of quality of life to be equal, or better than those without diabetes who did not exercise. This suggests that exercise helped to minimise the effects of diabetes on quality of life (Smith and McFall, 2005). It has been stated the domains of health related quality of life, which have the potential to improve with physical activity in people with diabetes, include physical and social functioning and subjective well-being (Zanuso et al., 2009).

Exercise has been prescribed to those with diabetes to combat the diminished quality of life with varying results. Several studies have found positive effects of exercise on quality of life in those with Type 2 diabetes. Levinger et al. (2007a) assessed the use of resistance training on the capacity to perform activities of daily living in individuals with high numbers of metabolic risk factors similar to those with diabetes. A ten week resistance training program was found to improve quality of life (by improved scores of the subscales of the SF-36 including physical function, general health and social function) independent of changes in body fat content or aerobic power (Levinger et al., 2007a). Similarly, Tamari (2009) used the SF-36 to assess quality of life after a three month resistance training program and found that overall, subscales of bodily pain, vitality, social functioning and mental health were all improved. However, this was based on a combined sample of people with and without diabetes, and it was concluded that those with diabetes were 80% less likely to improve within these domains noted in the previous sentence (Tamari, 2009).

Several researchers have also assessed the changes in quality of life through aerobic exercise. Bello et al. (2011) found that an eight week aerobic exercise program significantly improved quality of life as measured by the WHOQoL-BREF in people with Type 2 diabetes. Similarly, Snel et al. (2012) found a 16-week aerobic program significantly improved 11 of the 22 subscales of quality of life assessed across four commonly used quality of life instruments (SF-

36, MFI-20: Multidimensional Fatigue Inventory, HADS: Hospital Anxiety and Depression Scale, NHP: Nottingham Health Profile) in those with Type 2 diabetes, however this was in combination with a very low calorie diet intervention. Despite this, it was found the improvements in quality of life were longer lasting in those who also completed the exercise component when compared to those who did not (Snel et al., 2012). One study sought to compare changes in quality of life after a 22-week aerobic, resistance or a combination training program (Reid et al., 2010). Using the physical health status of the SF-36, Reid et al. (2010) found that resistance training was better than aerobic training for improving physical health status.

In contrast to above, several researchers have reported no effect from an exercise intervention on quality of life. In a 2007 systematic review it was reported that exercise did not improve quality of life in those with Type 2 diabetes (Kavookjian et al., 2007). Holton et al. (2003) conducted a ten week moderate intensity aerobic exercise program in people with diabetes without complications (such as peripheral neuropathy) and found that there was no significant changes in any quality of life scores as a result of aerobic training, suggesting that perhaps a combined aerobic and resistance training may have a greater effect (Holton et al., 2003). An earlier study by Tessier et al. (2000) looked at a 16-week combined aerobic and strength program in people with diabetes without complications to identify any link between physical activity, quality of life and attitudes in elderly patients with Type 2 diabetes. No significant change in the quality of life assessment for either the exercise or control group was found, however it was important to note that the program did not negatively affect the quality of life of the subjects in the exercise group (Tessier et al., 2000). Most recently a study was conducted which included the assessment of quality of life in three groups of participants assigned to either an endurance group, a combined exercise group, or a control group for a period of 12-weeks (Lambers et al., 2008). No difference in the quality of life between all three groups was reported (Lambers et al., 2008).

Possible explanations for the lack of evidence of the influence of exercise on quality of life noted in the studies above, include that the participants did not have any complications such as peripheral neuropathy, and therefore started the intervention with moderate to high quality of life scores (Kavookjian et al., 2007, Holton et al., 2003, Tessier et al., 2007). Tessier et al. (2000) also noted the small sample size (n=19) and the short duration of the intervention as possible

limitations of their study. Finally, in the systematic review the discrepancies of the different measures used to assess quality of life was noted (Kavookjian et al., 2007). None of the studies reviewed in the systematic review used diabetic-specific measures of quality of life and hence may not have been able to fully capture the impact of diabetes on general quality of life. Generic measures such as the SF-36 cannot always be sensitive to the unique experience of managing diabetes and its health consequences (Kavookjian et al., 2007). The SF-36 or variations of, were used in both Lambers et al. (2008) and Holton et al. (2003) as well as Tamari (2009) which reported mixed results of the impact of exercise on quality of life. A summary of the above mentioned studies is provided in Table 4.

Table 4 Summary of studies evaluating the effect of exercise on quality of life in people with diabetes

Reference	Participants	Research Design	Intervention			Quality of Life Instrument	Conclusions
			Mode	Duration	Frequency		
Studies which have reported a positive effect of exercise on QOL							
Bello et al. (2011)	T2D	RCT	Aerobic	8-wk	3 days/wk	WHOQoL-BREF	The program significantly improved quality of life.
Snel et al. (2012)	T2D	Pre-test, post-test with matched controls	Aerobic	16-wk	5 days/wk	SF-36, MFI-20, HADS, NHP	The exercise program (along with a very low calorie diet) significantly improved 11/22 subscales of quality of life assessed across four instruments.
Reid et al. (2010)	T2D	RCT	Aerobic, Resistance or Combined	22-wk	3 days/wk	SF-36	Resistance exercise was better than aerobic or no exercise for improving physical health status. No exercise was superior to resistance or combined exercise for improving mental health status.
Tamar (2009)	Elderly adults, including a subset of adults with diabetes	Prospective cohort observational	Resistance	12-wk	2 days/wk	SF-36	Overall quality of life was improved after the program, however people with diabetes were 80% less likely to improve in domains of pain, vitality, social functioning and mental health compared to those without diabetes.
Levinger et al. (2007a)	People with high metabolic risk factors	RCT	Resistance	10-wk	3 days/wk	SF-36	Resistance training improved quality of life in people with high metabolic risk factors, similar to diabetes, independent of changes in body fat content or aerobic power.

QOL: Quality of Life, T2D: Type 2 Diabetes, WHOQoL-BREF: World Health Organization Quality of Life Questionnaire, SF-36: Short-form 36, MFI-20: Multidimensional Fatigue Inventory, HADS: Hospital Anxiety and Depression Scale, NHP: Nottingham Health Profile, wk: week

Table 4 cont. Summary of studies evaluating the effect of exercise on quality of life in people with diabetes

Reference	Participants	Research Design	Intervention			Quality of Life Instrument	Conclusions
			Mode	Duration	Frequency		
Studies which have reported no effect of exercise on QOL							
Kavookjianet al. (2007)	T2D	Systematic Review	N/A				Exercise did not improve quality of life in those with Type 2 diabetes.
Lambers et al. (2008)	T2D	RCT	Aerobic or Combined Aerobic and Resistance	12-wk	3-days/wk	SF-36	There was no changes in quality of life in either exercise group (aerobic or combined aerobic and resistance) throughout the program.
Holton et al. (2003)	T2D	Pre-test, post-test with matched controls	Aerobic	10-wk	3-days/wk	SF-36	There were no significant changes in quality of life as a result of the training program.
Tessier, D et al. (2000)	T2D	RCT	Combined Aerobic and Resistance	16-wk	3-days/wk	Self-developed	No significant change in quality of life was observed.

QOL: Quality of Life, T2D: Type 2 Diabetes, WHOQoL-BREF: World Health Organization Quality of Life Questionnaire, SF-36: Short-form 36, MFI-20: Multidimensional Fatigue Inventory, HADS: Hospital Anxiety and Depression Scale, NHP: Nottingham Health Profile, wk: week

No studies were identified as part of this literature review that looked at the impact of exercise on quality of life in people with Type 2 diabetes and peripheral neuropathy, despite the numerous publications discussed above assessing the effect of various exercise programs on the quality of life in people with diabetes more broadly. The majority of research within those with Type 2 diabetes and peripheral neuropathy tends to lean towards the effect of exercise on peripheral nerve function as measured by electrophysiological and functional measures. However, it has been proposed within this review that diabetic peripheral neuropathy has an impact on the biological being (such as impaired nerve function), as well as the psychological and social being and, therefore, these domains also warrant attention.

The relationship between self-reported physical activity and quality of life

The role of exercise and its impact on quality of life in people with diabetes has now been discussed. In the studies reported above, exercise was of a structured nature, that is, part of a prescribed exercise program. However, exercise and physical activity is often not prescribed but rather self-driven and reported. The focus of this section is on the relationship between levels of self-reported physical activity and quality of life. This section will also focus on the relationship between quality of life and exercise and whether or not people were meeting physical activity recommendations. As there appears to be a lack of literature investigating self-reported physical activity and quality of life in people with Type 2 diabetes, with and without peripheral neuropathy, the following literature is based on a general adult population.

Bize et al. (2007) conducted a systematic review assessing levels of physical activity and health-related quality of life in adults, and found a consistent positive association between levels of self-reported physical activity and quality of life. Lustyk et al. (2004) used the Godin Leisure Time Physical Activity (LTPA) scale and Quality of Life Inventory (QOLI) to assess the relationship between self-reported physical activity and quality of life, and found a significant difference in quality of life scores between those who participated in low and high levels of physical activity. Specifically, the highest quality of life scores were found in the most frequently active group, however this consisted of light physical activity as opposed to strenuous activity (Lustyk et al., 2004). Acree et al. (2006) found a similar relationship between physical activity and quality of life using the Johnson Space Centre Physical Activity Scale and the SF-36. The study showed that health related quality of life in all eight domains of the SF-36 were significantly higher in

the group who reported higher levels of physical activity, however in comparison to Lustyk et al. (2004), this was adjudged to physical activity of at least moderate intensity for more than one hour per week (Acree et al., 2006). More recently, a study by Tessier et al. (2007) assessed if changes in physical activity over three years was associated with changes in quality of life, and found that increased physical activity was associated with higher scores in several domains of health related quality of life. The study used the SF-36, and the Modifiable Activity Questionnaire to attain self-reported physical activity data (Tessier et al., 2007).

Several researchers have gone further to categorise the level of self-reported physical activity into those who did, and did not, meet current physical activity recommendations. Brown et al. (2003) assessed whether recommended levels of physical activity, defined as at least 30 minutes of moderate intensity exercise on five or more days per week, or 20 minutes of vigorous activity on three or more days per week, were associated with better levels of health related quality of life through the number of 'unhealthy days' (decreased sense of physical or mental well-being) during the previous 30-day period. The study analysed data from the 2001 Behavioural Risk Factor Surveillance System (BRFSS) survey. The authors found a significant difference in unhealthy days between those respondents who were inactive compared to those who met physical activity recommendations. Further to the above mentioned study, Brown et al. (2004a) used data from the same survey to assess the dose-response relationship between self-reported physical activity and health related quality of life using the same physical activity recommendations. Similarly, it was reported that those who were classified as inactive reported more unhealthy days than those who engaged in some physical activity (but did not meet recommendations) and those who did meet recommendations (Brown et al., 2004a). Also of interest was that adults who participated in no vigorous activity, and those who engaged in vigorous activity for all seven days of the week were more likely to have more unhealthy days compared those who did not, indicating that doing too much vigorous activity may reduce any benefits related to quality of life (Brown et al., 2004a). Finally, Vuillemin et al. (2005) used the Modifiable Activity Questionnaire and the SF-36 to assess the relationship of meeting physical activity recommendations and quality of life using the same recommendations as Brown et al. (2003) and Brown et al. (2004a) mentioned above. Vuillemin et al. (2005) found that those who met these recommendations had a better health related quality of life compared to those who did not.

Despite the above evidence relating higher levels of physical activity to better quality of life, a review of the literature has failed to find the same level of evidence in those with diabetes, and those with diabetes and peripheral neuropathy. Taylor et al. (2010) assessed individuals with pre-diabetes, otherwise referred to as impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) using the Godin LTPA questionnaire and the RAND-12 Health Status Inventory. Physical activity recommendations were classified as 30 minutes of moderate intensity activity on five days of the week, or 20 minutes of vigorous activity on three days of the week. The results indicated that meeting physical activity recommendations was associated with better physical and mental quality of life functioning, with significant correlations between moderate MET-min/wk (METs: metabolic equivalent) and total MET-min/wk and physical health composite scores and mental health composite scores (Taylor et al., 2010).

This review thus far has highlighted that research into the effect of exercise in people with Type 2 diabetes and peripheral neuropathy is emerging. Despite this, the few studies which have been reported here often varied in methodology and outcomes, and mostly involved small sample sizes. The outcomes assessed included electrophysical and functional measures, yet no study reported the impact of an exercise program on quality of life. Despite various studies investigating the role of exercise interventions and self-reported physical activity on quality of life in adult populations, there is limited evidence of the effect of exercise and self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy.

Guidelines and Recommendations of Physical Activity and Exercise

Within this literature review it is proposed that physical activity is beneficial for people with diabetes and peripheral neuropathy due to its various biological, psychological and social benefits. Many recommendations have been made about the use of physical activity to reduce chronic disease risk, optimise general health, and specifically for those with diabetes, enhance glycemic control (Warren, 2010). Published physical activity recommendations for adults, older adults and for individuals with diabetes are presented in Table 5. It can be noted that the recommendations across these three groups are all very similar indicating moderate intensity physical activity is required to meet recommendations.

Although the majority of the recommendations are derived from the United States, it has been noted that physical activity recommendations for older Australians are in agreement with the American College of Sports Medicine and the American Heart Association (AHA) (Sims et al., 2010). Most recently, Exercise and Sports Science Australia (ESSA) released a position statement about physical activity for people with Type 2 diabetes indicating an accumulation of a minimum of 210 minutes of moderate intensity (40-59% HRR, 12-13 RPE) exercise per week, or 125 minutes of vigorous intensity exercise (60-84% HRR, 14-16 RPE) with two or more resistance training sessions (2-4 sets, 8-10 repetitions) included (Horden et al., 2012) is recommended for health.

Table 5 Aerobic physical activity recommendations as recommended by leading health bodies in the United States from 2000 to 2010

	Intensity	**Frequency**	**Duration**
Healthy Adults			
ACSM/AHA (2007)	3-6 METs (moderate) > 6 METs (vigorous)	5 d/wk (moderate) 3 d/wk (vigorous)	30 min/d (moderate) 20 min/d (vigorous)
ACSM (2010)	40-60% VO_2R (moderate), ≥ 60% VO_2R (vigorous)	3-5 d/wk	20-30 min/d
Older Adults (≥ 65 years)			
ACSM/AHA (2007)	5-6/10 effort (moderate), 7-8/10 effort (vigorous)	5 d/wk (moderate) 3 d/wk (vigorous)	30 min/d (moderate) 20 min/d (vigorous)
Adults with Type 2 diabetes			
ACSM(2000a)	40-70% VO_2max	3-5 d/wk	10-15min/d, progressing to 30 min/d
ADA (2004)	40-60% VO_2 max (moderate) > 60% VO_2max (vigorous)	3 d/wk	150 min/wk (moderate), 90 min/wk (vigorous)
ACSM(2010)	50-80% VO_2R, RPE 12-16/20	3-7 d/wk	150 min/wk

ACSM = American College of Sports Medicine, AHA = American Heart Association, ADA = American Diabetes Association, METs = Metabolic equivalents, VO_2max: maximal oxygen uptake, VO_2R: oxygen uptake reserve, RPE = Rate of perceived exertion, d/wk = days per week, min/d = minutes per day

Despite the apparent abundance of literature associated with the physical activity recommendations for people with Type 2 diabetes, only general recommendations for those with Type 2 diabetes and peripheral neuropathy have been reported. The ACSM and the ADA has released several papers over the past 20 years outlining these recommendations as shown in Figure 1. As can be seen from Figure 1, only general recommendations have been provided for people with diabetes and peripheral neuropathy, with only the most recent ADA/ACSM (2010) position statement indicating weight-bearing activity may be performed. However, it should be noted that the ADA and ACSM both described the level of evidence as:

> 'Limited randomised controlled trials which are small in size and results are inconsistent, or, evidence from well-constructed cohort studies including prospective cohort, or, a meta-analysis of cohort studies' (ACSM/ADA, 2010) p. 2284

The ADA/ACSM (2010) position statement cited two studies that led them to conclude that weight-bearing activity could be performed safely in people with diabetes and peripheral neuropathy. LeMaster et al. (2003) found that daily weight-bearing activity over a two year period did not increase the risk of foot re-ulceration in a sample of participants with diabetes with a history of foot ulceration. Furthermore, the authors concluded that weight-bearing activity duration appeared to have reduced foot ulcer risk (LeMaster et al., 2003). The second study cited by the ADA/ACSM has already been discussed in this literature review, and is the 'Feet First' randomised controlled trial by LeMaster et al. (2008). This study found that the promotion of weight-bearing activity did not lead to a significant increase in foot ulcers. This is in contrast to a previous study which concluded participants with diabetes and a history of previous ulcers may be susceptible to tissue injury even at low levels of cumulative stress (lower levels of physical activity)(Maluf and Mueller, 2003). This was supported by Armstrong et al. (2004) which found that participants with diabetes who develop ulcers may have a lower level of overall physical activity.

Recently, the position statement provided by ESSA again only provided general recommendations for physical activity including appropriate footwear, regular foot inspection and low impact exercises (Horden et al., 2012).

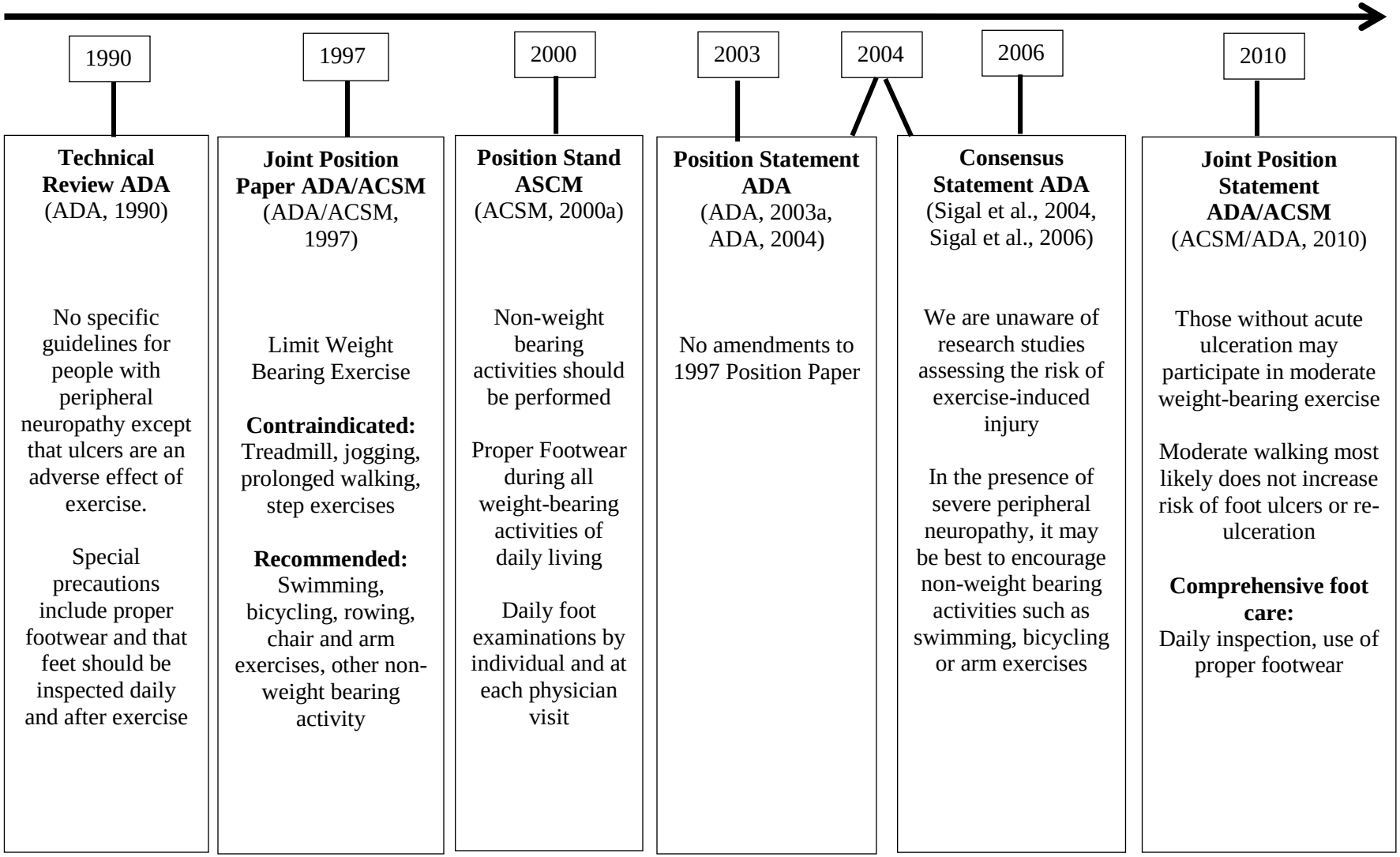


Figure 1 A timeline of ADA/ACSM recommendations for physical activity in people with diabetes and peripheral neuropathy 1990-2010

Despite the development of the above physical activity recommendations, a challenge remains in ensuring people with diabetes adhere to them and in particular, adhere to the correct intensity of the physical activity; a message which appears to be lost as shown in the studies below. In addition to people with diabetes being less likely to report regularly exercising, walking has been reported as the activity of choice for people with diabetes (Ford and Herman, 1995). More recently, Forbes et al. (2010) and Barrett et al. (2007) also found that walking was the most preferred form of physical activity. Walking may not satisfy the minimum moderate intensity level of exercise required to meet physical activity recommendations.

Several studies have been published in the past ten years assessing the levels of self-reported physical activity in people with Type 2 diabetes in the United States (as a sub-set of a larger population), and whether or not they met current physical activity recommendations (Table 6). A review of the current literature did not find similar articles for people with diabetes within Australia.

Table 6 Percentage (%) of physical activity adherence according to AHA, ADA or ACSM recommendations in people with diabetes in the United States

Author	Year Collected	n	Data Source	Recommendations	%
Resnick et al. (2006)	1999-2002	648	NHANES	150min/wk moderate or 90min/wk vigorous	28.2
Morrato et al. (2007)	2003	1825	MEPS		39
Zhao et al. (2011)	2007	18,370	BRFSS		25
Zhao et al. (2008)	2005	13,608	BRFSS		41.7
Nelson, Reiber & Boyko (2002)	1988-94	1480	NHANES	150min/wk moderate or 60min/wk vigorous	31
Strom, Lynch & Egede (2011)	2007	52, 817	BRFSS		35.9

AHA: American Heart Association
ADA: American Diabetes Association
ACSM: American College of Sports Medicine
BRFSS: Behavioural Risk Factor Surveillance System
NHANES: National Health and Nutrition Examination Survey
MEPS: Medical Expenditure Panel Survey
DM: Diabetes Mellitus
T2D: Type 2 diabetes
min/wk: minutes per week

No studies on self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy were found as part of this review, and accordingly, whether or not people are meeting current physical activity recommendations. Given the importance of physical activity in the management of people with Type 2 diabetes and peripheral neuropathy, further attention is warranted to investigate if these recommendations are being met.

Research into physical activity has broadened in recent years to include investigations into sedentary behaviours such as sitting and its effects on health and reported levels of physical activity. In direct opposition to being physically active, the sedentary behaviours of individuals may play a negative role in the challenge of promoting physical activity and exercise as a management tool within this group. Accordingly, sedentary behaviour such as sitting is an important factor to investigate in people with Type 2 diabetes and peripheral neuropathy.

People who sleep an average of eight hours per day and meet physical activity recommendations of 30 minutes of moderate intensity exercise per day, still have 15 ½ hours unaccounted for in a day (Hamilton et al., 2008). Whilst it is not uncommon for people to spend half of their waking day sitting, current public health recommendations focus largely on increasing physical activity, with little or no reference given to what people are doing during the non-exercising time (Hamilton et al., 2008, Hamilton et al., 2007, Patel et al., 2010). It has been calculated that the physical activity recommendations of 150 minutes of moderate intensity during the week only represents approximately 3% of the time most people spend awake (Katzmarzyk, 2010). Several authors have reported that people have been spending an increasing amount of time in sedentary behaviour involving extended periods of sitting and this trend is expected to continue with changes in transportation, communications, workplace, domestic and technological environments (Owen et al., 2010, Hamilton et al., 2007).

It has been noted by several authors that there may be significant adverse metabolic and health effects from extended periods of sitting such as obesity, waist circumference, body mass index, systolic blood pressure, fasting triglycerides, High Density Lipoprotein (HDL) cholesterol, 2-hour post load plasma glucose, and fasting insulin (Thorp et al., 2010, Bankoski et al., 2011, Owen et al., 2009, Patel et al., 2010). Furthermore, results from a recent study indicated leisure time spent sitting was positively associated with all-cause mortality in both men and women (Patel et al., 2010). Disturbingly, authors have also found that these detrimental effects from

sitting were independent of physical activity, meaning the positive effects of adhering to physical activity recommendations may be 'undone' if the remaining 15 ½ hours of waking time is spent sedentary (Hamilton et al., 2008, Owen et al., 2010, Patel et al., 2010). Accordingly, authors have been careful to note that the theory of 'too much sitting' is distinct from doing 'too little exercise' (Hamilton et al., 2008, Owen et al., 2010). This new area of research suggests that along with the promotion of current physical activity guidelines, public health guidelines should be implemented for sedentary behaviour, in particular sitting (Hamilton et al., 2008, Katzmarzyk, 2010).

A review of the literature has not detected a body of knowledge regarding the sitting behaviours of people with diabetes and people with diabetes and peripheral neuropathy. In light of the evidence cited above that excessive sitting may be detrimental to an individual despite the person meeting physical activity recommendations (Owen et al., 2010, Patel et al., 2010), it is therefore important to not only understand the levels of physical activity in people with diabetes and peripheral neuropathy, but to also to understand their sitting behaviours.

Safety precautions for people with Type 2 diabetes and peripheral neuropathy.

There are several precautions which must be taken to ensure the safety of participants during the implementation of an exercise program. Several studies described below have also noted the importance of these precautions and have provided details of the safety measures they undertook, and reported any adverse outcomes during the study period.

Studies that used a single mode of exercise in people with diabetes and peripheral neuropathy (strengthening or aerobic modes) did not report any serious adverse effects, however they did not provide a comprehensive explanation of the safety measures implemented. Richardson et al. (2001) reported one participant withdrawing from the intervention due to foot and ankle pain attributed to the exercise program, but did not detail any safety precautions used throughout the program, and whether or not these were adhered to. All of the participants of the Fisher et al. (2007) study completed the study and no adverse events were reported. Participants were advised to inspect their feet on a weekly basis at minimum, and were also required to measure their blood glucose levels before and after each exercise session. Ahn and Song (2012) reported that no adverse events occurred during their program, however similarly to Richardson et al. (2001),

they did not detail any other safety measures other than the monitoring of blood glucose levels before and after exercise. Despite the seemingly positive results above, it would seem important that more focus is given to reporting what safety measures or protocols were followed.

Studies involving the use of a combined aerobic and resistance training program in people with diabetes and peripheral neuropathy have provided more detail about the safety measures implemented, along with a more robust discussion about safety outcomes. Two participants did not complete the combined aerobic and resistance program by Otterman et al. (2011), however reasons for their withdrawal were not reported other than they were not due to an adverse event. Participants were required to check their blood glucose levels before and after each session. Foot examinations were performed immediately after the exercise sessions during the first week by a physiotherapist and thereafter participants were advised to complete the checks at home at least on every training day (Otterman et al., 2011). A total of 52 adverse events were recorded throughout the program, with only 16 of these being directly attributed to the exercise. Adverse events were classified as either being cardiovascular, foot, blood glucose regulation, musculoskeletal or other, with blood glucose regulation being the major contributor (Otterman et al., 2011).

Kluding et al. (2012) noted that there were no serious adverse events during testing or intervention stages, nor were there any infection or delayed healing at any biopsy site, and no ulcers were developed throughout the study (Kluding et al., 2012). The authors cited the CTC Common Toxicity Reporting Guidelines to report several Grade 2 (mild severity requiring minimal intervention) adverse events namely hyperglycemia, hypoglycemia prior to exercise, high resting blood pressure prior to exercise, pain in legs, knees, back or hands with exercise, and pain or itching at biopsy site (Kluding et al., 2012).

LeMaster et al. (2008) taught their participants foot related self-care skills, referred the participants to a podiatrist for therapeutic footwear, and provided the participants with a dedicated hotline to report any lesions to the feet. During study visits, investigators also examined all surfaces of each participant's feet. A total of 57 foot lesions were reported during the 12-month study, nine of which were due to self-inflicted self-care. The authors reported one non-ulcerative adverse event which may have been related to the strengthening program whereby one participant sustained a great toe fracture.

The highest level of safety precautions against foot injury came from Tuttle et al. (2012) who reported using visual inspection, digital photographs and foot skin temperature to document skin condition before and after each exercise session. Despite several occasions whereby the temperature difference between the left and right foot were enough to postpone the exercise session, no adverse events to the feet were reported in relation to the exercise program (Tuttle et al., 2012). Similarly, Mueller et al. (2013) reported using visual inspection and skin temperature assessments before and after each exercise session. A total of 13 lesions (in 12 participants) and four ulcers (in three participants) were documented throughout the study. All lesions were superficial with the average time to heal being 8.8 ± 7.2 days. The authors also reported several participants modifying their aerobic activity, or deferring the sessions because of pain.

Despite recent amendments to the physical activity recommendations for those with diabetes and peripheral neuropathy to allow moderate weight bearing activity (ACSM/ADA, 2010), it would seem sensible that safety protocols and reporting of adverse events are reported more routinely than seen to date, to help build the body of knowledge of what exercise is safe and what is not.

Within this review of the literature, the risk of ulceration and amputation within people with diabetes and peripheral neuropathy, and the impact these outcomes have on the functional status and quality of life for these individuals has been highlighted. Also discussed have been the sensory impairment, painful symptoms, and loss of lower limb strength in people with diabetes and neuropathy and how these factors are also linked with reduced functional capacity and quality of life. It is therefore important that these issues are included when assessing the safety of an exercise program. For these reasons, it is important that exercise is prescribed to people with Type 2 diabetes and peripheral neuropathy by trained exercise professionals who are able to monitor the individual's safety throughout training.

Modes of exercise for people with Type 2 diabetes and peripheral neuropathy

Within this review it has been proposed that physical activity and exercise is an appropriate management tool for people with Type 2 diabetes and peripheral neuropathy due to its biological, psychological and social benefits. However, the mode of activity is an important variable which must be assessed to ensure individuals are gaining maximum benefits within a safe environment. The most commonly assessed measure used to determine the efficacy of a mode of exercise reported in this review, whether it aerobic, resistance or a combination of the two for people with diabetes, appears to be HbA1c.

Aerobic training

Aerobic exercise is often prescribed to people with Type 2 diabetes as it provides many beneficial effects such as reducing metabolic risk factors for cardiovascular diseases including insulin resistance (Yokoyama et al., 2004) and it has been found to significantly decrease fasting plasma glucose levels (Short et al., 2003). Aerobic exercise has also been found to have a beneficial effect on insulin sensitivity (Cuff et al., 2003) and levels of HbA1c (Lambers et al., 2008, Sigal et al., 2007). The current recommendations of the duration and intensity of aerobic exercise for people with diabetes was provided in Table 5. The types of aerobic training typically recommended for people with diabetes and peripheral neuropathy have included low weight bearing activities such as swimming, rowing and cycling (Sigal et al., 2006), but now moderate weight bearing activities such as walking have been included (ACSM/ADA, 2010).

Resistance training

More recently several researchers have investigated the benefits of resistance training to those with Type 2 diabetes. Once considered to be unsafe in those with diabetes with correct monitoring, resistance training has the ability to arrest much of the functional decline associated with diabetes compared to aerobic exercise as it targets body composition, muscular endurance, muscular strength and flexibility (Colberg, 2013).

The effect of resistance training on long term glycemic control is uncertain with many studies finding varied results. Improvements in glycemic control have been reported in three recent systematic reviews which reported that resistance training was an effective intervention to improve glycemic control (Eves and Plotnikoff, 2006, Irvine and Taylor, 2009, Gordon et al.,

2009), with Irvine and Taylor (2009) reporting a significant reduction of 0.3% in HbA1c. Furthermore, Bweir et al. (2009) compared a ten week resistance training program to an aerobic program in people with Type 2 diabetes, and found that whilst both modes of exercise significantly decreased HbA1c the greatest reduction was noted in the resistance group with 40% of this group reporting a target HbA1c level of 7.0% or less.

However, several studies which were included in the above systematic reviews, reported no change in the levels of HbA1c after a resistance training program (Dunstan et al., 2005, Dunstan et al., 1998, Ibanez et al., 2005, Ishii et al., 1998). Possible reasons for the results include the short duration of the intervention (eight weeks or less) and low intensities (40-50% and 50-55% 1RM) for the Ishii et al. (1998) and Dunstan et al. (1998) studies respectively. Although Ibanez et al. (2005) did not observe any change in HbA1c levels, it is important to note that the study resulted in improved insulin sensitivity of the participants, and that the authors still recommended the use of resistance training as a potential adjunct therapy in the management of Type 2 diabetes. Finally, Dunstan et al. (2005) reported the changes in HbA1c during the second phase of an intervention whereby participants continued training from home. It was within this home setting that HbA1c levels increased suggesting that the most beneficial improvements come from a gym-based supervised program.

The ACSM has recommended that those with Type 2 diabetes participating in resistance training programs do so two to three days per week with a minimum of eight to ten exercises involving all the major muscle groups, and at a minimum of eight to 12 repetitions per set, at an intensity of 60-80% 1RM (ACSM, 2010). Of the studies described above, those programs which had a positive influence on long-term glycemic control used intensities at a minimum of 50% 1RM and up to a maximum of 85% 1RM (Cohen et al., 2008, Dunstan et al., 2002a).

Combined aerobic and resistance training

Many researchers have assessed the effects of a combined aerobic and resistance training program on HbA1c levels when compared to a control group, an aerobic group, a resistance group, or a combination of all three. Many of these studies have recently been compared in a systematic review by Oliveira et al. (2012). An extensive search of the literature yielded 28 studies meeting the specified search criteria, with publications dated between 2000 and 2011. The results found 17 studies where a combined program resulted in significant reductions in

HbA1c, and a further three studies with a clinically significant benefit (Oliveira et al., 2012). Furthermore, two studies found contrasting results concluding that separate aerobic and resistance programs produced a more noticeable absolute change in HbA1c than a combined program. Despite this, it was concluded that although there were vast differences in methods across all studies, a combined aerobic and resistance training program improves glycemic control when compared to either type alone (Oliveira et al., 2012). The literature presented above provides justification for the use of a combined aerobic and resistance training program due to its superior effect on levels of HbA1c, and the fact that a resistance component is beneficial to combating the functional decline associated with diabetes and peripheral neuropathy.

Summary of the review of literature

This review of the literature has identified that people with Type 2 diabetes and peripheral neuropathy experience a number of complications of the lower limb including impaired sensory feedback and painful symptoms (AIHW, 2008), risk of ulceration and amputation (Bansal, Kalita & Misra 2006), and decreased lower limb strength (Ijzerman et al., 2012). Activities of daily living are also said to be negatively affected in people with Type 2 diabetes and peripheral neuropathy (Liedberg and Vrethem, 2009). These issues lead to people with Type 2 diabetes and peripheral neuropathy having a poorer quality of life compared to those with Type 2 diabetes alone, and the healthy population (Vileikyte et al. 2005). Despite physical activity being recommended as an important management strategy for people with diabetes (Warren, 2010), the review conducted as part of this thesis found no specific recommendations for people with Type 2 diabetes and peripheral neuropathy. Despite the positive link between exercise and physical activity and improvement in physical function and quality of life, there is limited English-language literature available investigating the safety of physical activity and exercise for people with Type 2 diabetes and peripheral neuropathy.

Research Aims

The literature discussed within this review has provided justification for the three research studies conducted within this PhD. The research aims for each study are described below.

Study 1 – Chapter 4

- To investigate the amount of self-reported physical activity in those with Type 2 diabetes, and those with Type 2 diabetes and peripheral neuropathy, and determine whether or not they are meeting physical activity recommendations.

Study 2 – Chapter 5

- To investigate the level of self-reported quality of life in those with Type 2 diabetes and peripheral neuropathy and identify if any relationship exists between quality of life and self-reported physical activity. The study will also investigate whether or not there is a difference in self-reported quality of life between those who meet current physical activity recommendations, compared to those who do not.

Study 3 – Chapter 6

- To investigate a prescribed, supervised aerobic and resistance training program on people with Type 2 diabetes and peripheral neuropathy, assessing safety, quality of life, sensation and physical function.

CHAPTER 3: Theoretical Framework and Research Design

Theoretical Framework

Portney and Watkins (2000) discuss that the use of theories and models in research can aid in the development of new knowledge by providing a summary of previous findings, and thus predict how variables may be related when answering significant clinical questions. They also go on to say that upon the development of research questions, observations can be made to support, reject or modify the theory and thus create theoretical generalisations to predict future outcomes (Portney and Watkins, 2000). It has also been suggested that a theoretical framework provides the researcher with structure and boundaries to work within by identifying the major elements and variables which organise a study (Ennis, 1999).

As discussed in Chapter 2, diabetes and its complications, namely peripheral neuropathy, is multi-faceted and its effects are not restricted to biological outcomes, but also involve psychological and social aspects. Various frameworks within exercise and physical activity were investigated however were not deemed appropriate for this study due to their focus on behaviour change such as the Transtheoretical model (Prochaska and Velicer, 1997), or their focus on biomechanical outcomes of the human body, such as the Dynamical Systems Theory (Thelen and Smith, 2007). Within this thesis the Biopsychosocial (BPS) model was chosen because it encompasses the biological, sociological and psychological aspects of disease. Further exploration of the biopsychosocial model is presented below.

The Biopsychosocial Model

It has been reported that up until the late 1970s it was widely accepted that disease or illness could be fully attributed to deviations from standard measureable biological variables, otherwise known as the biomedical model. Engel (1977) described the then current state as a crisis within medicine as physicians were not concerning themselves with issues deemed to lie outside medicine's responsibility and authority, and hence neglecting any social, psychological and behavioural dimensions of illness. As such, Engel (1977) proposed a Biopsychosocial model:

> 'To provide a basis for understanding the determinants of disease and arriving at rational treatments and patterns of health care, a medical model must also take into account the patient, the social context in which he lives, and the complementary system devised by society to deal with the disruptive effects of illness, that is, the physician's role and the health care system. This requires a biopsychosocial model'

Furthermore, the BPS model can be viewed as both a philosophy of clinical care and a practical clinical guide. From a philosophical viewpoint, the BPS model is a way of understanding how disease and illness are affected through multiple levels of organisation from molecular through to societal, whilst practically, it is a way of understanding a patient's subjective experience as a contributing factor to diagnosis, health outcomes and humane care (Borrell-Carrio et al., 2004). Figure 2 is a representation of the BPS model.

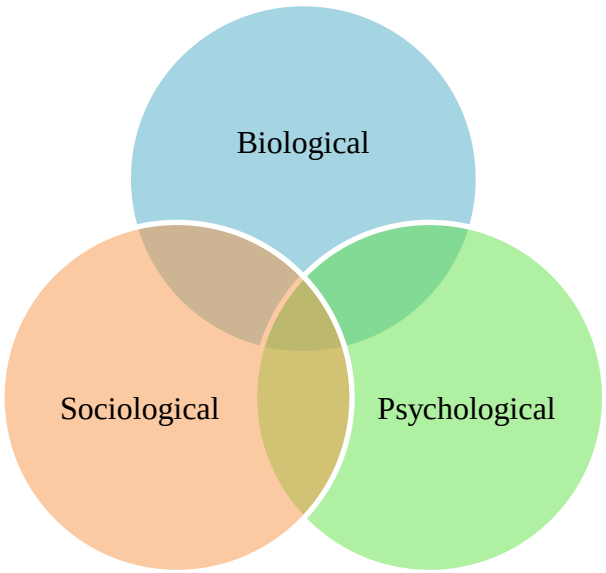


Figure 2 The Biopsychosocial Model (Engel, 1977)

From an exercise science perspective, the study of human movement is influenced by many factors including biological, health, and social factors, and therefore the methods, theories and knowledge of a wide range of disciplines including but not limited to, biological, physical and social sciences must be integrated (Abernethy et al., 2005). Accordingly, the studies outlined in this thesis will use the BPS model to understand the role of physical activity in those with Type 2 diabetes and peripheral neuropathy linking not only the biological and physical response to exercise, but assessing the sociological and psychological aspects through quality of life domains. Within this thesis, measures were used that underpin the core concepts of exercise and quality of life which places this research within a biopsychosocial domain. These measures include self-reported physical activity and quality of life, and the effects of an exercise program on safety, sensation, functional and quality of life domains.

Australian Safety and Quality Framework for Health Care

For the implementation of the exercise intervention in Chapter 6, the Australian Safety and Quality Framework for Health Care, developed by the Australian Commission on Safety and Quality in Healthcare was used to guide the study. As discussed in Chapter 2, only broad recommendations about exercise have been provided to those with Type 2 diabetes and peripheral neuropathy, most of which focus on the precautions and safety measures which must be taken due to the high risk associated with peripheral neuropathy. As discussed, there is a lack of research in this area leading to a lack of clarity about exercise prescription for people with diabetes and peripheral neuropathy. Accordingly, it was important in this thesis to follow the three underlying principles of the Australian Safety and Quality Framework, being that the exercise program was consumer centred, driven by information and organised for safety. Within these three principles are 21 areas for action, 11 of which specifically apply to those who work within a healthcare team, and nine of which can be applicable to this research. Table 7 provides a description of these areas for action, and how they were implemented into study three (Chapter 6) of this thesis.

Table 7 Application of the Australian Safety and Quality Framework for Health Care within this thesis

Core principle	Areas for action	Description	Application to this research
1. Consumer centred	1.2 increase health literacy	Use of patient decision aids (booklets, videos, websites) help people become involved in decision-making by providing information about different treatment options	Not applicable to a research setting
	1.3 partner with patients, families and carers to share decision making about their care		
	1.4 provide care that respects and is sensitive to different cultures	Check with patients they understand the information you are providing, particularly when there may be technical or complex information relevant to choices about treatment. Be aware and respect cultural beliefs	Aimed to use clear communication with all participants
	1.6 Improve continuity of care	Regularly and accurately update clinical records and intended treatment plan for other disciplines	Good records were kept and there was ongoing communication with other staff (podiatry, EP clinic)
	1.7 Minimise risks at handover	Make sure that clinical handover protocols are used when patients are transferred between services	Appropriate communication was used when different therapists were involved with participant care

EP: Exercise Physiology

Table 7 cont. Application of the Australian Safety and Quality Framework for Health Care within this thesis

2. Driven by Information	2.1 Use agreed guidelines to reduce inappropriate variation in the delivery of healthcare	Adopt clinical guidelines that you will use consistently, feedback your own experiences to any organisational or professional review process and adopt new information as it becomes available. Consistent application of well evidenced clinical guidelines is a part of high-quality, safe clinical practice	Extensive literature reviews were undertaken. Guidelines from ACSM, ADA, ESSA and WHO were considered when implementing the exercise intervention
	2.2 collecting and analysing safety and quality data to improve care 2.3 learn from patients' and carers' experiences	Participate in the gathering and analysis of safety and quality information within your organisation. Support and encourage patients and families to make their views and experiences known. Review any information, including reflecting on own performance, and identifying where changes and improvements can be made	Collected and analysed data for the study. Participants were encouraged to give feedback along the way. Exercise programs were individualised based on participant feedback (RPE).
	2.4 encourage and apply research that will improve safety and quality	Regularly check the key sources of safety and quality research results. Discuss findings with colleagues and broader clinical teams	Disseminating the research through thesis and publications
3. Organised for Safety	3.2 Health professionals take action for safety 3.8 Take action to prevent or minimise harm from healthcare errors	Follow processes for reporting patient incidences, take direct action to reduce or prevent risks of patient harm and participate in the ongoing analysis of adverse patient events. Also take an active role in adopting recommendations for change that come from incident analysis	Recorded all adverse events during exercise program and implemented strategies to prevent them from happening again.

ACSM: American College of Sports Medicine
ADA: American Diabetes Association
ESSA: Exercise and Sport Science Australia
WHO: World Health Organization
RPE: Rate of Perceived Exertion

Research Design

This section introduces the assessment of physical activity and quality of life, concepts important to study one (Chapter 4) and study two (Chapter 5), and single case experimental designs, the approach used in study three (Chapter 6).

Assessment of physical activity

Assessing physical activity levels within the population has become important in research to help determine relationships between physical activity and health outcomes (Westerterp, 2009). The range of techniques used to assess physical activity can be grouped into subjective, criterion, and objective methods (Vanhees et al., 2005). Subjective measures of physical activity were used in study one, presented in Chapter 4.

Subjective methods of physical activity assessment include behavioural observation and self-report measures which can be further divided into physical activity diaries, questionnaires, interviewer administered questionnaires and proxy-report questionnaires (Dale et al., 2002, Vanhees et al., 2005). In this thesis a self-report questionnaire was used to assess the levels of physical activity in people with Type 2 diabetes, and Type 2 diabetes and peripheral neuropathy. Self-report measures are commonly used as they are inexpensive, place a low burden on participants and are easily applicable to large populations, only requiring a pen and pencil to collect the data (Dale et al., 2002, Westerterp, 2009, Vanhees et al., 2005). However due to the subjective interpretation of the questions and perceptions of physical activity itself, the reliability and validity of self-report measures may be affected, with the possibility of over or under-estimation of actual physical activity (Prince et al., 2008, Vanhees et al., 2005).

For the purpose of assessing the physical activity of those with Type 2 diabetes and those with peripheral neuropathy, self-report measures are most desirable due to their low cost, and ability to attract large numbers of participants due to their simplicity. In the absence of other inexpensive, readily available, non-invasive and reasonably reliable and valid options, researchers are frequently using questionnaires to measure physical activity (Vandelanotte et al., 2010, Neilson et al., 2008).

Criterion methods include doubly labeled water and objective methods include motion sensors such as pedometers and accelerometers (Vanhees et al., 2005). The method of doubly labeled water is expensive and intrusive to the participants, making the method less desirable for larger studies, and therefore was not considered for use within this thesis (Shephard, 2003, Dale et al., 2002, Vanhees et al., 2005). Furthermore, motion sensors were not deemed appropriate for this thesis due to their cost and methodological issues such as compliance with protocols, frequency and sources of data error and the physical proximity of the participant for data collection (Schmidt et al., 2007, Prince et al., 2008). It has also been suggested that participants may show a reactive response as they know their physical activity is being assessed, with research finding that physical activity can increase by up to 2000 steps per day (Shephard and Aoyagi, 2010). Table 8, adapted from Dale et al. (2002) and Vanhees et al. (2005), summarises the advantages and disadvantages of some of the criterion, objective and subjective measures discussed here.

Table 8 The advantages and disadvantages of criterion, objective and subjective methods used to collect physical activity data

Method	Advantages	Disadvantages
Criterion		
Doubly labelled water	'Gold standard' Precision of Measurement	Invasive Expensive Not appropriate for large studies
Objective		
Pedometer	Non-invasive Inexpensive Used in a variety of settings	Promotes behaviour change Only assesses 'steps' ,does not account for intensity Does not account for upper body movements
Accelerometer	Non-invasive Used in a variety of setting Indicates intensity of activity	Promotes behaviour change Does not account for upper body movements Expensive for large studies
Subjective		
Direct observation	Non-invasive Provides qualitative and quantitative feedback	Time-intensive Promotes behaviour change Limited monitoring time
Self-report measures	Non-invasive Suitable for large studies Inexpensive Low participant burden	Decreased validity and reliability due to bias and misinterpretation of questions. May lack detailed information of physical activity

(Dale et al., 2002, Vanhees et al., 2005)

Shephard and Aoyagi (2010) have recognised that the questions need to be relative to the population being sampled. When assessing the physical activity habits of older adults, it is important to note many lack permanent employment and as such, questions about occupational activity, or extreme sports would not be valid, resulting in participant boredom and careless responses (Shephard and Aoyagi, 2010). Finally, when choosing the instrument, it is important that various techniques produce data which is not always comparable, and the ability to convert this raw data into a range of commonly used outcomes is necessary for comparison (Dale et al., 2002). Following an extensive review of commonly used physical activity questionnaires (Tables 9, 10 and 11), the short-form International Physical Activity Questionnaire (IPAQ) was deemed most appropriate to collect self-reported physical activity data in this thesis, and is discussed further in Chapter 4. Tables 9, 10 and 11 presents the measurement properties, validity and reliability of some commonly used physical activity questionnaires respectively, including the short-IPAQ.

Table 9 Measurement properties of commonly used physical activity questionnaires

Questionnaire	Reference	Type of activity recorded	Recall period	Administration	Number of questions	Measurement scale
Active Australia	(AIHW, 2003)	LTPA	Last 7-d	Interview: phone or face-to-face	8	Min/wk
Baecke	(Baecke et al., 1982)	Habitual PA	Not specified	Self-administered	16	Activity score
CHAMPS PA Questionnaire	(Stewart et al., 2001)	Daily, recreational activities & exercise	Typical wk in the past mo	Self-administered or interview	41	Frequency/wk Cal. expenditure/wk
EPIC PA Questionnaire	(Haftenberger et al., 2002)	Occupation, leisure, household domains	Typical wk in past yr	Self-administered or face-to-face interview	14	hr/wk MET-hrs/wk
Flemish PA Questionnaire	(Matton et al., 2007)	Dimensions of PA and sedentary behaviour	Usual wk	Self-administered Computerised	Up to 90	hr/wk kcal/hr kcal/wk
Godin	(Godin and Shephard, 1985)	LTPA	Usual wk	Self-administered	4	Frequency/wk
Harvard Alumnus Questionnaire	(Paffenbarger et al., 1978)	Stairs, walking, sport	Last 7-d	Self-administered	3	kcal/wk
IPAQ-Short	(Craig et al., 2003)	Health-related PA	Last 7-d	Self-administered or interview	7	MET-min/wk Categorical score
IPAQ-Long	(Craig et al., 2003)	Health-related PA	Last 7-d	Self-administered or interview	27	MET-min/wk Categorical score

CHAMPS: Community Healthy Activities Model Program for Seniors, PA: Physical Activity, EPIC: European Prospective Investigation into Cancer and nutrition, IPAQ: International Physical Activity Questionnaire, LTPA: Leisure Time Physical Activity, d = day, wk = week, min = minutes, Cal = Calories, hr = hour, MET = metabolic equivalent, kcal = kilocalorie

Table 9 cont. Measurement properties of commonly used physical activity questionnaires

Questionnaire	Reference	Type of activity recorded	Recall period	Administration	Number of questions	Measurement scale
Kaiser PA Survey	(Ainsworth et al., 2000)	Sport, recreation, occupation, transport, household	Last 12 mo	Self-administered	75	Activity Score Summary Index
Lagerros	(Lagerros et al., 2006)	Everyday PA	Usual d	Self-administered	9	kcal/day
LTPA Questionnaire	(Parker et al., 1988)	LTPA	last 3mo Last yr	Self-administered	47	kcal/wk/kg
Minnesota LTPA	(Taylor et al., 1978)	LTPA	Last 12mo	Self-administered and interview	62	kcal/day
OA-ESI	(O'Brien-Cousins, 1996)	Work, leisure, sport	7-d	Self-administered	43	kcal/wk
PA Frequency questionnaire	(Bernstein et al., 1998)	Total and activity specific EE	Last 7-d	Self-administered	70	kcal/day
PA Scale	(Aadahl and Jorgensen, 2003)	Sleep, work and leisure	Usual weekday	Self-administered	9	MET-time
Past yr total PA questionnaire	(Friedenreich et al., 2006)	Occupation, household, recreational	Last 12mo	Self-administered	Open Table format	hrs/wk MET-hrs/wk
Saint-Etienne PA questionnaire	(Berthouze et al., 1993)	Habitual PA	Last 7-d	Self-administered or interview	35	METs/day kcal/day kJ/day
Timperio	(Timperio et al., 2003)	Multiple domains of PA	Last 7-d	Self-administered	6	frequency/wk min/wk
Yale PA Survey	(Dipietro et al., 1993)	Occupation, household, exercise	Typical wk in last mo	Interview	40	hrs/wk kcal/wk Categorical index score

PA = Physical Activity, OA-ESI = Older Adult Exercise Status Inventory, LTPA = Leisure Time Physical Activity, EE = Energy Expenditure, mo = month, d = day, wk = week, kcal = kilocalorie, kg = kilogram, MET = Metabolic equivalent, hrs = hours, kJ = kilojoules, min = minute

Table 10 Validity of commonly used physical activity questionnaires

Questionnaire	Reference	Validity			
		Study population		Comparison measure	Results**
		n	Age (years) M ± SD*		
Active Australia	(Heesch et al., 2010)	53	65-89 (range)	Pedometer	ρ = 0.42 (Total PA) ρ = 0.31 (Moderate-Vigorous) ρ = 0.42 (Walking)
Baecke	(Baecke et al., 1982)	306	20-30 (range)	Lean body mass	b = 0.48-1.36 (work) b = 0.23-1.23 (sport) b = 0.15-0.27 (leisure)
CHAMPS PA Questionnaire	(Stewart et al., 2001)	249	74.1 ± 5.6	Measures of health	r = 0.02-0.30
EPIC PA Questionnaire	(Cust et al., 2008)	182	57.2 (mean)	Accelerometer	ρ = 0.29 (total PA)
Flemish PA Questionnaire	(Matton et al., 2007)	62 (employed/ Unemployed) 49 (retired)	39.2 ± 11.8 64.9 ± 5.2	Accelerometer	Employed/unemployed r = 0.27-0.88 Retired r = 0.15-0.85
Godin	(Godin and Shephard, 1985)	306	30.7 ± 9.8	%BF, % VO2 max	% BF r = 0.06-0.21 (range of intensities) r = 0.13 (total) %VO_2 max r = 0.04-0.38 (range of intensities) r = 0.24 (total)
Harvard Alumnus Questionnaire	(Albanes et al., 1990)	21 (Males only)	28-55 (range)	Caloric intake	ρ = 0.49
IPAQ-Short	(Craig et al., 2003)	n = 26-151 (across 5 Countries)	32.7 ± 10.9 to 48.9 ± 6.1 (range of Counties)	Accelerometer	ρ = 0.02-0.47 (PA) ρ = 0.12-0.49 (sitting)
IPAQ-Long	(Craig et al., 2003)	n = 26-151 (across 4 Countries)		Accelerometer	ρ = 0.05-0.52 (PA) ρ =0.25-0.51 (sitting)

*age presented as M ± SD, unless otherwise stated, ** text in parentheses is the comparator for validity, CHAMPS: Community Healthy Activities Model Program for Seniors, PA: Physical Activity, EPIC: European Prospective Investigation into Cancer and nutrition, IPAQ: International Physical Activity Questionnaire, BF = Body Fat, VO_2 = Maximal oxygen uptake

Table 10 cont. Validity of commonly used physical activity questionnaires

Questionnaire	Reference	Validity			
		Study population		Comparison measure	Results**
		n	Age (years) M ± SD*		
Kaiser PA Survey	(Ainsworth et al., 2000)	50 (Female only)	39.1 ± 12.0	VO2 peak, %BF, PA records, accelerometer	r = 0.59-0.62 (VO_2 peak) r = 0.53-0.56 (%BF) r = 0.35-0.42 (PA record) r = 0.49-0.53 (Accelerometer)
Lagerros	(Lagerros et al., 2006)	293	41.2 (mean)	Repeated 24-hr recall	r = 0.73
LTPA Questionnaire	(Parker et al., 1988)	166 (Males only)	43.0 ± 9.9	Physiological measures of PA status	r = 0.01-0.43
Minnesota LTPA	(Taylor et al., 1978)	175 (Males only)	48.4 ± 6.1	Treadmill performance	r = 0.303-0.576
OA-ESI	(O'Brien-Cousins, 1996)	327 (Females only)	77.0 (mean)	Other validated survey instruments	r = 0.411- 0.491
PA Frequency questionnaire	(Bernstein et al., 1998)	41	35-69 (range)	Energy expenditure, 24 hr recall PA	r = 0.76 (EE) r = 0.80 (PA recall)
PA Scale	(Aadahl and Jorgensen, 2003)	39	20-59 (range)	Accelerometer, activity diary	r = 0.20 (Accelerometer) r = 0.74 (Activity diary)
Past yr total PA questionnaire	(Friedenreich et al., 2006)	154	48.7 ± 7.7	Accelerometer, 7-day PA log	r = 0.26, ICC = 0.42 (Accelerometer) r = 0.42, ICC = 0.18 (7-day PA log)
Saint-Etienne PA questionnaire	(Berthouze et al., 1993)	20 (Males only)	56-72 (range)	Caloric intake assessment	r = 0.576
Timperio	(Timperio et al., 2003)	188	38.7 ± 14.9	Accelerometer	r = 0.10-0.40
Yale PA Survey	(Dipietro et al., 1993)	25	69.4 ± 5.5	Physiological measures, accelerometer	r = 0.01-0.60

*age presented as M ± SD, unless otherwise stated, ** text in parentheses is the comparator for validity, PA = Physical Activity, LTPA = Leisure Time Physical Activity, OA-ESI = Older Adults Exercise Status Inventory, VO_2 = maximal oxygen uptake, BF = Body Fat, hr = hour, EE = Energy Expenditure

Table 11 Reliability of commonly used physical activity questionnaires

Questionnaire	Reference	Reliability			
		Study population		Time interval	Results**
		n	Age (years) M ± SD*		
Active Australia Survey	(Brown et al., 2004)	356	18-75 (range)	1-d	ICC = 0.16 (moderate intensity) ICC = 0.56 (walking) ICC = 0.62 (gardening) ICC = 0.64 (vigorous intensity & total PA)
Baecke	(Baecke et al., 1982)	277	20-30 (range)	3 mo	r = 0.88 (Work) r = 0.81 (Sport) r = 0.74 (Leisure)
CHAMPS PA Questionnaire	(Harada et al., 2000)	80	> 65	2-wk	ICC 0.76 (moderate activities) ICC 0.62 (all activities)
EPIC PA Questionnaire	(Cust et al., 2008)	182	57.2 (mean)	10 mo	k = 0.62 (total PA)
Flemish PA Questionnaire	(Matton et al., 2007)	66 (Employed/ unemployed) 36 (Retired)	40.3 ± 12.1 63.5 ± 5.0	2-wk	Employed/unemployed ICC = 0.67-0.99 Retired ICC = 0.14-0.96
Godin	(Godin and Shephard, 1985)	56	18-65 (range)	2-wk	ICC = 0.94 (strenuous) ICC = 0.45 (moderate) ICC = 0.48 (light) ICC 0.74 (total)
Harvard Alumnus Questionnaire	(Jacobs et al., 1993)	78	37.3 ± 9.9	1 mo	r = 0.63 (walking) r = 0.72 (total index score) r = 0.75 (sports) r = 0.78 (stairs)
IPAQ-Short	(Craig et al., 2003)	292	18-65 (range)	3-7 d	ρ = 0.66-0.88 (total PA) ρ = 0.71-0.95 (sitting)

*age presented as M ± SD, unless otherwise stated, ** text in parentheses is the comparator for reliability, CHAMPS: Community Healthy Activities Model Program for Seniors, PA: Physical Activity, EPIC: European Prospective Investigation into Cancer and nutrition, IPAQ: International Physical Activity Questionnaire, d = day, mo = month, wk = week, ICC = intra class correlation

Table 11 cont. Reliability of commonly used physical activity questionnaires

Questionnaire	Reference	Reliability			
		Study population		Time interval	Results**
		n	Age (years) M ± SD*		
IPAQ-Long	(Craig et al., 2003)	294	18-65 (range)	3-7 d	ρ = 0.70-0.91 (total PA) ρ = 0.74-0.89 (sitting)
Kaiser PA Survey	(Ainsworth et al., 2000)	50 (Females only)	39.1 ± 12.0	1 mo	ICC = 0.01-0.85 (Index score) ICC = 0.82-0.83 (Summary score)
Lagerros	(Lagerros et al., 2006)	293	41.2 (mean)	3-wk	ICC = 0.55 (overall) ICC = 0.61 (printed questionnaire) ICC = 0.51 (web-based questionnaire)
LTPA Questionnaire	(Lamb and Brodie, 1991)	118	37.8 ± 11.6	2-wk	R = 0.86 (total)
Minnesota LTPA	(Folsom et al., 1986)	140	35-74 (range)	36 ± 10 d	r = 0.79 (light) r = 0.86 (moderate) r = 0.82 (heavy) r = 0.88 (total)
OA-ESI	(O'Brien-Cousins, 1996)	29	71.0 (mean)	7-d	r = 0.771
Past yr total PA questionnaire	(Friedenreich et al., 2006)	154	48.7 ± 7.7	9-wk	r = 0.64, ICC = 0.66 (total) r = 0.71, ICC = 0.58 (occupational) r = 0.65, ICC = 0.57 (household) r = 0.73, ICC = 0.64 (recreational)
Saint-Etienne PA questionnaire	(Berthouze et al., 1993)	20	23-54 (range)	6-wk	r = 0.997
Timperio	(Timperio et al., 2003)	188	38.7 ± 14.9	3-d	Frequency measures ICC = 0.38-0.80 Duration Measures ICC = 0.22-0.85
Yale PA Survey	(Dipietro et al., 1993)	76	71.5 ± 6.6	2-wk	r = 0.42-0.65

*age presented as M ± SD, unless otherwise stated, ** text in parentheses is the comparator for validity, IPAQ = International Physical Activity Questionnaire, PA = Physical Activity, LTPA = Leisure Time Physical Activity, OA-ESI = Older Adults Exercise Status Inventory, d = day, mo = month, wk = week, ICC = intra class correlation

Assessment of quality of life

The quality of life in people with Type 2 diabetes and peripheral neuropathy was assessed in studies two and three, discussed in Chapters 5 and 6 respectively. Quality of life has many definitions, however what is understood is that quality of life can take different interpretations for different people and therefore is best assessed only by subjective measurement (Fayers and Machin, 2000).

When deciding which type of quality of life instrument to use, several considerations should be made, particularly the decision whether to use a generic or disease specific measurement. A disease-specific questionnaire (NeuroQol) was deemed most appropriate for use in this thesis and is described in Chapters 5 and 6. Disease-specific instruments are used to assess the special concerns of a particular diagnostic group and are generally more sensitive to the small clinical changes which are important for the patient and clinician (Patrick and Deyo, 1989, Huang et al., 2008). Some advantages of disease specific instruments are that they may reduce the respondent's burden and increase participation by including relevant quality of life dimensions (Fletcher et al., 1992). A disadvantage of using this type of instrument is that it limits comparability of quality of life results with other populations without disease (Fletcher et al., 1992). Generic instruments cover a broad range of quality of life dimensions that are applicable to a variety of diseases, interventions, treatments, demographics and cultural groups (Patrick and Deyo, 1989, Fletcher et al., 1992, Huang et al., 2008, O'Connor, 2004). Having such broad domains, however, may reduce the responsiveness of the questionnaire (Fletcher et al., 1992).

Research has been conducted into the use of generic and disease-specific quality of life questionnaires with regards to diabetes. Diabetes has a unique effect on one's quality of life through affecting physical, psychological and social functioning. Achhab et al. (2008) recently conducted a systematic review into diabetes specific quality of life instruments among adults and found 16 instruments meeting their inclusion criteria. Many of these questionnaires were designed for those with Type 1 diabetes, the elderly, or did not directly address quality of life. The six remaining relevant instruments are presented in Table 12. Many of the dimensions of these instruments include areas which are specific to diabetes such as diabetes worry, diet adherence, monitoring barriers, treatment frequency and frequency of symptoms (Boyer and Earp, 1997, Bradley et al., 1999, DCCT, 1988, Fitzgerald et al., 1996, Meadows et al., 1996,

Shen et al., 1999). Despite the systematic review being conducted in 2008, these diabetes specific instruments were developed between 1988 and 1999 and may not capture the advances in the Type 2 diabetes and its management over the past decade.

Table 12 Diabetes specific quality of life instruments as discussed by Achhab et al. (2008).

Title	Author	Year	Dimensions/scales/domains	Items
DQoL (Diabetes Quality of Life)	(DCCT)	1988	4 scales: satisfaction, impact, social worry, diabetes worry	46
Diabetes Care Profile (DCP)	(Fitzgerald et al.)	1996	14 scales: control problems, social and personal factors, positive attitude, negative attitude, self-care ability, importance of care, self-care adherence, diet adherence, medical barriers, exercise barriers, monitoring barriers, understanding management practice, long-term care benefits and support attitudes	234
Diabetes Health Profile (DHP-1)	(Meadows et al.)	1996	3 dimensions: psychological distress, barriers to activity and dis-inhibited eating	32
Diabetes-39 (D-39)	(Boyer and Earp)	1998	5 dimensions: energy and mobility, diabetes control, anxiety and worry, social burden, and sexual functioning	39
Diabetes Quality of Life Clinical Trials Questionnaire (DQLCTQ)	(Shen et al.)	1999	8 domains: physical function, energy/fatigue, health distress, mental health, satisfaction, treatment satisfaction, treatment flexibility and frequency of symptoms	57
Audit of Diabetes-dependent Quality of Life (ADDQoL)	(Bradley et al.)	1999	13 domains: employment, social life, family relationships, friendships, sex life, leisure, travel, future (self), future (family), motivation, physicality, perception of peer burden, enjoyment of food	20

Despite the apparent abundance of diabetes specific quality of life questionnaires, Polonsky (2000) concluded that confusion exists when choosing appropriate instruments and that researchers were following three broad principles. These were to use whatever instrument everyone else was using, to assume that health related quality of life is synonymous with psychological status, and hence use any instrument which appears to assess the patient's psyche such as depression, and to choose a questionnaire based on its name, as long as it includes the terms 'quality of life' and 'diabetes' (Polonsky, 2000). These issues were perhaps further highlighted in a recent systematic review which outlined the ten most frequently used tools for assessing quality of life in people with diabetes between 1995 and 2008 (Speight et al., 2009). Of

the ten instruments identified, only three were deemed to assess quality of life (DQoL, ADDQoL, and WHOQoL), with the remaining seven more appropriately judged to assess health status, well-being and satisfaction (Speight et al., 2009). Furthermore, six of the ten questionnaires were diabetes-specific and four were considered generic leading Speight et al. (2009) to suggest that whilst generic measures allow comparison across various diseases, they may be unable to understand the impact of diabetes on quality of life.

Other factors which must be taken into account when selecting an appropriate instrument include its measurement properties, namely validity, reliability and responsiveness, and the method of administration, whether it be self-administered or interviewer administered (Fletcher et al., 1992). A self-administered questionnaire was selected for use in this thesis. Whilst self-administered questionnaires may exclude participants who are illiterate, interviewer administered questionnaires require the need for extra resources, staff and appropriate training (Fletcher et al., 1992). Interviewer administered questionnaires may also be susceptible to the systematic errors associated with observer effects and the conditions under which the measurement is made (Cox et al., 1992). Considerations must be made into the length of the questionnaire, as lengthy and complicated questionnaires are an imposition to the respondents (Cox et al., 1992, Fletcher et al., 1992). As such, it has been suggested that there is no advantage in offering any more than between 5-7 responses categories for each question (Cox et al., 1992).

Single Case Experimental Design (SCED)

Study three of this thesis (discussed in Chapter 6) used a single case experimental ABA design to assess the effects of a prescribed exercise intervention in people with Type 2 diabetes and peripheral neuropathy. Direct and systematic replication was used to enhance the methodological quality of the study, as in discussed below.

Single subject research designs provide a quasi-experimental approach to evaluate the effectiveness of a treatment on an individual, or small group of individuals, where by the individuals act as their own control (Backman and Harris, 1999). Single subject research is idiographic in nature as the entire research from conceptualisation to observation and measurement is directed towards drawing inferences at an individual level (Morgan and Morgan, 2009, Ottenbacher, 1990). It is important to note that the term ‘single subject’ does not mean

only one participant completes the study, as several participants may be assessed using single subject methodology (Morgan and Morgan, 2009). By using a variety of strategies discussed in this thesis, single subject designs are able to provide a clinically viable, controlled experimental approach to the study of an individual, whilst maintaining the flexibility to observe any changes throughout ongoing interventions (Portney and Watkins, 2000). Single case designs are particularly useful in situations whereby there are rare diseases, unique study populations, isolated environments, emergency situations and public health urgency (Bryson-Brockmann and Roll, 1996, Janosky, 2005). In particular, these designs are a useful research tool in a clinical practice setting as they are able to identify cause-effect relationships without requiring large sample sizes or large budgets, a feature highlighted when compared to larger group designs (Evans, 2003, Janosky, 2005).

Continuous assessment

The single subject design is characterised by repeating outcome measurements during one or more baseline and intervention phases; the term used to describe testing periods (Kazdin, 1982, Palisano, 2007, Zhan and Ottenbacher, 2001). The systematic collection of repeated measures is required to observe the trends and patterns within the data to evaluate variability of the behavioural response over a length of time (Ottenbacher, 1990, Portney and Watkins, 2000, Repper, 1998). Importantly, the continuous measurement prior to treatment allows the researcher to examine the pattern or stability of performance so that when the intervention is implemented, the researcher is able to examine whether any change in target behaviour coincides with the intervention (Kazdin, 1982). This is not applicable to group comparison studies as behaviour is only measured on two occasions, namely before and after the intervention (Evans, 2003, Kazdin, 1982, Ottenbacher, 1990, Portney and Watkins, 2000). The use of repeated measures helps to improve the validity of the study because a trend of behaviour over multiple data points decreases the probability that the result was due to chance (Backman and Harris, 1999).

ABA design

The foundation of single case research is known as the AB design whereby a series of baseline (A) measures are taken to measure the participant's target behaviour, prior to an intervention (B) being implemented (Backman et al., 1997). The ABA design used in this thesis is an extension of the AB design where the intervention is withdrawn in the third phase, providing greater

confidence in the ability to determine the impact of the treatment (Zhan and Ottenbacher, 2001). In single case research, the intervention is considered to be the independent variable, whilst the dependent variable is the patient response or target behaviour which is an observable, quantifiable and valid indicator of the intervention's effectiveness (Portney and Watkins, 2000). The independent variable discussed in Chapter 6 is a 12-week supervised combined aerobic and resistance training program, while the dependent variables includes measures of sensation, quality of life and function.

The first stage of a single subject design is to establish what the target outcome looks like prior to the commencement of the intervention (Morgan and Morgan, 2009). This initial observation phase reflects the natural state of the target outcome, and is referred to as the 'baseline phase' (Kazdin, 1982, Morgan and Morgan, 2009, Portney and Watkins, 2000). Using conventional notation, the baseline phase is denoted using the letter 'A' (Janosky, 2005, Portney and Watkins, 2000). The baseline phase provides information about responses during a period of non-treatment, mimicking that of a control condition (Portney and Watkins, 2000). As the baseline phase serves the function of describing current levels of performance it is important that the data is relatively stable (Kazdin, 1982). Being able to achieve a reasonable steady state is important for the researcher to draw conclusions about the effects of an intervention, as the comparison between baseline and intervention is used to identify meaningful change (Morgan and Morgan, 2009). A stable baseline is one which is considered to have minimal variability in the measurements (Kazdin, 1982).

Once the baseline data has been collected, the manipulation of the independent variable occurs (Morgan and Morgan, 2009). The independent variable, otherwise known as the intervention is denoted by the letter 'B' (Janosky, 2005). The intervention phase has similar purposes to that of the baseline phase in that it is used to describe current performance and to predict future performance if the conditions remained the same (Kazdin, 1982). During the intervention phase, the researcher is able to examine whether or not the target outcomes have deviated from the projected level of the baseline, and in what direction the change is, indicating a change in performance (Kazdin, 1982).

The withdrawal of the intervention is used to demonstrate that changes in target behaviour only occur in the presence of the intervention, and therefore any changes in the dependent variable can be more confidently linked to the presence of the independent variable (Backman et al., 1997, Portney and Watkins, 2000). The principle of the withdrawal phase lies in its ability to show that changes in the target behaviour are only evident during the intervention phase (B) (Portney and Watkins, 2000). If the changes that occurred during the intervention are not maintained in this phase, then it can be logically assumed that the intervention was the factor that caused the changes in the target behaviour (Evans, 2003, Morgan and Morgan, 2009, Portney and Watkins, 2000). This allows the internal validity to be controlled, as it is highly improbable that any observed changes in target behaviour would be due to other factors which coincidentally occurred at the same time as the onset and ceased at the conclusion of the intervention (Morgan and Morgan, 2009, Portney and Watkins, 2000, Zhan and Ottenbacher, 2001).

The obvious problem associated with the withdrawal phase is that in order to be effective in its roles listed above, the target behaviour must be reversible (Portney and Watkins, 2000). The need to be able to show a reversal of the target behaviour is crucial if causal inferences are to be made in relation of the efficacy of the intervention (Kazdin, 1982). However, this is not always the case as changes resulting from a systematic intervention often become lasting even after the removal of the treatment and as such the withdrawal phase does not always result in a return of behaviour to the initial baseline, pre-intervention level (Morgan and Morgan, 2009). In particular, rehabilitation programs aimed at increasing strength and endurance are difficult to explore using a withdrawal phase, as the removal of the intervention is unlikely to result in an immediate decrease of these measures (Backman and Harris, 1999). Secondly, it may also be seen as ethically unreasonable, or on occasions even dangerous, to withdraw a treatment which is providing benefits to the participant (Portney and Watkins, 2000). If attempting to return the target behaviour to baseline levels is the equivalent to making the condition worse, such a reversal would be difficult to defend ethically, particularly in a clinical environment (Kazdin, 1982).

Methodological quality of single subject research

In order to assess the methodological quality of single subject research, a scale has been devised enabling the critical appraisal of these designs in order to improve their standards (Tate et al., 2008). The SCED scale is a ten item scale which provides a valid evaluation of methodological quality, inter-rater reliability, as well as providing a pre-commencement checklist for researchers (Tate et al., 2008). The development of this scale was based upon the issues with single subject research, and how to improve them, as displayed in Table 13 (Tate et al., 2008). A dichotomous response format of either present or absent is used, with one point awarded for each criterion which is met, with a score ranging between zero to ten, with higher values indicating better methodology (Tate et al., 2008).Whilst Tate et al. (2008) have recognised the SCED scale does not include all criteria representing sound methodology, this minimum set of core values has been shown to be a reliable and valid instrument. The study discussed in Chapter 6 scores eight out of ten (observer bias was not controlled for), however it should be noted that for some outcome measures for some participants, a stable baseline was not achieved. However, due to the factors discussed above relating to stable baselines, it was determined that the intervention commence after four weeks of baseline measurements.

Table 13 Method used to develop items for the SCED Scale (Tate et al. 2008)

Issues with Single Subject design	Possible solutions and SCED Scale criteria
Understanding of the problem	Operationally define and specify the target behaviours, with use of relevant, precise and repeatable measures
Determining treatment efficacy	Build a control condition into the design i.e. withdrawal
Variability in behaviour	Establish a stable baseline over at least three occasions
	Take continuous measures of behaviour during the intervention
	Present raw data record for each phase in tabular or graphical form
Observer bias	Establish inter-rater reliability for observations of target behaviours
	Assessor is independent from therapist
Verification of treatment efficacy	Use statistical analyses or describe effect sizes
Generalisation	Use of replication
	Provide evidence to generalisation beyond specific target behaviour

SCED: Single Case Experimental Design

There are several notable differences between single subject research and group comparison designs. Importantly, group statistical analyses may make it difficult to understand clinical significance rather than just statistical significance (Bryson-Brockmann and Roll, 1996). The use of a binary decision of whether results are significant or not significant as the standard to which the effectiveness of the research in group designs is assessed, may mask any clinical changes (Morgan and Morgan, 2009). In a clinical environment, the extent to which an intervention is significant is shown through noticeable, real-world change in the functioning of the client. This standard, referred to as clinical significance may be a more relevant criterion for evaluating the effectiveness of an intervention rather than statistical significance alone (Morgan and Morgan, 2009). Table 14 provides a summary of the difference between group comparison designs and single subject research designs.

Table 14 Comparison of group comparison and single subject methods for clinical research adapted from Ottenbacher (1990)

Research Design	Group Comparisons	Single Subject
Comparisons	At least two groups selected from a target population	Within subject performance for one subject or a small group
Observations	Outcome measures collected infrequently; usually pre-test and post-test only	Performance is monitored repeatedly over a period corresponding to the requirements of the design
Patient Feedback	Little or no data is gathered on patient performance or feedback until study is complete; the emphasis is on outcome	Patient feedback is monitored across design phases, and the emphasis is on studying process as well as outcome
Methodology	The research design is fixed and changes are not permitted once the intervention is introduced	Modifications in design are possible; the methodology is flexible and allows the addition or elimination of design phases
Costs/Expense	Relatively high and the procedures are difficult to implement in clinical settings without some outside resources and support	Relatively small, and the procedures can often be incorporated as part of a clinical routine
Methods of data analysis	Well established and accepted as scientifically legitimate; rules for statistical inference are clearly defined	Relatively new; statistical and inferential limitations are not completely understood
Inferences	Made between individuals and reflect group performance	Made at a within-subject level and reflect the performance of a single individual or a small group
Generalisability	Established through the use of a statistical model based on random sampling from a target population	Established through a planned program of replication

Despite the positive features, the primary limitation within single subject designs is the inability to generalise the findings to the greater population (Kazdin, 1982, Kennedy, 1979, Palisano, 2007). Whilst larger group comparison designs do not allow the deep understanding of the effect of a treatment on an individual client which is possible in single case designs, this method is sometimes preferred as it is assumed the results can be generalised, when compared to single subject designs (Kazdin, 1982, Kennedy, 1979, Ottenbacher, 1990). This includes the fact that the statistical techniques associated with group comparison studies permits the researcher to estimate the generalisability of the findings, a criterion which a single subject design cannot meet (Kennedy, 1979). This criticism of single subject designs is also referred as limited external validity, essentially, the limited extent to which data from an individual can be generalised to the population as a whole (Backman et al., 1997, Morgan and Morgan, 2009, Repper, 1998). Despite the results of a single subject design being able to provide positive findings of the effectiveness of an intervention for a particular participant, the portion of the population who would experience similar results remain unknown (Janosky, 2005).

Various methods were used within this thesis to combat this limitation. Several authors have identified the use of replication to enhance the generalisability of single subject research (Backman et al., 1997, Bryson-Brockmann and Roll, 1996, Janosky, 2005, Repper, 1998). Replication is able to demonstrate evidence of external validity, ultimately leading to the identification of a general principle (Kazdin, 1982, Morgan and Morgan, 2009). The use of replications can examine the magnitude to which results of one study with one participant extend across a variety of settings, behaviours, researchers and other variables, as only when a finding can be repeated again and again, does it become established scientific knowledge (Kazdin, 1982, Morgan and Morgan, 2009).

There are two ways in which replication may be used and were explored in this thesis. Direct replication consists of applying the exact procedures across a number of different participants to evaluate the intervention under the same conditions (Kazdin, 1982, Morgan and Morgan, 2009). By using direct replication, researchers are able to determine whether the findings are restricted to the initial participant, or whether the results are consistent across many (Kazdin, 1982). As such, direct replication of single subject experimental designs using a relatively small group can play an integral part in demonstrating generalisable results (Bryson-Brockmann and Roll, 1996).

It has been argued that the use of interventions using different clinical settings, combinations of interventions, and therapists can help to resolve the issue of generalisability, a method known as systematic replication (Backman et al., 1997, Bryson-Brockmann and Roll, 1996, Janosky, 2005, Kazdin, 1982, Repper, 1998). Systematic replication means the researcher repeats the intervention whilst purposely allowing features of the intervention to vary from the original experiment, such as the use of different clinical settings, combinations of interventions and therapists (Kazdin, 1982, Morgan and Morgan, 2009). If the varying designs across a number of individual cases shows common patterns on treatment outcomes then causal inference and the generalisation inference is strengthened (Kazdin, 1982, Repper, 1998). This systematic replication can take place intra-subject or inter-subject (Morgan and Morgan, 2009).

CHAPTER 4: Self-reported Physical Activity in people with Type 2 Diabetes and Peripheral Neuropathy

Introduction

This chapter focuses on the self-reported physical activity in a sample of people with Type 2 diabetes and in those with Type 2 diabetes and peripheral neuropathy, using the International Physical Activity Questionnaire (IPAQ). The aim of this study was to better understand the activity levels of people living in the community with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy, having established throughout the introduction and literature review that physical activity is a useful management tool for this population.

Literature Review

As outlined in Chapter 2, physical activity has a moderating effect on Type 2 diabetes through glucose control, as well as providing many other biological advantages (ACSM, 2000a, Dunstan and Daly, 2007, WHO, 2006, Warren, 2010). Physical activity has been reported to reduce the impact of the sensory deficits, painful symptoms and loss lower limb strength experienced in those with diabetes and peripheral neuropathy and led to improvement in functional outcomes (Fisher et al., 2007, Kluding et al., 2012, Otterman et al., 2011). Furthermore, Snel et al. (2012) and Bello et al. (2011) have suggested that physical activity improves the quality of life in people with Type 2 diabetes. Given the various advantages of physical activity presented in the literature review, it is important to understand whether or not people with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy are participating in regular physical activity, and to what extent.

In order to educate the community of the quantity and intensity of physical activity required to gain health benefits, several organisations have developed recommendations for participation. Recently, ESSA released a position statement about physical activity for people with Type 2 diabetes that recommended an accumulation of a minimum of 210 minutes of moderate intensity exercise per week (or 125 minutes of vigorous intensity exercise) and two or more resistance training sessions (2-4 sets, 8-10 reps) (Horden et al., 2012). However, during the conception of this study, the recommendations were that people with Type 2 diabetes should undertake 150 minutes of at least moderate physical activity per week (ACSM/ADA, 2010). Therefore in this thesis, this was considered to be the current recommendations.

While these recommendations help to inform people with Type 2 diabetes as to the appropriate amounts of physical activity they should undertake, they also provide researchers with a measure of quantifying whether or not the population adheres to them. The Australian Institute of Health and Welfare (2008) reported that two out of three people with diabetes did insufficient physical activity (defined as less than 150min/wk over five days of the week) during 2004 and 2005. Furthermore, citing physical activity recommendations from the AHA, ADA and ACSM, researchers have found between 25% and 42% of people with diabetes were participating in sufficient physical activity (Zhao et al., 2011, Zhao et al., 2008).

Physical activity recommendations are not solely a question of duration, but for greater health benefits, the intensity at which physical activity is performed is equally important. The recommendations of 150 minutes per week for people with diabetes is only relevant if done at least at a moderate intensity (ACSM/ADA, 2010). As it has been suggested that walking is the most preferred activity for people with diabetes (Barrett et al., 2007, Forbes et al., 2010), it is important to assess the intensity of self-reported physical activity in people with diabetes as walking may not be considered moderate intensity. The challenge for people with Type 2 diabetes and peripheral neuropathy may not lie within promoting more physical activity, rather different types of physical activity to ensure a moderate intensity is being met. Furthermore, researchers have suggested that the amount of sedentary behaviour in the form of excessive sitting may be detrimental to individuals, independent of whether they are meeting physical activity recommendations (Owen et al., 2010, Patel et al., 2010). Considering these variables, it is important to attain a full physical activity profile including walking, moderate and vigorous physical activity behaviours, as well as the amount of sitting in people with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy.

Given the lack of research reporting the physical activity behaviour of people with Type 2 diabetes and peripheral neuropathy, the investigation of self-reported physical activity in this population is supported. Furthermore, a review of the literature failed to find previous research studies investigating whether or not this group were meeting current physical activity recommendations. Due to the importance of physical activity for people with Type 2 diabetes and peripheral neuropathy, further investigation is warranted to determine the duration and

intensity of self-reported physical activity, and compliance with physical activity recommendations.

Aim and research questions

The aim of this study was to investigate the amount of self-reported physical activity in people with Type 2 diabetes, with and without peripheral neuropathy, and determine whether physical activity recommendations were being met For the purpose of this thesis, physical activity recommendations were defined as 150 minutes of moderate physical activity per week (ACSM/ADA, 2010). The following research questions guided this study.

1. What is the amount of self-reported physical activity in people with Type 2 diabetes?
2. What is the amount of self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy, and is there a difference between people with without peripheral neuropathy?
3. Do people with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy meet current physical activity recommendations?
4. What is the amount of self-reported sitting in people with Type 2 diabetes?
5. What is the amount of self-reported sitting in people with Type 2 diabetes and peripheral neuropathy, and is there a difference between those without peripheral neuropathy?

Methodology

Participants

Participants were recruited from Diabetes SA through several mail-outs using random sampling. Diabetes SA is an association established with the purpose of providing support to people with diabetes. Diabetes SA has over 30,000 members from all areas of South Australia with 82% of members estimated to have Type 2 diabetes. The sole inclusion criteria for this study were that respondents were required to have Type 2 diabetes and there were no exclusion criteria. Participation was voluntary and anonymous and the return of the questionnaire was deemed as consent. Ethical clearance was obtained from the University of South Australia (UniSA) Human Research Ethics Committee.

Description of tools and instruments

The short International Physical Activity Questionnaire (IPAQ) (Craig et al., 2003) (Appendix 1) was used to assess self-reported physical activity. The self-administered short form of the questionnaire was preferred over the longer version due to its simplicity of use, as an attempt to increase the response rate. Therefore from this point forward, the short IPAQ will simply be referred to as the IPAQ. The IPAQ focuses on the amount of physical activity performed over the past 7-day period. The IPAQ is designed for use by adults aged 18-65 years and provides information on time spent in four domains, namely leisure time physical activity, domestic and gardening activities, work-related physical activity and transport related physical activity. The IPAQ includes questions about three specific types of physical activity undertaken within the four domains namely, walking, moderate-intensity activities and vigorous-intensity activities. The IPAQ also has questions about time spent sitting, however it is recommended this question be analysed independently from the remaining questions (IPAQ, 2005).

The IPAQ is shown to be reliable ($\rho = 0.76$) and at least as valid as other self-reported physical activity measures (concurrent= 0.58; criterion= 0.30 against Computer Science Accelerometer) (Craig et al., 2003). Although it was originally intended that the IPAQ to be used for adults aged between 18-65 years, it has since been tested in older adults to assess its suitability. Several articles have assessed its reliability (ICC = 0.47-0.94) and validity (ρ = 0.28-0.53) across all categories of the IPAQ and supported its use in older adults over 65 years of age (Jancey et al., 2007, Tomioka et al., 2011, Hurtig-Wennlof et al., 2010).

The data obtained from the IPAQ was used to estimate the total amount of physical activity completed in a 7-day period by weighting the reported minutes per week in each category by a MET (metabolic equivalent) energy expenditure estimate. The weighted MET-minutes per week were calculated by multiplying the duration, frequency and MET intensity, and then summing across the activity domains (vigorous, moderate, walking) to produce a weighted estimate of total physical activity per week ($MET \cdot min \cdot wk^{-1}$) as explained in Table 15 (Craig et al., 2003).

Table 15 Calculation of MET-min/wk variables for the IPAQ (Craig et al. 2003)

MET-min/wk	Formula
Walking	3.3 * walking minutes * walking days
Moderate	4.0 * moderate minutes * moderate days
Vigorous	8.0 * vigorous minutes * vigorous days
Total	Walking MET-min/wk + moderate MET-min/wk + vigorous MET-min/wk

IPAQ: International Physical Activity Questionnaire MET: Metabolic Equivalent

Procedures

An envelope containing a cover letter from Diabetes SA (Appendix 2), study information sheet (Appendix 3), and the questionnaire was mailed to 4000 Diabetes SA members. Individuals were asked to fill out the demographic data sheet which asked for their age, gender, years since diagnosis of Type 2 diabetes and whether or not they had been diagnosed by their medical officer with peripheral neuropathy. Below the demographic section, was a slip where those interested in participating in an exercise intervention could write their contact details (Appendix 4). This formed the basis of recruitment for the study described in Chapter 6. Following this, all respondents were asked to complete the IPAQ and return all the relevant papers within 2 weeks. In order to distinguish each section, the cover letter, information sheet, and demographic data sheet were printed on white paper, with the IPAQ printed on yellow paper. Due to the confidential nature of the Diabetes SA database, blank envelopes were sealed by the principal researcher and provided to Diabetes SA where a volunteer staff member attached the address labels.

A total of three mail-outs (4000 questionnaires) were conducted over a nine month period. The first mail-out occurred throughout March and April 2009 and involved 1000 Diabetes SA members with Type 2 diabetes. A second mail-out occurred throughout June and July 2009 involving another 1000 Diabetes SA members with Type 2 diabetes. A final mail-out consisting of 2000 questionnaires was completed in January 2010. All mail outs used a random sampling of Diabetes SA members with Type 2 diabetes. Strategies used to enhance response rates included reminder emails sent by Diabetes SA and letters sent by the Principal researcher to those who had not yet responded within two to three weeks of the initial mail-out. An example of a reminder letter is provided in Appendix 5.

Data Analysis

Prior to analysis, physical activity data from the IPAQ were processed according to the authors' instructions which included the following recommendations (IPAQ, 2005). If 'don't know/not sure' was selected or if data were missing, that case was removed from the analysis. Physical activity data which was unreasonably high were considered outliers and excluded from analysis. This included any case by which the sum of all walking, moderate and vigorous time variables were greater than 960 minutes (16 hours), assuming an average person sleeps for eight hours per day. Those who reported minimum values of activity (<10 min) were re-coded to zero minutes based on evidence that suggests that physical activity in minimum bouts of ten minutes is required to achieve health benefits. Finally, data was truncated in an attempt to normalise the distribution of the levels of physical activity. It was recommended that any variable exceeding three hours or 180 minutes be re-coded to 180 minutes, permitting a maximum of 21 hours of activity in a week to be reported for each category (IPAQ, 2005). Sitting data was analysed separately from physical activity data.

Assessment of the data expressed as both MET-min/wk and min/wk data revealed that it was not normally distributed, and thus a logarithmic transformation was performed in order to use parametric statistics. Independent two-sample t-tests were used to detect differences between male and female participants, and those who had been diagnosed with peripheral neuropathy compared to those who had not. Descriptive statistics (means and standard deviations) were used to describe the age and years since diagnosis of Type 2 diabetes, but due to the non-normal distribution of the sample and the unequal sample size within groups, 95% confidence intervals were used to detect any differences. Data were considered to be statistically different if confidence intervals did not overlap (Portney and Watkins, 2000).

Given the non-normal distributions of physical activity and energy expenditure in many populations, it was recommended by the authors of the IPAQ that physical activity data be presented using medians (*Mdn*) and inter-quartile ranges (*IQR*) rather than means (IPAQ, 2005).

Results

Physical Activity

A response rate of 15.1% or 605 responses were received from the 4000 questionnaires of which 481 valid responses were used for analysis. Of those valid responses, a total of 465 respondents (96.7%) provided their gender, while 463 respondents (96.3%) indicated whether or not they had been diagnosed with peripheral neuropathy. There were 124 responses (20.5%) excluded from the analysis for various reasons described in Figure 3. Of the valid responses, 11.4% identified as being diagnosed with peripheral neuropathy which is below the estimated 18.6% prevalence of peripheral neuropathy in Australia (NADC, 2009). Of the valid responses, the majority were male (58.8% male, 37.8% female, 3.3% unknown). This information is presented in Figure 3.

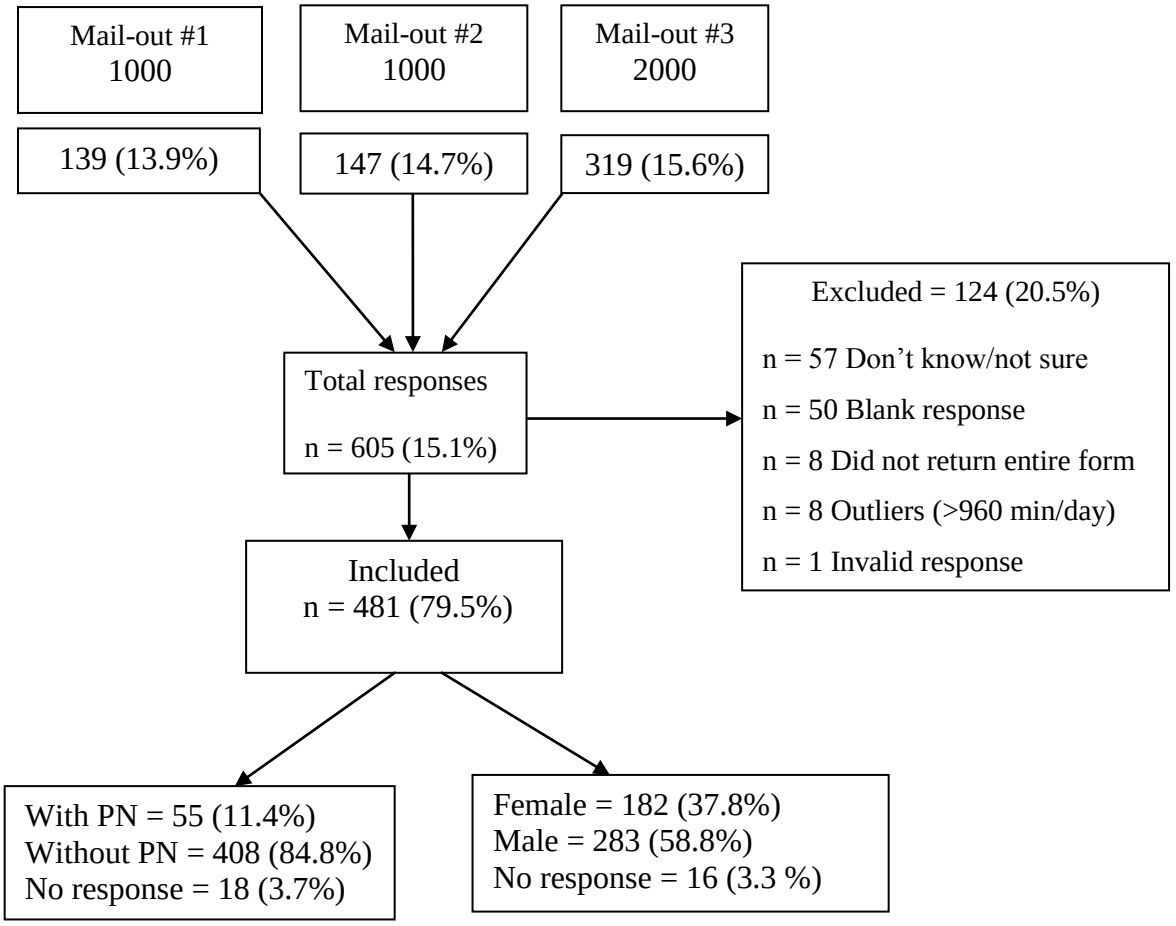


Figure 3 Respondents of the physical activity component of the IPAQ

PN: Peripheral Neuropathy
Min/day: minutes per day

Demographics

The mean, standard deviations, 95% confidence intervals and the proportion of participants by age group are displayed in Table 16. The age of the participants ranged between 33-83 years. Males were significantly older than females (95% CI: 63.2 – 65.1). Respondents who had indicated they had been diagnosed with peripheral neuropathy were significantly older than those with Type 2 diabetes alone. The largest proportion of the respondents were aged between 61-70 years for all groups (36.8% - 42.8%) except for those who have been diagnosed with peripheral neuropathy, as the largest proportion of these respondents (37.7%) were aged between 71-80 years.

Table 16 Age (years) of respondents of the physical activity component of the IPAQ

	n[+]	**Age (years)** ***M ± SD***	**95% CI**	**Range (years) (%)**					
				31-40	**41-50**	**51-60**	**61-70**	**71-80**	**>80**
All	481	63.2 ± 8.6	62.4 - 63.9	1.3	6.0	31.0	40.3	21.2	0.2
Male	283	64.1 ± 7.9	63.2 - 65.1*	0.7	2.5	30.7	42.8	23.0	0.3
Female	182	61.8 ± 9.4	60.4 - 63.1	2.2	11.0	31.3	36.8	18.7	0.0
With PN	55	66.6 ± 8.2	64.4 - 69.0*	0.0	1.9	24.5	35.9	37.7	0.0
Without PN	408	62.7 ± 8.6	61.8 - 63.5	1.5	6.6	31.9	40.7	19.1	0.2

M = mean, SD = Standard Deviation, CI = Confidence Interval, PN = peripheral neuropathy, [+] n = 16 did not provide their gender, n = 18 did not provide their PN status , * statistically significant within group (95%CI)

Participants were also asked how long since they had been diagnosed with Type 2 diabetes. There was no significant difference between the years since diagnosis between males and females however those who had been diagnosed with peripheral neuropathy had been diagnosed with Type 2 diabetes for a significantly longer period of time (95% CI: 9.3 – 14.6). The largest proportion of participants had been diagnosed with Type 2 diabetes for five years or less (41.6%), however the largest proportion of those who had also been diagnosed with peripheral neuropathy were diagnosed with Type 2 diabetes between five and ten years (33.3%) (Table 17).

Table 17 Years since diagnosis of Type 2 diabetes of respondents to the physical activity component of the IPAQ.

	n[+]	Years since diagnosis (*M* ± *SD*)	95% CI	Range (years) (%)					
				0-5	>5-10	>10-20	>20-30	>30-40	>40
All	481	8.4 ± 6.8	7.8 - 9.1	41.6	31.8	21.8	3.7	0.9	0.2
Male	283	8.7 ± 6.5	8.0 - 9.5	39.9	29.9	25.9	4.0	0.0	0.3
Female	182	8.0 ± 7.3	6.9 - 9.1	43.9	35.5	15.6	3.3	2.2	0.0
With PN	55	12.0 ± 9.5	9.3 - 14.6*	31.4	33.3	23.5	5.9	3.9	2.0
Without PN	408	8.0 ± 6.3	7.4 - 8.6	42.9	31.8	21.3	3.5	0.5	0.0

M = mean, SD = Standard Deviation, CI = Confidence Interval, PN = peripheral neuropathy, [+] n = 16 did not provide their gender, n = 18 did not provide their PN status , * statistically significant within group (95%CI)

Physical activity

The results for each category of physical activity (total, vigorous, moderate and walking) are presented separately. Firstly those who reported engaging in that particular category of physical activity for at least 10 minutes were analysed, followed by those who did not complete any physical activity for that category. Finally, an analysis of the demographics of those who did and did not complete that category of physical activity was undertaken.

Total Self-Reported Physical Activity

There were 450 participants (94%) from the total sample (n = 481) who reported they had completed at least 10 minutes of physical activity during the previous 7-days. There were 51 participants (93%) with peripheral neuropathy who reported they had completed at least 10 minutes of physical activity during the previous 7-days. Table 18 shows the total self-reported physical activity (reported in MET.min/wk) for these participants, separated by those with and without peripheral neuropathy.

Table 18 Median and interquartile ranges for those who reported engaging in any physical activity (MET.min/wk)

	n[+]	Median (MET.min/wk)	*IQR*	p
All	450	2076	798 – 4285	
With PN	51	1433	495 – 3390	0.04*
Without PN	383	2106	876 – 4380	

PN = peripheral neuropathy, [+] n = 16 did not provide their PN status, * statistically significant within group ($p<0.05$)

Participants reported engaging in a median of 2076 MET.min/wk during the previous 7-days. Further analysis revealed that males (*Mdn* = 2340, *IQR* = 891-5175 MET.min/wk) reported participating in significantly greater amounts of physical activity compared to females (*Mdn* = 1581, *IQR* = 693-3116 MET.min/wk) ($p = 0.003$). Figure 4 shows the distribution of participants who reported participating in some exercise during the past 7-days. The large interquartile range (*IQR* = 798 – 4285 MET.min/wk) can be explained through the frequency distribution being heavily skewed to the left, indicating the majority of participants engaged in smaller amounts of physical activity, with less participants engaging in larger amounts of MET.min/wk.

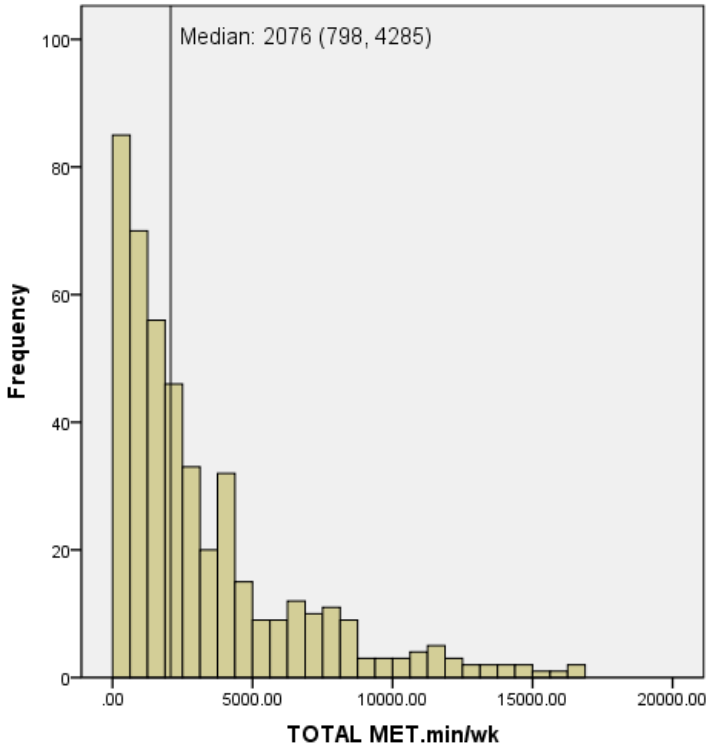


Figure 4 Frequency distribution of all the total physical activity (MET.min/wk) during the past 7-days

People with Type 2 diabetes and peripheral neuropathy participated in significantly less physical activity compared to those with Type 2 diabetes alone (p = 0.04) as shown in Table 18. Further analysis revealed that those with Type 2 diabetes and peripheral neuropathy who reported participating in physical activity in the previous 7-days were older (*M* = 66.06 ± 8.27, 95%CI = 63.69-68.44 years) and had been diagnosed with Type 2 diabetes for longer (*M* = 11.23 ± 8.44, 95%CI = 8.76-13.71 years) than those without peripheral neuropathy.

There were 31 participants or 6.4% of the total sample (n = 481) who reported that they had not participated in any walking, moderate or vigorous physical activity during the previous 7-days. There were more inactive females than males, with 9% of females (n = 16) and 5% of male participants (n = 14) reporting not engaging in any physical activity. Of the participants who reported being diagnosed with peripheral neuropathy, 8% (n = 4) reported not participating in any physical activity during the past 7-days. Of those who reported engaging in physical activity compared to those who reported doing no physical activity, no significant differences in age and years since diagnosis of Type 2 diabetes were found.

Vigorous Self-reported Physical Activity

A total of 228 participants of the total sample (n = 481) indicated they had engaged in some vigorous physical activity during the past 7-days, representing 47% of the whole sample, which included 143 males (51%) and 80 females (44%). Of the participants who reported being diagnosed with peripheral neuropathy, 18 (33%) reported engaging in vigorous physical activity. Table 19 shows the median and interquartile ranges of vigorous activity (MET.min/wk) for all participants, separated by presence of peripheral neuropathy.

Table 19 Median and interquartile ranges for those who reported engaging in vigorous physical activity (MET.min/wk)

	n[+]	**Median (MET.min/wk)**	***IQR***	**p**
All	228	1140	720 – 3240	
With PN	18	1440	780 – 2520	0.64
Without PN	204	1440	720 - 3540	

PN = peripheral neuropathy, [+]n = 6 did not provide their PN status, *statistically significant (P < 0.05)

Overall, participants reported engaging in a median of 1140 vigorous MET.min/wk during the previous 7-days. Further analysis revealed that males (*Mdn* = 1920, *IQR* = 960-4320 MET.min/wk) reported participating in significantly more vigorous physical activity compared with females (*Mdn* = 960, *IQR* = 500-2100 MET.min/wk) ($p < 0.001$). There were no significant differences in the amount of vigorous activity completed by those with and without peripheral neuropathy. The distribution of all participants is shown in Figure 5. The distribution is skewed to the left indicating the majority of participants engaged in smaller amounts of vigorous physical activity.

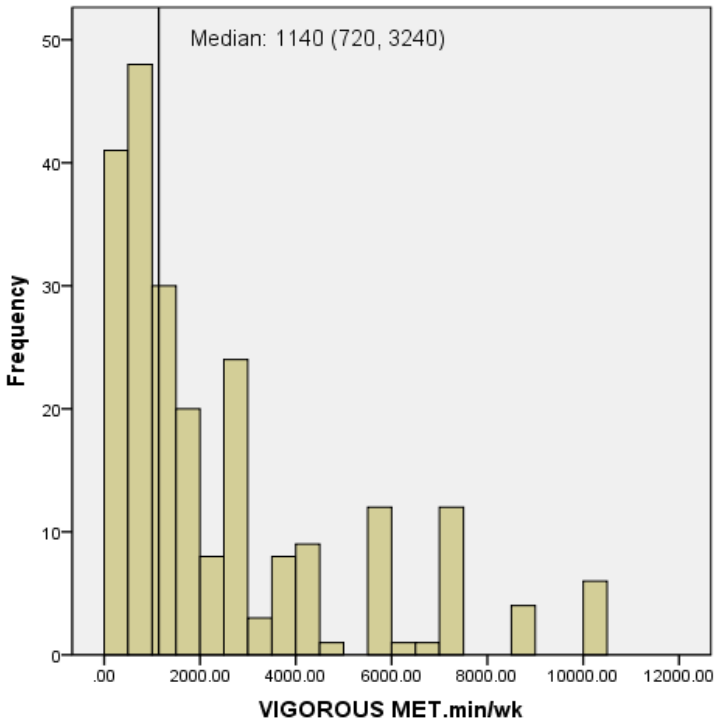


Figure 5 Frequency distribution of all participants who engaged in vigorous physical activity (MET.min/wk) during the past 7-days

The majority of participants (n = 253/481, 53%) reported not engaging in any vigorous physical activity during the previous 7-days. Those participants with peripheral neuropathy who did not engage in any vigorous physical activity were significantly older (*M* = 67.03, *SD* = 8.56, 95%CI = 64.09-69.97 years) than those without peripheral neuropathy who did not engage in vigorous physical activity. An analysis of the age and the years since diagnosis of Type 2 diabetes between those participants who did and did not engage in any vigorous physical activity found there was no difference between groups.

Moderate Self-reported Physical Activity

A total of 274 participants (57.0%) indicated they had engaged in some moderate physical activity during the past 7-days which included 59% (n = 167) of males and 53% (n = 96) of females. Of those with peripheral neuropathy, 47% (n = 26) reported participating in moderate physical activity. Table 20 below shows the median and interquartile ranges for all participants, separated by presence of peripheral neuropathy.

Table 20 Median and interquartile ranges for those who reported engaging in moderate physical activity (MET.min/wk)

	n[†]	**Median (MET.min/wk)**	***IQR***	**p**
All	274	960	480 – 1920	
With PN	26	1320	540 – 2340	0.70
Without PN	237	960	480 - 1860	

PN = peripheral neuropathy, [†]n = 11 did not provide their PN status

Overall participants reported engaging in a median of 960 moderate MET.min/wk during the previous 7-days. Further investigation revealed that males (*Mdn* = 1200, *IQR* = 560-2400 MET.min/wk) reported participating in significantly more moderate physical activity compared to females (*Mdn* = 720, *IQR* = 360-1680 MET.min/wk) (p = 0.004). There was no significant difference in the self-reported levels of moderate physical activity between participants with and without peripheral neuropathy. Figure 6 shows the distribution of all participants who reported participating in some moderate exercise during the past 7-days (MET.min/wk). The distribution of all those who participated in moderate activity is skewed to the left indicating the majority of participants engaged in smaller amounts of moderate physical activity.

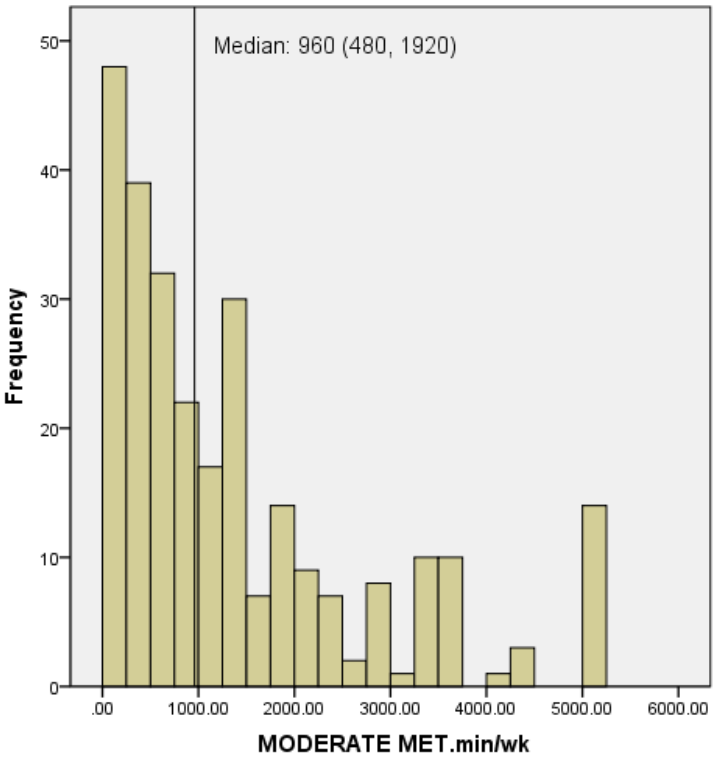


Figure 6 Frequency distribution of all participants who engaged in moderate physical activity (MET.min/wk) during the past 7-days

There were a total of 207 participants (43%) who reported not engaging in any moderate physical activity during the previous 7-days. There were no demographic differences in age and duration of Type 2 diabetes diagnosis between respondents with and without peripheral neuropathy, who did not complete any moderate physical activity. An analysis of the age and years since diagnosis of Type 2 diabetes between those participants who did, and did not engage in any vigorous physical activity found there was no difference between groups.

Walking

A total of 433 participants (90% of whole sample) indicated they had completed some walking during the previous 7-days. This included 91% (n = 258) of males, 88% (n = 161) of females, and 85% (n = 47) of people with peripheral neuropathy, meaning walking was the preferred activity compared to vigorous and moderate activities. Table 21 shows the median and interquartile ranges for the amount of walking of all participants, separated by presence of peripheral neuropathy.

Table 21 Median and interquartile ranges for those who reported walking **(**MET.min/wk)

	n[+]	Median (MET.min/wk)	*IQR*	p
All	433	693	297 – 1386	
With PN	47	594	198 – 1386	0.20
Without PN	371	693	330 – 1386	

*statistically significant (P<0.05), PN = peripheral neuropathy, [+] n = 15 did not provide their PN status

Participants reported walking for a median of 693 MET.min/wk during the previous 7-days. Further analysis revealed that males (*Mdn* = 693, *IQR* = 330-1485 MET.min/wk) reported walking significantly more than females (*Mdn* = 594, *IQR* = 297-1188 MET.min/wk) (*p* = 0.04). There was no difference in the amount of self-reported walking between participants with and without peripheral neuropathy. Figure 7 shows the distribution of all participants who reported walking during the past 7-days. The distribution of all those who walked is skewed to the left indicating the majority of participants engaged in smaller amounts of walking, with a few participants indicating a longer duration of walking during the past week.

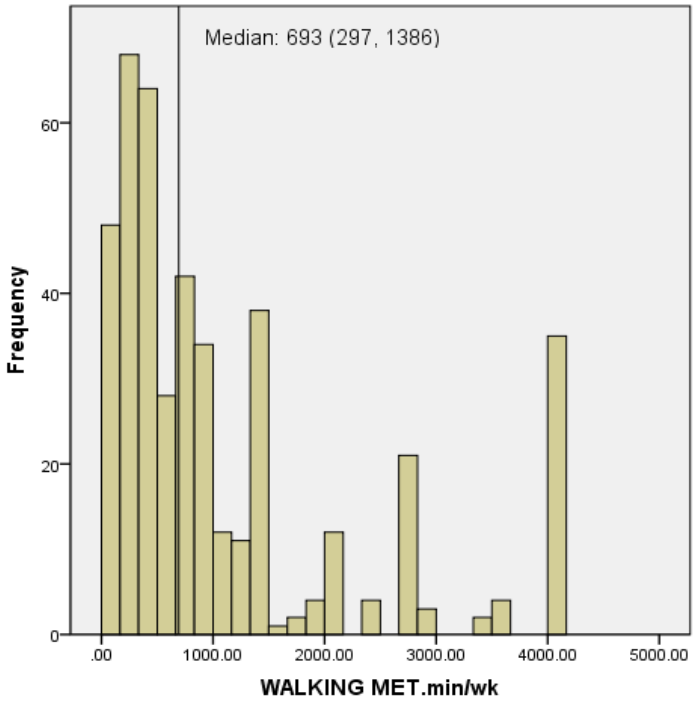


Figure 7 Frequency distribution of all participants who engaged walking during the past 7-days (MET.min/wk)

There were a total of 48 participants (10% of whole sample) who reported not engaging in any walking during the previous 7-days. An analysis of the age and years since Type 2 diabetes diagnosis between those who did and did not complete any walking during the previous 7-days, found no difference between groups.

Physical Activity Profile

As highlighted in the results thus far, walking appeared to be the most prevalent activity for all participants. Figure 8 represents the physical activity profile for the domains of reported physical activity of the participants, and is a breakdown of the contribution of vigorous, moderate and walking activities in those participants who participated in some physical activity during the previous week (n=450). Mean, standard deviations and 95% confidence intervals of the percentage contribution of vigorous, moderate and walking activities can be found in Appendix 6 (Tables 47-49).

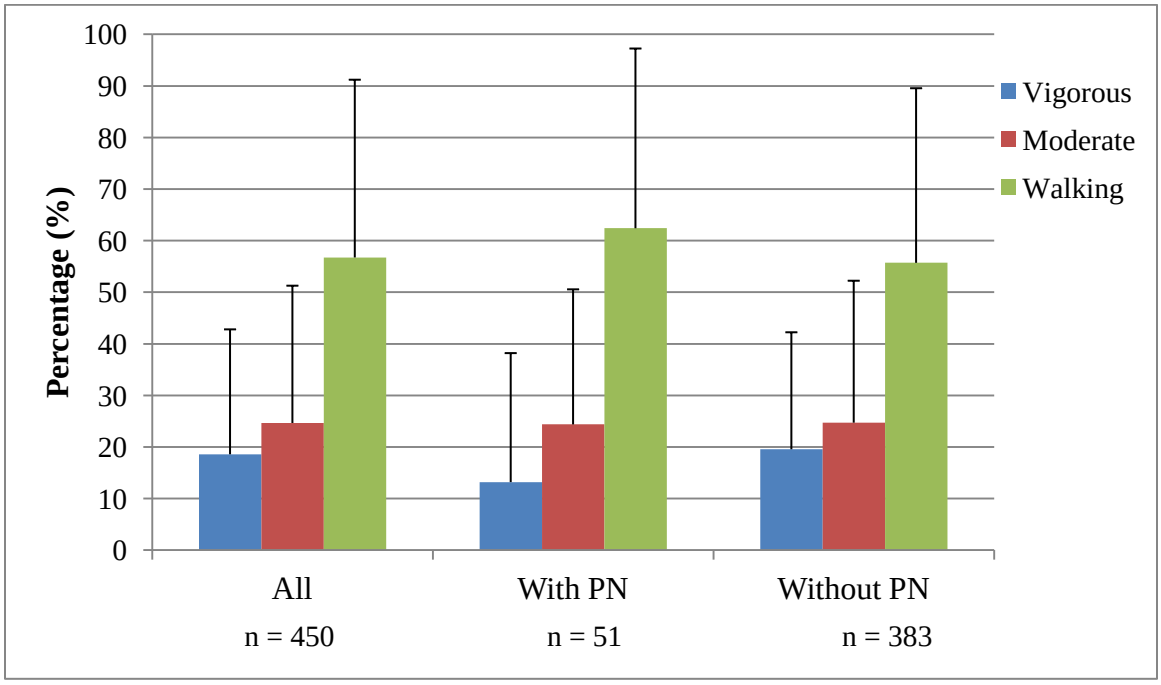


Figure 8 Percentage contribution of vigorous, moderate and walking activities of participants who reported engaging in any physical activity in the previous 7-days

As can be noted from Figure 8, all participants spent the majority of their physical activity profile walking, followed by moderate intensity activity, and vigorous intensity physical activity. There were no differences in intensity contribution between participants with and without peripheral neuropathy. The large standard deviations are an indication of the variance of percentage contribution of each intensity. For example, walking was the most popular type of activity, with all participants indicating walking contributed to an average over 50% of their total physical activity profile. Furthermore, 29% (n = 131) of respondents indicated walking was the only form of physical activity they had participated in during the previous 7-days, contributing to 100% of their profile.

Physical Activity Recommendations

Table 22 shows the minutes of physical activity achieved by those participants who indicated they had engaged in some physical activity (n=450) during the previous 7-days. As previously described, there were 31 participants who did not engage in any physical activity.

Table 22 Median and interquartile ranges for those who reported engaging in any physical activity **(**min/wk)

	n[+]	**Median (min/wk)**	***IQR***	**p**
All	450	460	210 – 990	
With PN	51	300	130 – 840	0.03*
Without PN	383	480	210 - 1080	

PN = peripheral neuropathy, *statistically significant ($p<0.05$), [+]n = 16 did not provide their PN status

Participants who indicated they had been physically active during the previous 7-days, engaged in physical activity for a median of 460 minutes. Further analysis found that males (*Mdn* = 555, *IQR* = 220-1200 min/wk) reported participating in significantly more minutes of physical activity than females (*Mdn* = 330, *IQR* = 208-773 min/wk) (p = 0.004). People with peripheral neuropathy completed significantly less minutes of physical activity than those without peripheral neuropathy (p = 0.03) as shown in Table 22. Figure 9 presents the frequency distribution of minutes per week for all participants which is skewed to the left, indicating that participation decreased as the minutes of physical activity increased.

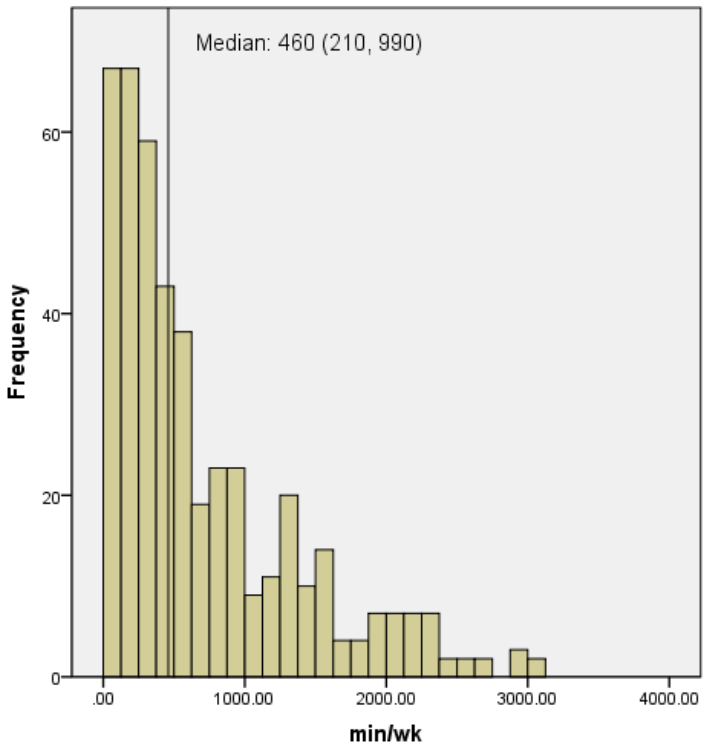


Figure 9 Frequency distribution of all participants who engaged in some physical activity during the past 7-days (min/wk)

Using the minutes per week data for each of the intensities within the IPAQ, each participant could be classified as either adhering or not adhering to physical activity recommendations of 150 minutes per week of at least moderate intensity (ACSM, 2010, Sigal et al., 2004). The results indicated 57% of all respondents met current physical activity recommendations. Less than half (49%) of people with Type 2 diabetes and peripheral neuropathy met physical activity recommendations. There were no significant differences in age and duration of Type 2 diabetes diagnosis between those who did, and those who did not meet physical activity recommendations.

Figure 10 provides a box-plot representation of those who did (yes) and did not (no) meet physical activity recommendations. Those who met physical activity recommendations reported a median of 720 (*IQR* = 400, 1440) minutes per week of physical activity, compared to those who did not meet physical activity recommendations reporting a median of 150 (*IQR* = 50, 315) minutes per week. This difference was analysed to be significant ($p < 0.01$).

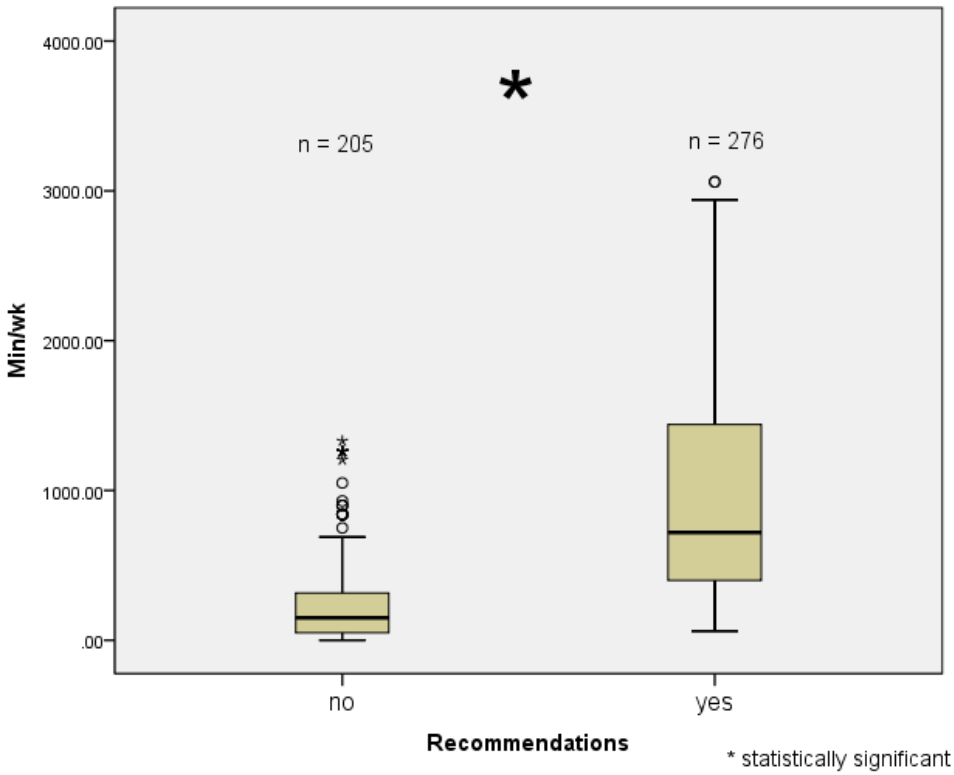


Figure 10 Total physical activity (min/wk) of those who met (yes) and did not meet (no) physical activity recommendations ($p<0.01$)

An important feature of Figure 10 is the large amount of outliers within those who did not meet physical activity recommendations who appear to be exceeding 150 minutes of physical activity per week. This is further highlighted by people who did not meet physical activity recommendations reporting of a median of 150 (*IQR* = 50-315) minutes per week. The majority (n = 106, 52%) of respondents who did not meet physical activity recommendations reported engaging in physical activity for at least 150 minutes per week as shown in Figure 11.

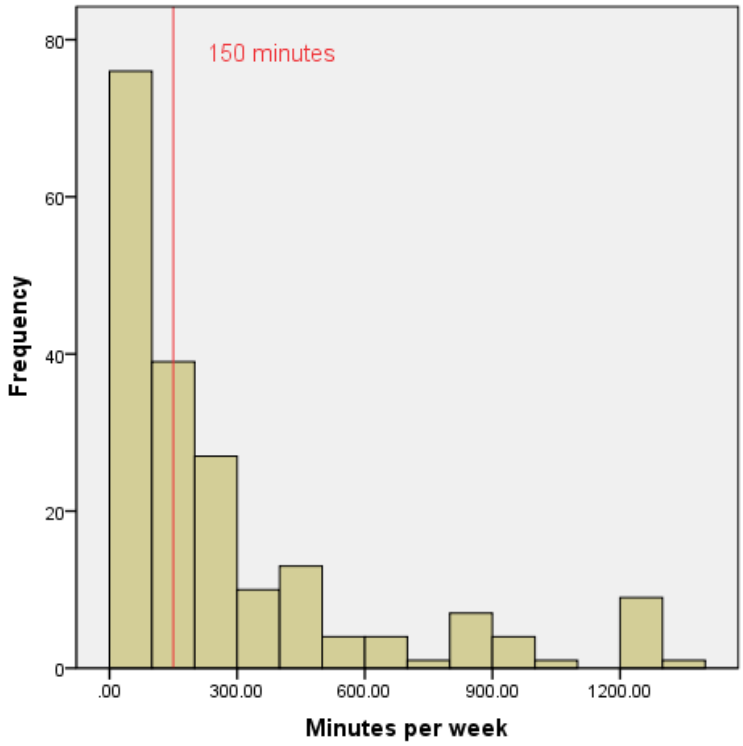


Figure 11 Physical activity (min/wk) of those who did not meet physical activity recommendations

Despite reporting at least 150 minutes of physical activity in the previous week, n = 106 respondents were classified as not meeting physical activity recommendations as they did not engage in a sufficient amount of moderate intensity activity. An analysis of the percentage contribution of walking, moderate intensity and vigorous intensity for this subset found walking contributed to almost 92% of their physical activity expenditure, with moderate and vigorous activities accounting for the remaining 8%. This is compared to those who met physical activity recommendations whereby a more even contribution between walking, moderate intensity and vigorous intensity activities were reported. Figure 12 is a side by side representation of percentage distribution of vigorous intensity, moderate intensity and walking reported by the respondents who achieved 150 minutes of physical activity but not at the correct intensity, and those who were classified as meeting current physical activity recommendations.

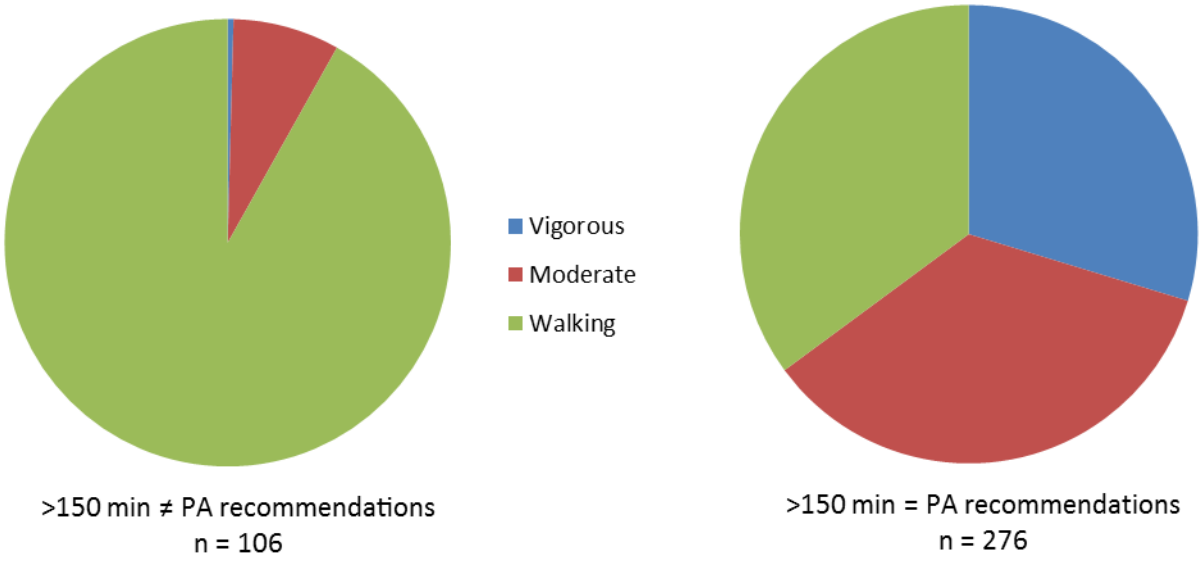


Figure 12 Percentage contribution of vigorous, moderate and walking activities reported by those who reported some physical activity (PA) and achieved at least 150 minutes of PA, by whether or not they met PA recommendations

These results indicate that 79% (n = 382) of all respondents reported engaging in at least 150 minutes of physical activity in the previous week, however 28% (n = 106) of this group did not exercise at the required moderate intensity to be classified as meeting physical activity recommendations.

Sitting

Of the 605 responses received, 513 valid responses (84.8%) for the sitting component of the IPAQ were used for analysis. Of those valid responses, a total of 495 respondents (96.5%) provided their gender, while 493 (96.1%) indicated whether or not they had been diagnosed with peripheral neuropathy. There were 92 responses (15.2%) excluded for analysis for various reasons provided in Figure 13. The majority of respondents were male, and 11.7% of respondents indicated they had been diagnosed with peripheral neuropathy, which is below the estimated prevalence (18.6%) of peripheral neuropathy in Australia (NADC, 2009). This information is presented in Figure 13.

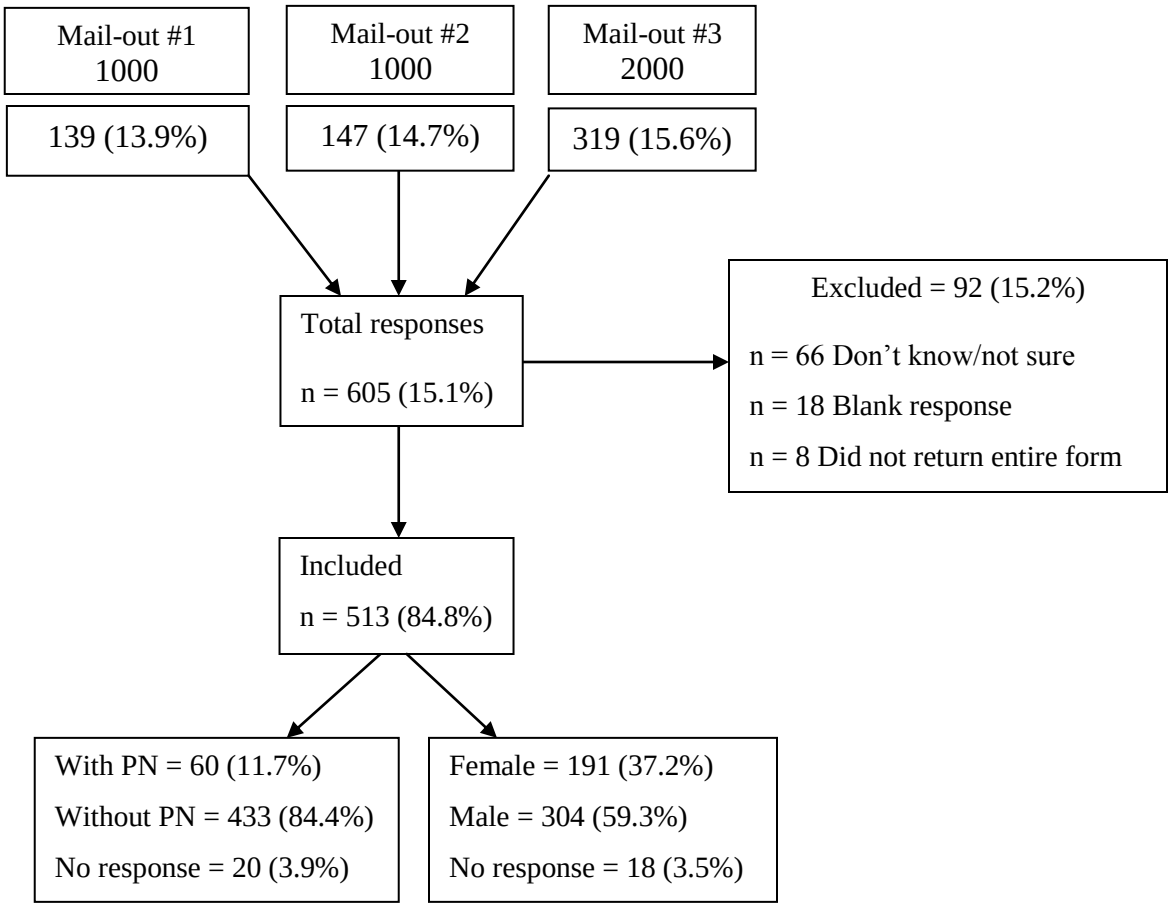


Figure 13 Respondents of the sitting component of the IPAQ

PN = Peripheral Neuropathy

Demographics

The age of all participants who completed the sitting questionnaire (n=513) are provided in Table 23. Males were significantly older than females (95% CI: 63.69 - 65.46), and those with Type 2 diabetes and peripheral neuropathy were significantly older than those with Type 2 diabetes alone (95% CI: 64.48 – 68.76). The highest proportion of participants were aged between 61-70 years of age with the exception of people with Type 2 diabetes and peripheral neuropathy, with the highest proportion (37.9%) aged between 71-80 years. Table 23 provides the mean, standard deviation, 95% confidence intervals and range of ages for all participants.

Table 23 Age (years) of respondents of the sitting component of the IPAQ

	n[+]	Age (years) *M* ± SD	95% CI	Range (years) (%)					
				31-40	41-50	51-60	61-70	71-80	>80
All	513	63.58 ± 8.37	62.84 – 64.32	0.8	5.3	30.7	40.4	22.6	0.2
Males	304	64.58 ± 7.81	63.69 – 65.46*	0.3	2.3	28.7	43.6	24.8	0.3
Females	191	62.09 ± 8.94	60.82 – 63.37	1.6	9.4	34.0	35.6	19.4	0.0
With PN	60	66.62 ± 8.15	64.48 – 68.76*	0.0	1.7	25.9	34.5	37.9	0.0
Without PN	433	63.12 ± 8.34	62.33 – 63.91	0.9	5.8	31.7	41.0	20.4	0.2

M = mean, SD = standard deviation, CI = confidence Interval, PN = peripheral neuropathy, [+] n = 18 did not provide their gender, n = 20 did not provide their PN status, *statistically significant (95% CI)

Table 24 provides the results for the years since diagnosis of Type 2 diabetes for all participants. The highest proportion of respondents reported being diagnosed with Type 2 diabetes for five years or less (40.9%), however the highest proportion of those with peripheral neuropathy (32.1%) were diagnosed between five to ten years ago. Respondents with peripheral neuropathy had been diagnosed with Type 2 diabetes for significantly longer than those without peripheral neuropathy (95% CI: 9.52 – 14.89).

Table 24 Years since diagnosis of Type 2 diabetes of respondents to the sitting component of the IPAQ.

	n[+]	Years since diagnosis *M* ± SD	95% CI	Range (%)					
				0-5	>5-10	>10-20	>20-30	>30-40	>40
All	513	8.61 ± 6.91	8.00 – 9.23	40.9	31.8	22.1	3.9	1.1	0.2
Male	304	8.98 ± 7.06	8.17 – 9.77	40.1	29.8	24.1	5.0	0.7	0.3
Female	191	7.84 ± 6.67	6.88 – 8.80	43.1	34.6	18.6	2.1	1.6	0.0
With PN	60	12.21 ± 10.03	9.52 – 14.89 *	30.3	32.1	25.0	5.4	5.4	1.8
Without PN	433	8.05 ± 6.30	7.45 – 8.65	43.1	31.4	21.3	3.7	0.5	0.0

M = mean, SD = standard deviation, CI = confidence Interval, PN = peripheral neuropathy, [+] n = 18 did not provide their gender, n = 20 did not provide their PN status , *statistically significant (95% CI)

Sitting Results

All participants, and those without peripheral neuropathy reported sitting for a median of 300 minutes per day as shown in Table 25. However, people with Type 2 diabetes and peripheral neuropathy reported sitting for a median of 360 minutes per day. There was no difference in the level of self-reported sitting between participants with and without peripheral neuropathy

Table 25 Median and interquartile ranges for those who reporting sitting (min/day)

	n[†]	Min/day Median (25^{th}-75^{th})	
All	513	300 (210, 465)	
With PN	60	360 (240, 600)	p = 0.06
Without PN	433	300 (210, 420)	

PN = peripheral neuropathy, [†]n = 20 did not provide their PN status

Figure 14 shows the distribution of minutes of sitting for all participants. The distribution of all those who reported sitting is skewed to the left indicating the majority of participants reported smaller amounts of sitting.

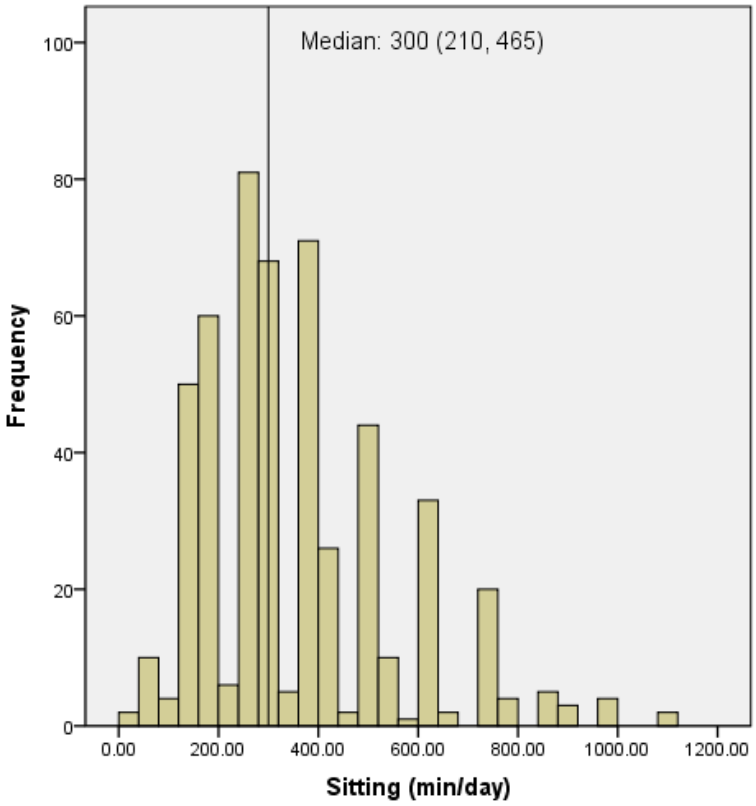


Figure 14 Frequency distribution of sitting (min/day) for all participants

Discussion

A review of the literature provided evidence that physical activity was beneficial for people with Type 2 diabetes and people with Type 2 diabetes and peripheral neuropathy, for its biological, sociological, and psychological benefits. However there was a lack of research into the levels of self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy and their level of compliance to physical activity recommendations. This study appears to the first to assess the self-reported levels of physical activity in people with Type 2 diabetes and peripheral neuropathy and whether or not they were meeting current physical activity recommendations. The results of this study found that people with Type 2 diabetes and peripheral neuropathy were significantly less active than those with Type 2 diabetes alone, with the majority of respondents not meeting physical activity recommendations.

Self-reported physical activity in people with Type 2 diabetes

Respondents with Type 2 diabetes reported engaging in 2076 (*IQR* = 796, 4285) MET-min/wk (median and interquartile ranges reported) of self-reported physical activity in the past 7-days. A total of 31 respondents (6.4%) reported not engaging in any physical activity during the past 7-days. Over half (57%) of the respondents reported engaging in moderate intensity activity during the previous 7-days, making it more popular than vigorous activities (47%). However, the most popular type of activity reported was walking, with 90% of the sample indicating they had participated in at least one bout of walking for at least ten minutes during the previous 7-days. This finding supports previous research whereby authors have reported that walking was the most common and preferred method of physical activity in people with Type 2 diabetes (Barrett et al., 2007, Forbes et al., 2010). A further analysis of the data revealed that males completed significantly more overall self-reported physical activity than women which confers with some previous literature (ABS, 2010, ABS, 2006). Specifically, males engaged in significantly more vigorous, moderate and walking activities than females.

Direct comparison of this study to others is limited as the current study reported medians and inter-quartile ranges rather than means due to the non-normal distribution of physical activity and energy expenditure (IPAQ, 2005). Two studies were found to have used the short IPAQ in people with Type 2 diabetes however reported their results using means. Huang (2009) found a mean of 1078.86 MET-min/wk which is almost half the amount of physical activity that was

reported in the current study. However, it should be noted that Hunag (2009) included those who reported doing no physical activity in the past week in the mean calculation. In the current study, those who reported not participating in any physical activity (n = 31) were removed from the analysis due to the logarithmic transformation of the data. Most recently Mynarski et al. (2012) used the short IPAQ in those with Type 2 diabetes and found a mean of 2469 (*SD* = 1326) MET-min/wk which is more comparable to the current study, although they had a considerably smaller sample size (n = 31) as the primary aim of their study was to compare the participants' declared physical activity against the actual volume as measured using an accelerometer.

Self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy

Respondents with Type 2 diabetes and peripheral neuropathy engaged in a median of 1433 (*IQR* = 495, 3390) MET-min/wk of physical activity in the past 7-days. Almost 10% of the sample reported doing no physical activity in the past week. Respondents with Type 2 diabetes and peripheral neuropathy were significantly less active that those with Type 2 diabetes alone.

A review of the literature during conception of this study identified few studies which assessed self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy. However recently, Van Schie et al. (2011) used acceleromtery to assess the level of physical activity in people with peripheral neuropathy, whilst comparing these results with self-reported physical activity assessed using the IPAQ. The authors found that participants reported almost twice as much physical activity compared to the current study, with a median of 2517 (*IQR* = 686, 10016) MET-min/wk. The authors reported that there was a significant association between self-reported physical activity and the accelerometer (ρ=0.49), noting that self-reported physical activity was underestimated in people with low activity levels (Van Schie et al., 2011). A possible reason for the difference between the two studies could be the younger age of the participants in the Van Schie et al. (2011) study (*M* = 60, *SD* = 9 years), compared to the current study whereby the average age was *M* = 66.6, *SD* = 8.2 years. Secondly, as the study conducted by Van Schie et al. (2011) was primarily aimed at assessing the validity of an accelerometer, the inclusion criteria stipulated that participants had to be able to walk for at least four minutes. The present study did not have any inclusion criteria of this nature, and therefore the sample may have included more sedentary or functionally impaired individuals.

No studies were identified which compared the self-reported physical activity levels of people with Type 2 diabetes compared to Type 2 diabetes and peripheral neuropathy using the IPAQ, however, the two groups have been compared using objective measures (Van Sloten et al., 2011). Van Sloten et al. (2011) found that when assessing physical activity using a pedometer, those with peripheral neuropathy took a significantly less number of steps per day compared to those without peripheral neuropathy. This is in agreement with the current study which found people with peripheral neuropathy were significantly less active than those with Type 2 diabetes alone.

Meeting physical activity recommendations

It appears that as a group, those with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy are achieving physical activity recommendations as indicated by the median for these groups exceeding 150 minutes per week. However, further investigation into the intensity of these reported minutes revealed that 57% and 63% of the reported physical activity was classified as walking as opposed to the recommended moderate intensity for those with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy respectively. This finding supports previous research whereby authors have found that walking was the most common and preferred method of physical activity in people with Type 2 diabetes (Barrett et al., 2007, Forbes et al., 2010).

It was noted that in fact, 57% and 49% of respondents with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy, actually achieved current physical activity recommendations respectively. Of the literature presented in Table 6 in Chapter 2 using the same physical activity recommendations, the proportion of people with Type 2 diabetes meeting recommendations from this study were up to double that of previous research which reported adherence levels between 25% and 41.7% (Morrato et al., 2007, Resnick et al., 2006, Zhao et al., 2011, Zhao et al., 2008). A possible reason for this discrepancy include that aside from Resnick et al. (2006), n = 648, the other studies used a substantially larger sample, up to 20,000 participants. A review of the literature failed to find any data on those with Type 2 diabetes and peripheral neuropathy and whether or not they were meeting current physical activity recommendations.

Comparison of such studies should be done with caution as researchers have found that varying frequency and duration requirements of scoring algorithms can yield different results. Mealing et al. (2011) found that the percentage of respondents who met physical activity recommendations varied dependent on whether they were assessed according to ≥ 150min/wk (39.8%) or ≥ 150min/wk and ≥ 5 sessions/wk (20.3%). Similarly, Sarkin et al. (2000) found the proportion of a sample meeting physical activity recommendations varied between 32% to 59%, depending on the scoring protocol and instrument used (Sarkin et al., 2000).

However, the results of this study should be interpreted with caution as the IPAQ regards the categories of moderate physical activity and walking to be mutually exclusive, such that participants who reported walking may have been doing so at a moderate intensity. The results of this study found that walking was the most preferred activity for the participants, however whether or not this activity was done at a moderate intensity cannot be definitively answered using the protocols of the IPAQ.

Self-reported sitting in people with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy

This study appears to be the first to investigate the self-reported levels of sitting in people with Type 2 diabetes and peripheral neuropathy. This information is important as it has been suggested that the amount of sedentary behaviour in the form of excessive sitting may be detrimental to individuals, independent of whether they are meeting physical activity recommendations (Owen et al., 2010, Patel et al., 2010).

Respondents with Type 2 diabetes reported sitting for a median of 300 (210, 450) minutes per day, or 5.0 hours per day. Due to the relatively new nature of research into sitting, there is a lack of comparable data within this population, however, much of the recent research focuses on television viewing time, as it has been noted that this is the most predominant leisure-time sedentary behaviour (Dunstan et al., 2010). Two recent studies used subjective self-reported measures to assess sitting and yielded similar results. Thorp et al. (2010) assessed data from the 2004-05 Australian Diabetes, Obesity and Lifestyle (AusDiab) study in those yet to be diagnosed with diabetes, and found a significant difference between men (M = 5.71, 95% CI = 5.60-5.82 h/day) and women (M = 5.19, 95% CI = 5.09-5.29 h/day). Data was not presented for the overall sample. Most recently, Gill et al. (2011) used the IPAQ to assess the time spent sitting in a

sample which were enrolled in a Type 2 diabetes prevention trial and found that respondents spent on average $M = 5.75$, $SD = 2.90$ hours per day sitting.

In the current study, respondents with Type 2 diabetes and peripheral neuropathy reported sitting for slightly longer with a median of 360 ($IQR = 240, 600$) minutes per day (a median of 6 hours). No research using subjective measures of sitting were found for comparison. Najafi et al. (2010) used objective accelerometry to find that 13 participants with diabetes and peripheral neuropathy spent approximately 37% of their day sitting, which equates to approximately 530 minutes.

Limitations of Study

A limitation of this study is the limited response rate of 15.1%, or 605 responses. Portney and Watkins (2000) have suggested that a realistic response rate between 30%-60% should be expected for questionnaires, which is at least twice that received in this study. A possible reason for the low response rate may have been expired details on the Diabetes SA database as indicated by the large number of 'return to sender' envelopes sent back to the principal researcher. This low response rate was despite several strategies being used which have been shown to increase postal questionnaire responses, such as using a short questionnaire, using reply paid envelopes, being issued from a University, follow-up contact with non-respondents and the assurance of confidentiality (Edwards et al., 2002, Edwards, 2010, Nakash et al., 2006, Edwards et al., 2009). The low response rate, along with the single channel of recruitment through Diabetes SA may mean the sample is not representative of the broader population of people with Type 2 diabetes and peripheral neuropathy.

Self-reported physical activity questionnaires are most appropriate tool when sampling large populations and have been extensively used by other authors. Self-reported questionnaires were deemed as the only viable method to collect physical activity data in this study due to its inexpensive nature, low participant burden, and because it can be so easily applied to large populations (Dale et al., 2002, Vanhees et al., 2005). In order to reduce the effect of over-reporting, data cleaning procedures of the IPAQ included the exclusion of unreasonably high data, and the truncation of data in an attempt to normalise its distribution (IPAQ, 2005). Further research may indicate the use of objective measures of physical activity, such as accelerometry.

Conclusions

This study appears to be the first to estimate the self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy, and whether or not they are meeting physical activity recommendations. This study identified that people with Type 2 diabetes and peripheral neuropathy had lower levels of physical activity compared to those with Type 2 diabetes alone, with less than half (49%) of respondents with Type 2 diabetes and peripheral neuropathy meeting physical activity recommendations of 150 minutes of moderate intensity per week (ACSM/ADA, 2010). The most prevalent form of physical activity was walking, which lead to many participants not meeting physical activity recommendations, as the IPAQ does not consider walking to be a moderate intensity activity. It is important to promote the use of moderate intensity physical activity in this population, given its positive effects of the biological, sociological and psychological outcomes of peripheral neuropathy which were highlighted in the literature review.

CHAPTER 5: Physical Activity and Quality of Life in people with Type 2 Diabetes and Peripheral Neuropathy

Introduction

In keeping with the biopsychosocial model, this chapter investigates the self-reported quality of life of people with Type 2 diabetes and peripheral neuropathy using the NeuroQol. Having demonstrated through the literature provided in Chapters 1 and 2 that Type 2 diabetes and its complications also impact on social and psychological aspects of people's lives, it is important to understand how Type 2 diabetes and peripheral neuropathy affects quality of life. Having established in Chapter 2 that physical activity may improve the quality of life in this population, and that this population reported insufficient physical activity in Chapter 4, this study will investigate the relationship between self-reported physical activity assessed using the IPAQ, and quality of life assessed using the NeuroQol.

Literature Review

It has been suggested that people with Type 2 diabetes have a poorer quality of life due to the chronic nature of the condition, its association with complications, and its relationship with depression (Egede and Ellis, 2010, Sundaram et al., 2009). Furthermore, it has been established that people with peripheral neuropathy, a common complication of Type 2 diabetes, have a diminished quality of life compared to those without peripheral neuropathy (Chyun et al., 2006, Currie et al., 2006, Olaleye et al., 2001, Vileikyte et al., 2005, Lloyd et al., 2001, Mold et al., 2004, Ovayolu et al., 2008). Several authors have identified that the loss of sensation and decline in physical function associated with peripheral neuropathy may contribute to the diminished quality of life (Mold et al., 2004, Padua et al., 2005, Vileikyte et al., 2005).

Not only has physical activity been noted as a management strategy of Type 2 diabetes due to its health benefits, it has also be considered to provide psychosocial benefits which can reduce morbidity and mortality, and improve quality of life in those with diabetes (Glasgow et al., 1997, Smith and McFall, 2005, Zanuso et al., 2009, Dunstan and Daly, 2007). There is evidence that higher levels of self-reported physical activity are associated with a better quality of life in adult populations as investigated in a systematic review by Bize et al. (2007). Furthermore, several authors have found that adults who met physical activity recommendations had a better quality of life compared to those who did not (Brown et al., 2004a, Vuillemin et al., 2005). However it appears there is limited research into whether this same relationship applies to those with Type 2

diabetes and peripheral neuropathy, as a review of literature did not find any studies which investigated this relationship in this population.

Aim and research questions

The aim of this study was to investigate the level of self-reported quality of life in those with Type 2 diabetes and peripheral neuropathy and determine whether or not there was a relationship between quality of life and self-reported physical activity. The study will also address whether or not there is a difference in self-reported quality of life between those who meet current physical activity recommendations compared to those who do not. The following research questions guide the study in this chapter.

1. What is the quality of life of people with Type 2 diabetes and peripheral neuropathy as measured using the NeuroQol domain, domain summary and overall summary scores and is there a difference by gender?

2. Is there a relationship between the level of self-reported physical activity as measured using the IPAQ MET-min/wk and min/wk variables and self-reported quality of life as measured using the NeuroQol domain, domain summary and overall summary scores?

3. Is there a difference in self-reported quality of life as measured by the NeuroQol domain, domain summary and overall summary scores between those who met current physical activity recommendations and those who did not?

Methodology

Participants

A total of 79 participants (13.1%) out of the 605 respondents initially recruited for the physical activity questionnaire discussed in Chapter 4, agreed to participate in this study. The sole inclusion criteria were that all participants were required to have Type 2 diabetes and peripheral neuropathy as diagnosed by their medical practitioner. There were no exclusion criteria. Participation was voluntary and anonymous and the return of their questionnaire was deemed as consent. Ethical clearance was obtained from the UniSA Human Research Ethics Committee.

Description of tools and instruments

The NeuroQoL is a quality of life instrument which is used to assess physical and social problems associated with Type 2 diabetes and peripheral neuropathy and was developed by Vileikyte et al. (2003) (Appendix 7). It is a disease specific instrument which is hierarchically organised, consisting of 35 items assessing the symptoms of diabetic peripheral neuropathy and psychosocial functioning in six primary domains including pain, symptoms of lost feeling in the feet, sensory motor symptoms, and limitations in daily activities, interpersonal problems and emotional burden. Following each domain, a single item (Domain Summary A-F) assesses the effect of that domain on the individual's quality of life, with two final summary questions (Question 28 & 29), asking how much the respondent's foot problems interfere with their quality of life, and finally, what is their overall quality of life. A diagram of the hierarchical model is shown in Figure 15.

Within each domain of the NeuroQol, respondents were asked to rate the frequency with which each specific item occurs on a five point scale from never = 1, to all of the time = 5. To yield a score for a domain, the mean of the questions are calculated in order to produce what is referred to as a 'scale' score, whereby higher scores represent more severe symptoms or a greater disruption of function.

Each question within a domain is then scored by the respondent according to its 'bother' or 'importance' with 1 = none; 2 = some; 3 = very. A 'weighted' score is then calculated by multiplying the frequency score by the corresponding bother/importance score to provide a more detailed picture of the degree to which the specific experience impacts on an individual's satisfaction or quality of life.

To score the domain summary questions (A-F), respondents are asked how much that domain reduces their quality of life and is coded between 1 = not at all, to, 5 = very much, with higher scores indicating a greater impact on quality of life. There are two final summary questions of the NeuroQol (Questions 28 and 29). Firstly, participants are asked how their foot problems affect their quality of life with scores between 1 = not at all, to, 5 = very much, with higher scores indicating a greater impact on quality of life. Finally, participants are then asked to rate what their overall quality of life is between 1 = poor, to, 5 = excellent, with higher scores indicating a better quality of life.

Psychometric tests of the NeuroQol included factor analyses and internal consistency of scales and a series of multivariate analyses were performed to establish its criterion, construct and incremental validity (Vileikyte et al., 2003). The results were compared with those obtained using the Short Form (SF)-12 measure of health-related functioning. The authors found the NeuroQol to be reliable (α= 0.86-0.95), valid (β = 0.17-0.40, p = 0.001), and more strongly associated with measures of neuropathic severity than the SF-12 (Short Form-12), as it mediated the relationship of diabetic peripheral neuropathy with overall quality of life and significantly explained variance in overall quality of life compared with the SF-12 (Vileikyte et al., 2003).

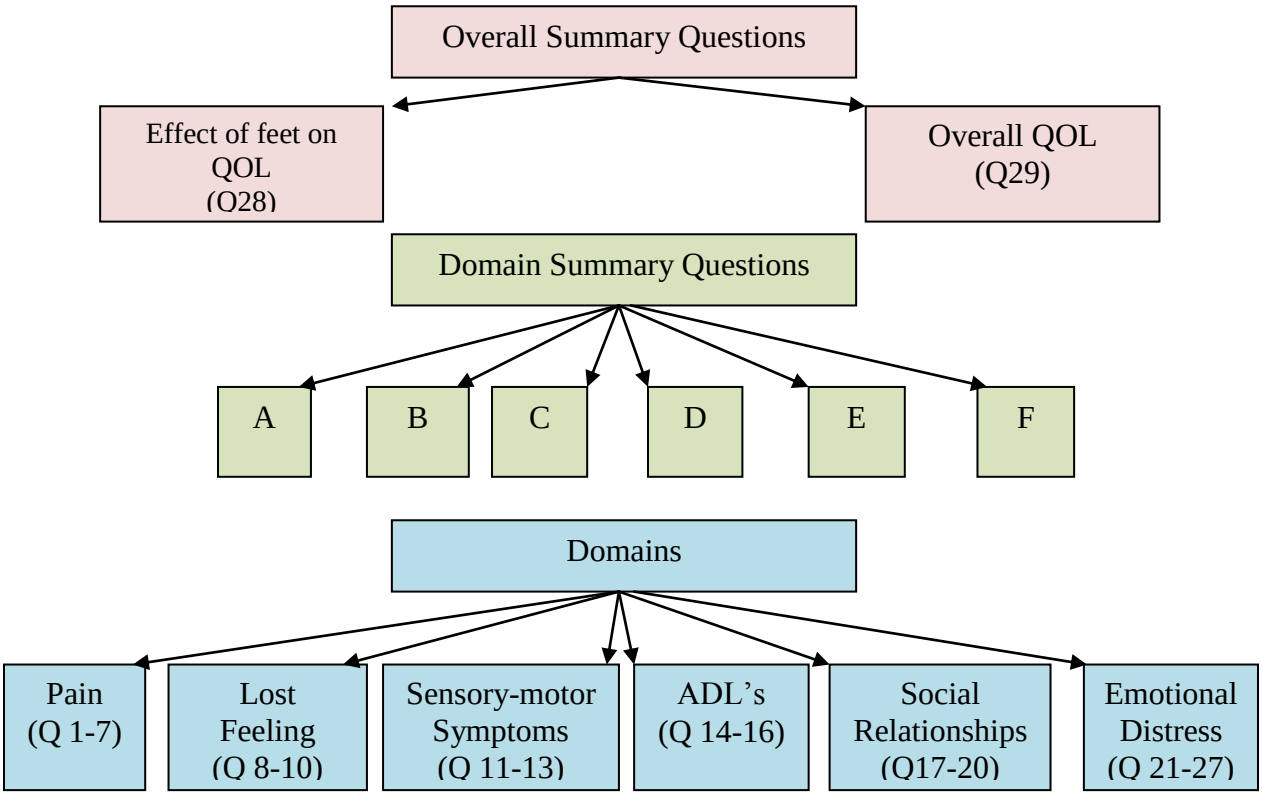


Figure 15 Hierarchical model of the NeuroQol as described by Vileikyte et al. (2003)

Procedures

The procedures followed for the data collection were the same as those outlined in Chapter 4. The only variation for the present study was following the completion of the demographic data sheet and the IPAQ, those participants who indicated they had been diagnosed with peripheral neuropathy by their medical officer were then asked to complete the NeuroQol. The NeuroQol

was printed on blue paper to identify it from the demographic sheet, printed on white paper, and the IPAQ which was printed on yellow paper.

Data analysis

Participants were advised to complete the NeuroQol only if they had responded 'yes' to being diagnosed with peripheral neuropathy. Those who had indicated they did not have peripheral neuropathy, but still completed the NeuroQol, were excluded from analysis. Respondents were also excluded from analysis if they had indicated the presence of peripheral neuropathy, but did not return the NeuroQol.

Data from the NeuroQol was prepared for analysis according to the authors' instructions which are detailed here (Vileikyte et al., 2003). Only respondents who provided a frequency for each question within that domain were able to obtain a 'scale' score. If a respondent failed to provide a frequency for a question, they were excluded from analysis within that domain. Only respondents who provided both a frequency and a bother score for each question within a domain were able to obtain a 'weighted' score. Accordingly, it was possible for a respondent to obtain a scale score, but not a weighted score within a domain. In order to be included in the analysis of research questions two and three (the relationship between quality of life (NeuroQol) and physical activity (IPAQ); and the difference in quality of life in those who meet physical activity recommendations compared to those who do not meet recommendations), respondents were required to have correctly provided a score for both the NeuroQol and IPAQ. Data analysis procedures for the IPAQ were discussed in Chapter 4.

Assessment of the NeuroQol results revealed a non-normal distribution. Accordingly, 95% confidence intervals and the Mann Whitney-U test were used to detect differences between groups for the NeuroQol data. In order to determine if there was a relationship between quality of life and self-reported physical activity in those with Type 2 diabetes and peripheral neuropathy, Spearman's rank correlation coefficient (rho, ρ) was used due to the non-parametric nature of the data sets. Relationships were categorised according to Portney and Watkins (2000).

Results

A total of 4000 questionnaires were distributed across three separate mail-out procedures, with a response of 605 questionnaires (15.1%) as described in Chapter 4. Of the 605 responses, a total of 79 participants (13.5%) indicated they had been diagnosed with peripheral neuropathy as can be seen in Figure 16.

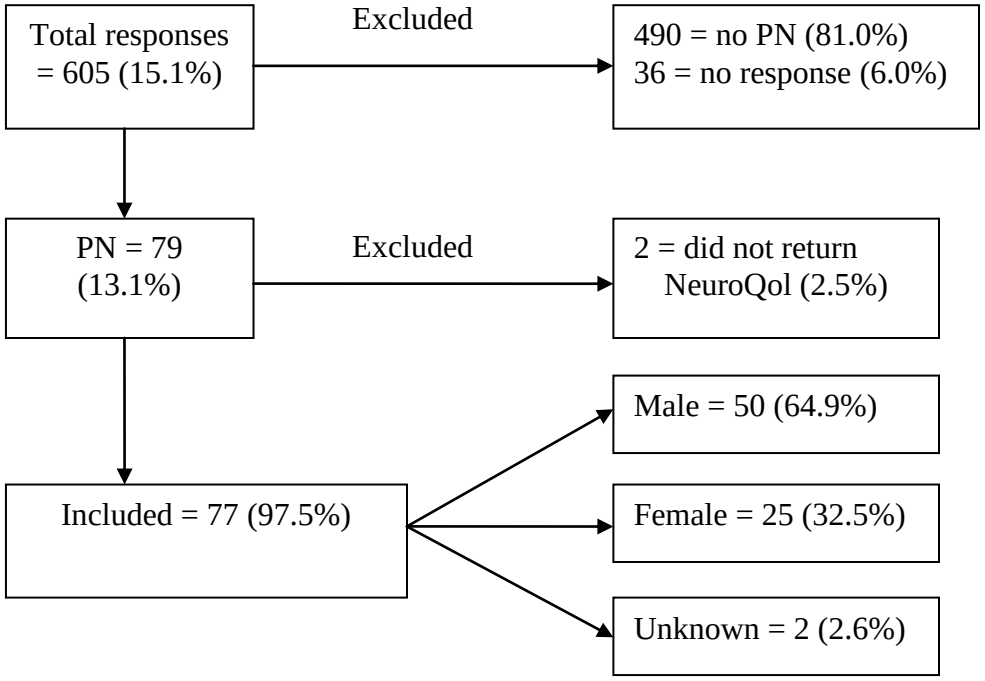


Figure 16 Response rate and gender for respondents with Peripheral Neuropathy (PN) who completed the NeuroQol

Of the 79 responses received a total of 77 responses (97.5%) were used for analysis. The age and years since diagnosis of Type 2 diabetes of the sample are shown in Table 26 with twice as many male respondents than females, and two failing to indicate their gender. Females were older and had been diagnosed with diabetes for longer than their male counterparts, however this was not to a level of significance as shown by the 95% confidence intervals.

Table 26 Age (years) and years since Type 2 diabetes diagnosis for all respondents of the NeuroQol

	n[+]	Age (years) (*M*±*SD*)	95% CI	Years since diabetes diagnosis (*M*±*SD*)	95% CI
All	77	66.21 ± 8.20	64.19 – 68.24	12.03 ± 10.10	9.68 – 14.39
Male	50	65.54 ± 8.91	63.01 – 68.07	10.42 ± 8.90	7.83 – 13.00
Female	25	67.56 ± 8.64	63.99 – 71.13	15.14 ± 11.65	10.33 – 19.95

[+]n = 2 did not provide their gender, M = mean, SD = standard deviation, CI = confidence interval

Scale Scores

Figure 17 shows the mean scale score for each domain for all respondents, by gender. The scale scores have a maximum value of five, with higher scores indicating a greater frequency of symptoms or problems in that domain. The highest scoring scale scores for all respondents included lost feeling (*M* =2.65, *SD* = 1.22), emotional distress (*M* = 2.57, *SD* = 1.30) and activities of daily living (M = 2.56, SD = 1.36). Females reported a significantly worse scale score for activities of daily living compared to males (*M* = 3.09, *SD* = 1.52 versus *M* = 2.32, *SD* = 1.23, p = 0.02). A detailed presentation of results is presented in Appendix 8 (Table 52).

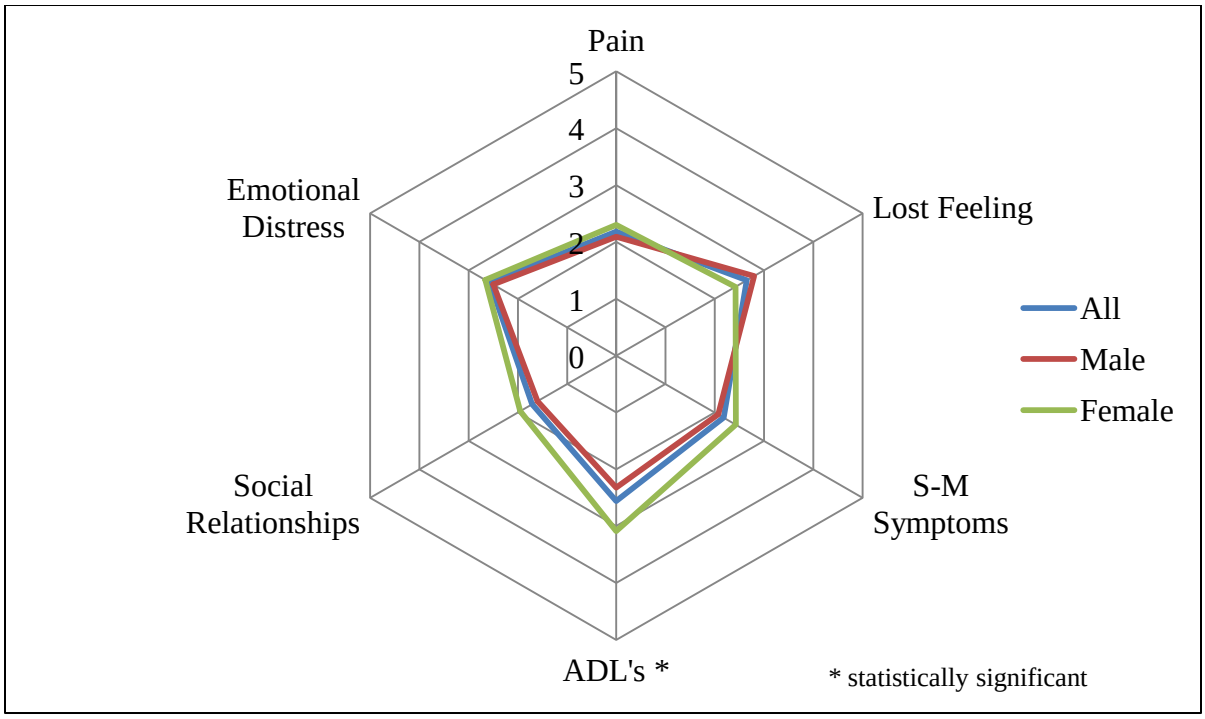


Figure 17 Mean scale scores (/5) for domains of the NeuroQol, by gender
S-M = Sensory-motor, ADLs = Activities of Daily Living

Weighted Scores

Figure 18 shows the mean weighted score for each domain of the NeuroQol for all respondents, by gender. The weighted scores have a maximum score of 15 due to the multiplication of the frequency (/5) and the bother (/3) reported for each domain. The domains which recorded higher weighted scores were the same as those with the higher scale scores, being activities of daily living (*M* = 6.23, *SD* = 4.27), lost feeling (*M* = 5.46, *SD* = 3.77) and emotional distress (*M* = 4.97, *SD* = 3.89). Statistical analysis revealed no significant difference between males and females for any of the six domains. Exact values can be found in Appendix 8 (Table 52).

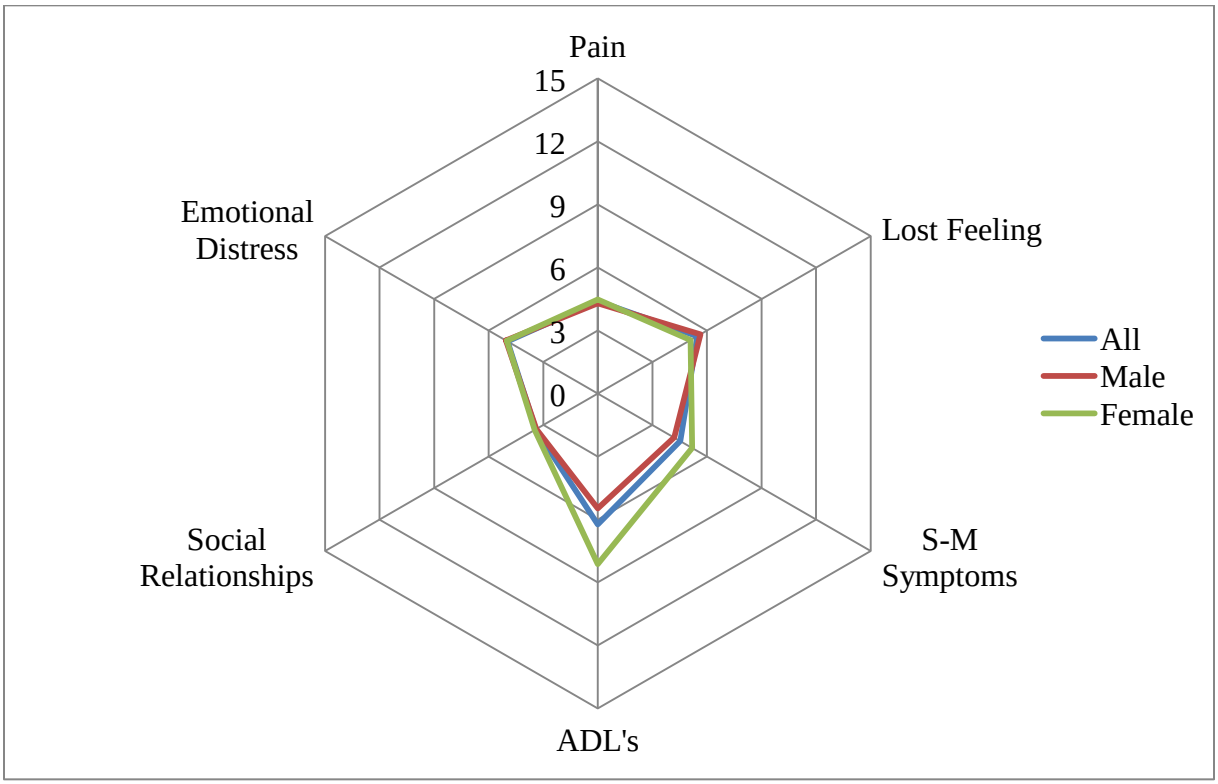


Figure 18 Mean weighted scores (/15) for domains of the NeuroQol, by gender

S-M = Sensory-motor, ADLs = Activities of Daily Living

Domain Summary Scores

Figure 19 displays the mean domain summary scores for all respondents, males and females. The domain summary score assesses the effect of that domain on a participant's quality of life. The highest domain summary scores were activities of daily living (*M* = 2.63, *SD* = 1.40), pain (*M* = 2.55, *SD* = 1.26), and sensory-motor symptoms (*M* = 2.48, *SD* = 1.42), indicating that these domains affected the respondents quality of life more than the other domains. Females reported a significantly higher domain summary score for social relationships compared to males (*M* = 1.89, *SD* = 1.32 versus *M* = 2.57, *SD* = 4.41, p = 0.05) indicating females found their quality of life with respect to this domain was significantly worse. A detailed presentation of results is presented in Appendix 8 (Table 52).

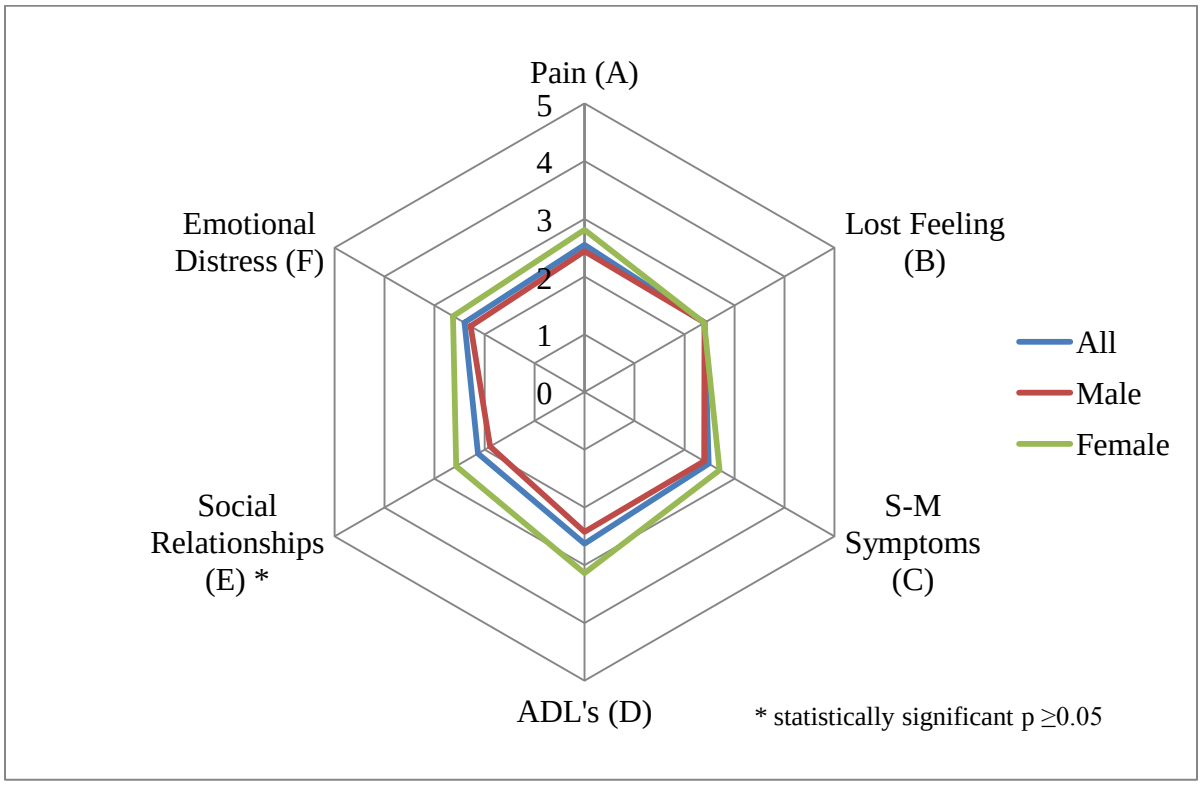


Figure 19 Mean domain summary scores (/5) for domains of the NeuroQol, by gender

S-M = Sensory-motor, ADLs = Activities of Daily Living

Overall Summary Scores

Table 27 provides the results of the overall summary scores of the NeuroQol. Participants were asked to identify to what extent the problems with their feet affected their quality of life, and finally, what was their overall quality of life. Females perceived the problems with their feet to affect their quality of life more negatively than their male counterparts as indicated by a higher score. This is supported by females also rating their overall quality of life worse than males as noted in the lower quality of life scores. However, neither of these differences in gender reached a level of significance.

Table 27 Overall summary questions of the NeuroQol, by gender (*M* ± *SD*)

	n[+]		
Effect of feet on Quality of life			
All	74	2.54 ± 1.24	
Male	47	2.45 ± 1.21	p = 0.47
Female	25	2.68 ± 1.31	
Overall Quality of life			
All	74	2.99 ± 1.05	
Male	47	3.15 ± 1.02	p = 0.11
Female	25	2.76 ± 1.09	

[+] n = 2 did not provide their gender, M = mean, SD = standard deviation

Quality of life and self-reported physical activity

Correlation coefficients were calculated for the scale and weighted scores of the six NeuroQol domains against total MET-min/wk and total min/wk variables of the IPAQ (Table 28). There was no relationship between scale and weighted domain scores of the NeuroQol and total self-reported physical activity as measured by MET-min/wk and min/wk.

Correlation coefficients were also calculated for the scale and weighted scores of the six NeuroQol domains against vigorous, moderate and walking self-reported physical activities (Table 29). There was a significant fair relationship between moderate intensity activity and the scale ADL score (p = 0.05), and the weighted social relationships score (p= 0.02). There was also a significant fair relationship between walking and the scale (p = 0.01) and weighted (p = 0.04) sensory-motor symptom scores, and the ADL scale score (p = 0.02).

Table 28 Spearman's rho (ρ) correlation coefficient for scale and weighted domain scores and total self-reported physical activity (MET.min/wk and min/wk)

		Self-reported physical activity				
		n	**MET.min/wk (ρ)**	**p**	**Min/wk (ρ)**	**p**
Pain	Scale	47	-0.00	0.99	-0.03	0.83
	Weighted	38	0.02	0.91	-0.02	0.92
Lost Feeling	Scale	51	0.04	0.76	0.00	1.00
	Weighted	42	0.08	0.60	0.04	0.81
S-M Symptoms	Scale	52	-0.21	0.13	-0.22	0.11
	Weighted	43	-0.27	0.08	-0.27	0.08
ADLs	Scale	47	-0.20	0.17	-0.24	0.11
	Weighted	40	-0.14	0.38	-0.19	0.25
Social Relationships	Scale	37	-0.07	0.68	-0.04	0.79
	Weighted	25	-0.03	0.87	-0.01	0.95
Emotional Distress	Scale	48	-0.17	0.25	-0.18	0.22
	Weighted	41	-0.05	0.74	-0.08	0.62

S-M = sensory motor, ADLs = Activity of Daily Living

Table 29 Spearman's rho (ρ) correlation coefficient for scale and weighted domain scores and vigorous, moderate and walking physical activities (min/wk)

		n	**Vigorous (ρ)**	**p**	**Moderate (ρ)**	**p**	**Walking (ρ)**	**p**
Pain	Scale	47	0.20	0.19	-0.10	0.50	-0.15	0.31
	Weighted	38	0.18	0.29	-0.15	0.39	-0.10	0.55
Lost Feeling	Scale	51	0.19	0.18	-0.11	0.46	-0.13	0.36
	Weighted	42	0.24	0.13	-0.13	0.42	-0.10	0.53
S-M Symptoms	Scale	52	0.10	0.50	-0.22	0.13	-0.35	0.01*
	Weighted	43	0.04	0.82	-0.29	0.06	-0.31	0.04*
ADLs	Scale	47	0.23	0.13	-0.29	0.05*	-0.34	0.02*
	Weighted	40	0.27	0.10	-0.25	0.13	-0.30	0.06
Social Relationships	Scale	37	0.08	0.66	-0.23	0.16	0.06	0.71
	Weighted	25	0.04	0.87	-0.48	0.02*	0.20	0.35
Emotional Distress	Scale	48	0.15	0.30	-0.25	0.09	-0.16	0.28
	Weighted	41	0.24	0.13	-0.19	0.24	-0.16	0.34

*correlation is significant at the 0.05 level (2-tailed). S-M = sensory-motor, ADLs = Activities of Daily Living

Table 30 displays the relationship between total physical activity as measured by MET-min/wk and min/wk variables of the IPAQ, and the overall summary and domain summary (A-F) questions of the NeuroQol.

Table 30 Spearman's rho (ρ) correlation coefficients for summary quality of life questions and total self-reported physical activity (MET.min/wk and min/wk)

Overall Summary Scores	n	MET.min/wk (ρ)	p	Min/wk (ρ)	p
Overall QOL	51	0.43	<0.01*	0.42	<0.01*
Effect of feet on QOL	51	-0.05	0.74	-0.06	0.67
Domain Summary Scores (A-F)					
Pain (A)	50	-0.14	0.34	-0.14	0.33
Lost Feeling (B)	51	-0.07	0.62	-0.11	0.43
Sensory Motor Symptoms (C)	49	-0.25	0.09	-0.24	0.10
ADLs (D)	48	-0.26	0.07	-0.28	0.05*
Social Relationships (E)	48	-0.04	0.79	-0.04	0.81
Emotional Distress (F)	51	-0.04	0.80	-0.06	0.68

*correlation is significant at the 0.05 level (2-tailed), QOL = quality of life, ADLs = Activities of Daily Living

As can be noted from Table 30, the strongest relationship was between total physical activity and overall quality of life. A non-parametric correlation found a significant fair relationship between overall quality of life and physical activity as measured in MET-min/wk ($\rho = 0.43$, $p < 0.01$) and min/wk ($\rho = 0.42$, $p < 0.01$). A significant fair relationship was also found for the summary ADL domain score ($\rho = -0.28$, $p = 0.05$).

Further analysis sought to determine if there was any relationship between the summary scores of quality of life and the duration of vigorous, moderate and walking intensities of physical activity (min/wk) as shown in Table 31.

Table 31 Spearman's rho (ρ) correlation coefficients for summary quality of life questions and vigorous, moderate and walking intensities of self-reported physical activity (min/wk)

Overall Summary Scores	n	Vigorous (ρ)	p	Moderate (ρ)	p	Walking (ρ)	p
Overall QOL	51	0.12	0.42	0.43	0.00*	0.25	0.08
Effect of feet on QOL	51	0.14	0.33	-0.20	0.15	-0.07	0.64
Domain Summary Scores (A-F)							
Pain (A)	50	0.10	0.50	-0.25	0.08	-0.13	0.38
Lost Feeling (B)	51	0.24	0.09	-0.28	0.04*	-0.14	0.32
Sensory-Motor Symptoms (C)	49	0.01	0.94	-0.34	0.02*	-0.20	0.18
ADLs (D)	48	0.26	0.17	-0.35	0.01*	-0.32	0.03*
Social Relationships (E)	48	0.16	0.27	-0.19	0.20	-0.06	0.67
Emotional Distress (F)	51	0.23	0.10	-0.16	0.26	-0.14	0.35

*correlation is significant at the 0.05 level (2-tailed), QOL = quality of life, ADLs = Activities of Daily Living

A significant relationship ($p < 0.05$) was found between the level of self-reported moderate physical activity (min/wk) and overall quality of life, and the domain summary scores of lost feeling, sensory-motor symptoms and activities of daily living. These relationships are considered fair ($\rho = 0.25$-0.50) as shown in Table 31. A significant relationship ($p < 0.05$) was also found between the level of self-reported walking (min/wk) and the domain summary score of activities of daily living. This relationship is also considered fair ($\rho = 0.25$-0.50). There were no relationships between the summary quality of life scores and self-reported vigorous activity.

Quality of life and physical activity recommendations

An analysis was conducted as to whether there were differences in the level of quality of life between those participants who were deemed to meet the current physical activity recommendations of 150 minutes of at least moderate activity per week. Figure 20 shows the mean scale score of all domains of the NeuroQol for those who did meet current physical activity recommendations compared to those who did not. There was no significant difference in the scale scores between those who did, and did not meet current physical activity recommendations. Results can be found in Appendix 8 (Table 52).

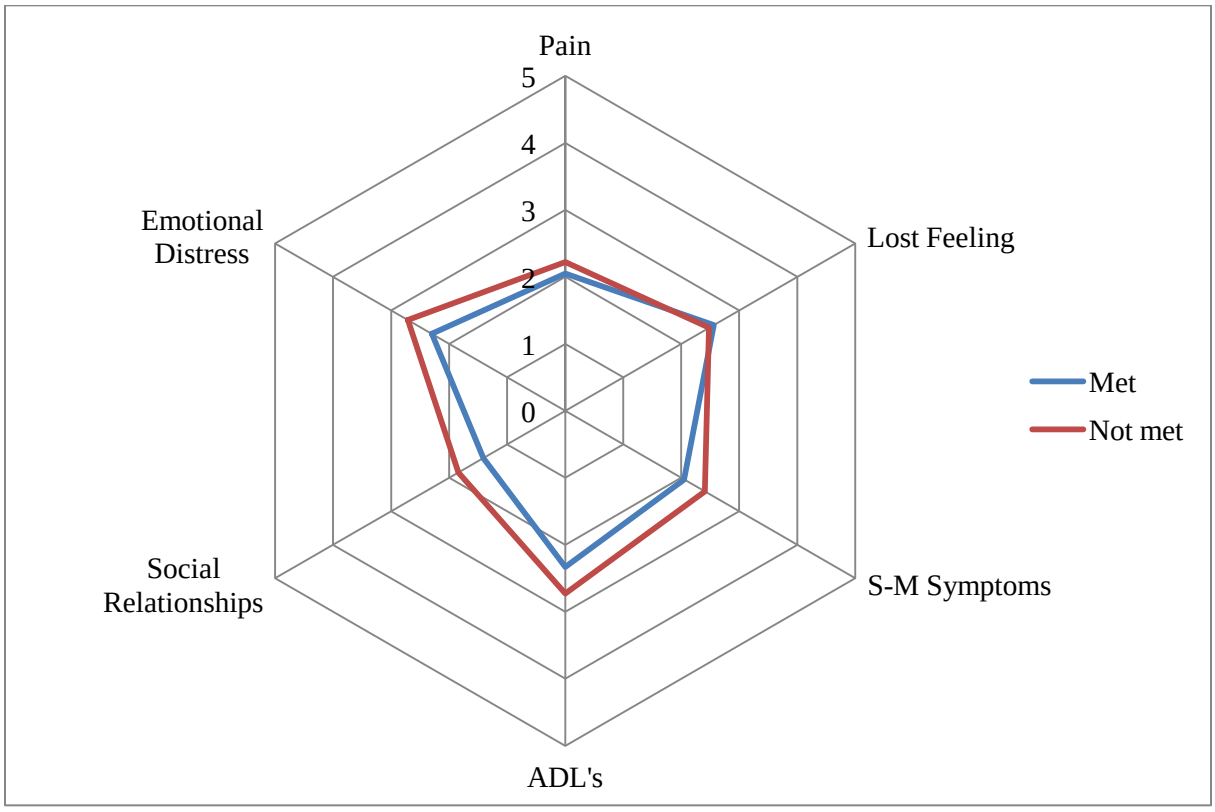


Figure 20 Mean scale score (/5) of domains of the NeuroQol comparing those who did (met), and did not (not met) meet current physical activity recommendations

S-M = Sensory-Motor, ADLs = Activities of Daily Living

Figure 21 shows the mean weighted scores for domains of the NeuroQol, comparing those who did meet current physical activity recommendations to those who did not. Those who met current physical activity recommendations were significantly less affected by problems associated with their social relationships than those who did not meet current physical activity recommendations ($p = 0.04$). Results can be found in Appendix 8 (Table 52).

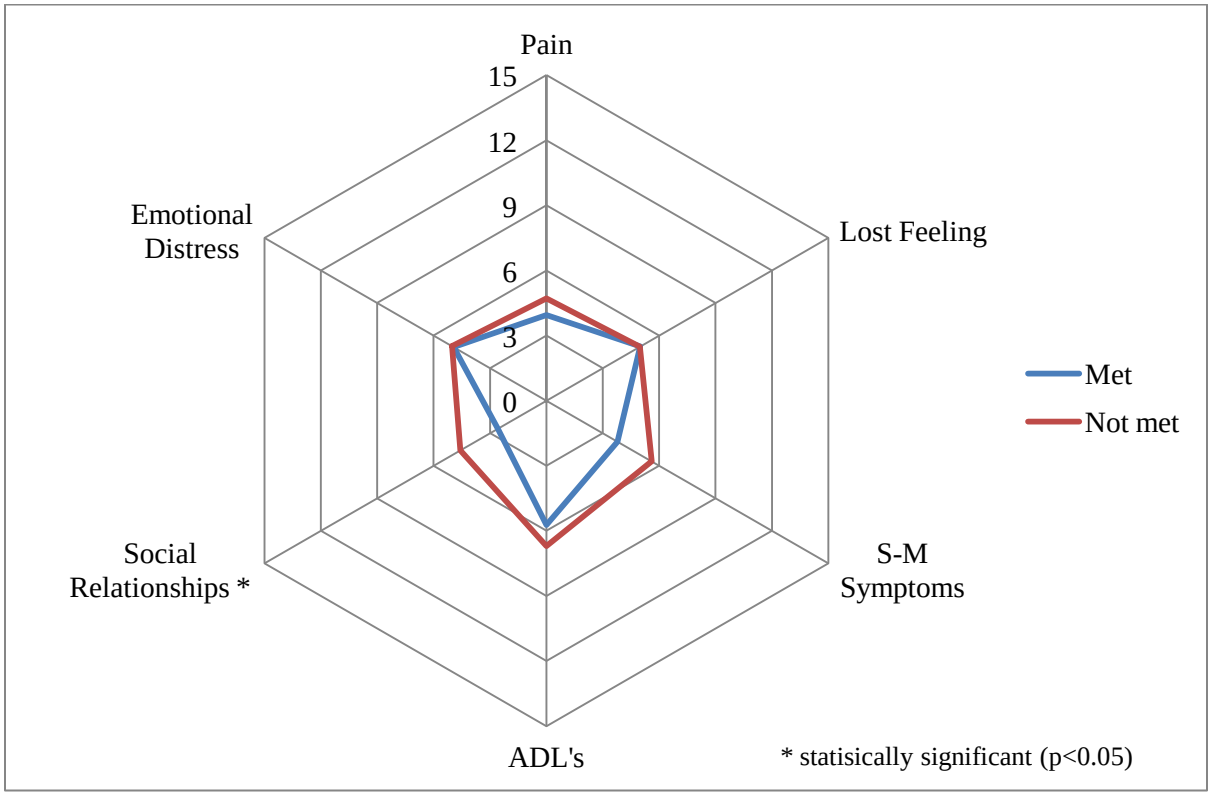


Figure 21 Mean weighted scores (/15) of domains of the NeuroQol comparing those who did (met) and did not (not met) meet current physical activity recommendations.

S-M = Sensory-Motor, ADLs = Activities of Daily Living

Figure 22 displays the mean domain summary scores of the NeuroQol between those who did, and did not meet current physical activity recommendations. Those who met current physical activity recommendations were significantly less likely to have sensory-motor symptoms impact their quality of life compared to those who did not meet recommendations (p = 0.04). Exact values can be found in Appendix 8 (Table 52).

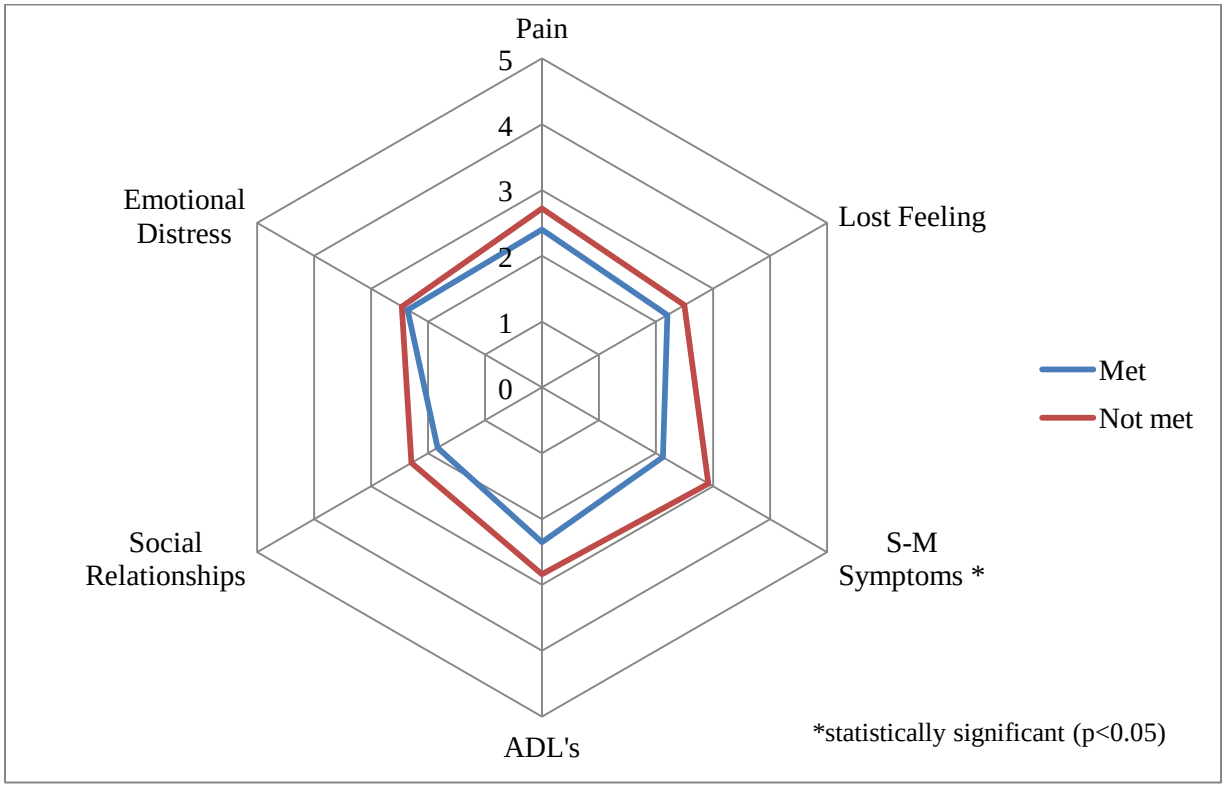


Figure 22 Mean domain summary scores (/5) of domains of the NeuroQol comparing those who did (met) and did not (not met) meet current physical activity recommendations

S-M = Sensory-Motor, ADLs = Activities of Daily Living

A comparison also investigated the difference between those who met and did not meet the current physical activity recommendations for the overall summary questions of the NeuroQol. Table 32 displays these results. Those who met physical activity recommendations had a significantly better quality of life than those who did not meet the recommendations ($p < 0.001$).

Table 32 Comparison of overall summary questions of the NeuroQol between those who met (met) current physical activity recommendations compared to those who did not (not met)

	n	Overall, I would say problems with my feet reduced my quality of life: (*M* ± *SD*)	
Met	25	2.36 ± 1.22	p = 0.42
Not met	26	2.65 ± 1.29	
		Overall, I would rate my quality of life as: (*M* ± *SD*)	
Met	25	3.48 ± 1.08	p = 0.00
Not met	26	2.58 ± 0.90	

Discussion

The results of this study demonstrate for the first time that those with Type 2 diabetes and peripheral neuropathy, who reported engaging in the recommended 150 minutes of moderate intensity activity per week, had a significantly better overall quality of life compared to those who did not meet recommendations. The results of this study support the promotion of moderate physical activity for people with Type 2 diabetes and peripheral neuropathy due to its positive effects on the sociological and psychological roles of the disease.

In this thesis the NeuroQol was separated into three types of scores being domain, domain summary and overall summary scores. Furthermore, domain scores were separated into scale and weighted scores, with scale scores indicating the frequency or severity of a symptom or dysfunction, and a weighted score indicating a bother or importance of that symptom or dysfunction to the participant. As was the case in this study, a domain could have a high scale score compared to other domains, but have a low weighted score, implying that although the frequency or severity may be high, it may not bother or be deemed important to the participant. Domain summary scores came from an independent question which asked the participant to rate the effect that domain had on their quality of life. Therefore, it was possible for a domain to have

a high scale or weighted score, however if it was deemed not to have a great impact on quality of life, then the domain summary score may in contrast, be low.

Quality of life in people with Type 2 diabetes and peripheral neuropathy

The highest scoring scale and weighted domains were emotional distress, lost feeling and activities of daily living, suggesting that these domains have the greatest frequency and severity, and importance and bother in people with Type 2 diabetes and peripheral neuropathy. The higher domain summary scores included activities of daily living, pain and sensory-motor symptoms indicating these domains affected the respondents' quality of life more than the other domains.

Activities of daily living had higher scale, weighted and domain summary score compared with other domains. This suggests that the presence of peripheral neuropathy results in greater dysfunction, bother and effect on quality of life in the daily activities of the participants compared with other domains. This is supported in the literature whereby peripheral neuropathy has been associated with severe consequences in the daily lives of those diagnosed including tasks such as walking, occupational performance, housework and leisure (Liedberg and Vrethem, 2009). The questions asked in the domain of activity of daily living refers to the participant's ability to perform paid work, perform tasks around the house and garden, and take part in leisure activities (Appendix 7).

Several studies have investigated the quality of life in those with Type 2 diabetes and peripheral neuropathy, however many of these results are not comparable to the current study due to the use of various generic quality of life instruments such as the SF-36 and the WHOQoL-BREF (Chyun et al., 2006, Lloyd et al., 2001, Ovayolu et al., 2008). Although some studies described below have previously used the NeuroQol to assess quality of life in those with Type 2 diabetes and peripheral neuropathy, not all have used the questionnaire to its full capacity. Davies et al. (2006) combined the means of the six domains to produce a single quality of life score, while Lavery et al. (2008) used a composite category score of selected questions. Vileikyte et al. (2005) reported the scale scores of the pain (M = 1.96, SD = 0.86), lost feeling (M = 2.85, SD = 1.48) and ADLs (M = 2.51, SD = 1.38) domain in a large sample (n = 494) of respondents from the US and UK, and reported similar scores to the scale scores found in this study (Appendix 8, Table 52). Although Vileikyte et al. (2005) also collected and reported scores for sensory-motor symptoms

and the emotional distress domains, not all questions within that domain were used, and therefore are unable to be compared to the current study. Vileikyte et al. (2009) followed up their 2005 study and found similar results, with scores of the lost feeling domain increasing over the 4 year period. The study presented in this chapter appears to be the first to use the NeuroQol in its entirety to investigate the quality of life in people with Type 2 diabetes and peripheral neuropathy.

The relationship between self-reported physical activity and quality of life

This study appears also to be the first to investigate the relationship between self-reported physical activity and quality of life in people with Type 2 diabetes and peripheral neuropathy.

The results demonstrated there was a fair and significant relationship between overall quality of life and total physical activity. The positive relationship suggests that as the level of total physical activity increases, so does overall quality of life (or vice versa), supporting the promotion of exercise for people with Type 2 diabetes and peripheral neuropathy. This is supported by Glasgow et al. (1997) who found that self-reported physical activity was the only significant self-management behaviour able to predict the quality of life in people with diabetes. Similarly, Smith and McFall (2005) found that exercise was associated with a reduction of impaired days per month on all measures of quality of life in people with diabetes. It was noted that those respondents who exercised, reported several domains equal or even better than those without diabetes who did not exercise, suggesting that exercise helped to eliminate the negative effects of diabetes on quality of life (Smith and McFall, 2005).

A fair and significant relationship was also found between the activities of daily living domain summary score and the total minutes per week of self-reported physical activity. This relationship indicated that an increase in the minutes of physical activity per week would result in a decrease in the domain summary score of activities of daily living, which is a positive outcome for the individual. As the results described earlier, activities of daily living had the greatest effect on quality of life, therefore, physical activity is supported to decrease this burden.

The relationship between domain summary scores and vigorous activity indicated that as levels of vigorous physical activity increase, quality of life decreased. This suggests that vigorous activity may not be as beneficial for those with Type 2 diabetes and peripheral neuropathy when

aiming to improve their quality of life. The results indicated that the strongest relationship between physical activity and summary scores of the NeuroQol were for moderate intensity physical activity suggesting this type of exercise should be promoted among this population. All of the relationships between moderate and walking intensities and domain summary scores indicated that as moderate and walking intensity activity decreases, the impact of peripheral neuropathy on their quality of life within these domains increases. Despite the lack of previous literature addressing this question using the same instruments as the current study, previous studies using healthy participants and other instruments also found stronger relationships between self-reported physical activity of a light to moderate intensity and quality of life compared to more vigorous activities (Acree et al., 2006, Lustyk et al., 2004).

Quality of life and physical activity recommendations

All variables of quality of life measured by the NeuroQol between those who did and did not meet physical activity recommendations were compared. The most important finding of this study was that people who met physical activity recommendations had a significantly better quality of life than those who did not meet recommendations. This finding suggests that physical activity performed at an intensity to meet current recommendations has a positive effect on quality of life. Given it has been suggested that those with Type 2 diabetes and peripheral neuropathy have a poor quality of life (Chyun et al., 2006, Currie et al., 2006, Vileikyte et al., 2005, Ovayolu et al., 2008), the promotion of moderate intensity physical activity within this population to a level which meets current physical activity recommendations may aid in improving quality of life.

A review of the literature found no comparative studies using the IPAQ and the NeuroQol to assess the relationship physical activity recommendations and quality of life indicating the unique results of this study. Furthermore, there is an absence of literature investigating this relationship in those with Type 2 diabetes and peripheral neuropathy using other self-reported instruments. Only one similar study whereby those with pre-diabetes were assessed using the Godin LTPA questionnaire and the RAND-12 Health Status Inventory was located during the literature review (Taylor et al., 2010). Taylor et al. (2010) found a significant difference in the physical and mental health in those who met physical activity recommendations compared to those who did not. Comparing the results of the present study to Taylor et al. (2010) should be

done with caution given the use of a disease-specific quality of life (NeuroQol), in the present study versus a generic questionnaire (Godin LTPA). However similarities do exist in that meeting current physical activity recommendations in both studies resulted in a significant improvement in quality of life compared to those who did not, regardless of the population and instruments used. This may also be supported by various other authors already highlighted in the literature review who found a relationship between self-reported quality of life, and meeting current physical activity recommendations in other healthy populations (Brown et al., 2003, Brown et al., 2004a, Vuillemin et al., 2005).

Limitations

A limitation of this study is the smaller than anticipated sample size as previously discussed in Chapter 4. A response rate of 15.1% or 605 responses was received, of which 79 respondents indicated they had been diagnosed with peripheral neuropathy with two of these being excluded from analysis. A discussion of response rates and the strategies used in an attempt to increase the response rate was explored in Chapter 4.

A second limitation of this study is the amount of incomplete data received from the respondents, which was largely attributed to participants' failing to indicate a 'bother' or 'importance' score for questions within a domain. This meant a number of respondents were unable to receive a weighted score for a domain. Whilst this double-barreled approach to questions within the NeuroQol may be seen as confusing to the participant, the NeuroQol was considered to be the most suitable instrument to collect quality of life information from those with Type 2 diabetes and peripheral neuropathy due to its disease specific nature.

As this study focused on the relationship between the two variables, it was not able to determine causality; whether the increase in physical activity lead to an improved quality of life or vice versa. Finally, as discussed in Chapter 4 the IPAQ considers moderate physical activity and walking to be mutually exclusive and therefore the determination of participants as either meeting physical activity recommendation or not meeting physical recommendations was made according to these protocols, and may not be comparable to other physical activity recommendations.

Conclusions

The most significant finding of this study is that respondents who self-reported meeting physical activity recommendations had a better quality of life compared to those who did not meet recommendations. Furthermore, moderate physical activity had the strongest relationship with better scores of quality of life compared to walking and vigorous activities. These findings support the implementation of a moderate intensity physical activity program in people with Type 2 diabetes and peripheral neuropathy.

CHAPTER 6: The effect of a combined exercise program in people with Type 2 Diabetes and Peripheral Neuropathy

Introduction

In this chapter the effects of a combined aerobic and resistance training program on safety, quality of life, sensation and function in a sample of people with Type 2 diabetes and peripheral neuropathy are investigated. Having established the positive biological, social and psychological effects of physical activity on those with Type 2 diabetes in the review of the literature in Chapter 2, it is important to investigate these effects on those with Type 2 diabetes and peripheral neuropathy. Furthermore, the study presented in Chapter 4 identified that people with Type 2 diabetes and peripheral neuropathy were not participating in sufficient activity at the correct intensity deemed to be meeting recommendations, whilst Chapter 5 established that there was a positive association between physical activity and quality of life. Therefore, it is important to investigate the effects of a prescribed exercise program on people with Type 2 diabetes and peripheral neuropathy, not only on quality of life, but to also assess the safety of the program, and its impact on lower limb sensation and physical function.

Literature Review

The role of physical activity and exercise for people with Type 2 diabetes and peripheral neuropathy has received much less attention than in those with Type 2 diabetes alone. However, as discussed in Chapter 2 of this thesis the positive effects of various exercise programs in people with Type 2 diabetes and peripheral neuropathy have recently been reported (Fisher et al., 2007, Otterman et al., 2011, Tuttle et al., 2012). The conclusions of these recently published studies were that exercise was not contraindicated in people with Type 2 diabetes and peripheral neuropathy, as long as it was carefully prescribed and monitored. In addition, it has been reported that people with Type 2 diabetes have a diminished quality of life (Papelbaum et al., 2010, Pena et al., 2010) and whilst various studies have reported the effects of physical activity on quality of life, there have been varying results.

Despite the physical activity guidelines for those with diabetes and peripheral neuropathy recently being amended to recommend moderate weight bearing (ACSM/ADA, 2010), there remains little research in this area of exercise with people with Type 2 diabetes and peripheral neuropathy. Due to the increased risk of ulceration and amputation as a result of the sensory loss associated with peripheral neuropathy, it has been recognised that it is important to assess and

monitor sensation to determine safe levels of physical activity or exercise (Bansal et al., 2006, Duby et al., 2004, Vinik and Mehrabyan, 2004). In several studies where exercise was prescribed as part of an intervention, there was limited information about the safety measures implemented, or whether or not any adverse events resulted (Ahn and Song, 2012, Fisher et al., 2007, Richardson et al., 2001). However, other studies which provided greater detail of the safety procedures implemented, indicated that poorly controlled blood glucose levels were the largest contributing factor to adverse events (Kluding et al., 2012, Otterman et al., 2011).

Although there have been recent efforts to investigate the effect of various exercise programs in people with Type 2 diabetes and peripheral neuropathy, this area of research is still in its infancy. It remains unclear if exercise is safe, beneficial and improves quality of life in people with Type 2 diabetes and peripheral neuropathy.

Aim and research questions

The aim of the study reported in this chapter was to investigate the effect of a prescribed aerobic and resistance training program in people with Type 2 diabetes and peripheral neuropathy with respect to safety, quality of life, sensation and function. A single case experimental design using the ABA withdrawal method with direct and systematic replication was used to answer the following research questions.

1. Is a prescribed exercise intervention safe for people with Type 2 diabetes and peripheral neuropathy?

2. Does a prescribed exercise intervention improve self-reported quality of life in people with Type 2 diabetes and peripheral neuropathy?

3. Does a prescribed exercise intervention improve sensation as measured by protective sensation and vibration perception threshold in people with Type 2 diabetes and peripheral neuropathy?

4. Does a prescribed exercise intervention improve the functional capacity as measured by the Physical Performance Test and muscle strength in those with Type 2 diabetes and peripheral neuropathy?

Methodology

Participants

Participants were recruited from Diabetes SA and the UniSA Podiatry Clinic using a variety of methods. Questionnaires (n=2000) were mailed out to members of Diabetes SA (as described in Chapter 4), and participants were asked to provide their contact details if they were interested in participating in an exercise program. Those who showed interest in participating were subsequently sent an information sheet (Appendix 9).

Participants were also recruited from Diabetes SA through information provided at education sessions and through an advertisement in a quarterly membership magazine, 'Living'. Diabetes SA has over 30,000 members, 82% of whom have Type 2 diabetes. The number of members with Type 2 diabetes and peripheral neuropathy was difficult to determine, however with 45% of Diabetes SA clients residing within the metropolitan area, and given the prevalence of peripheral neuropathy is approximated at 18.9% (NADC, 2009), it was estimated the advertisement could have reached approximately 4,500 people in the target population.

Participants were also recruited from the UniSA Podiatry Clinic. A letter of invitation was sent to those clients with Type 2 diabetes (n = 355) (Appendix 10). Clients who were interested in participating were urged to contact the principal researcher whereby a separate information sheet (Appendix 11) was sent out for further information.

The inclusion and exclusion criteria for the study are outlined in Table 33.

Table 33 Inclusion and exclusion criteria for the exercise program

Inclusion Criteria	Exclusion Criteria
Type 2 diabetes for greater than 6 months and controlled by diet and or hypoglycaemic agents	Type 1 diabetes or Type 2 controlled by insulin
The presence of peripheral neuropathy as diagnosed by a medical officer	History of recurrent hypoglycaemic episodes within past 6-months
Not currently participating in regular aerobic exercise or resistance training nor had been during the previous 6 months.	The presence of any comorbidities or injury which would inhibit physical activity such as severe cardiovascular disease, retinopathy, severe arthritis
Aged 18 years and over	The presence of any foot ulceration, gangrene or amputation

Participants were assessed by an independent Accredited Exercise Physiologist with four years' experience prior to the commencement of the program to assess pre-existing conditions or injuries other than those described in the exclusion criteria. Participants who had experienced symptoms relating to peripheral neuropathy, but who had not been diagnosed by their medical practitioner were assessed by a Podiatrist at the UniSA Podiatry Clinic. Participants who were deemed ineligible were offered sessions in the Diabetes Exercise Clinic at the UniSA. All participants who satisfied the inclusion criteria and agreed to participate in the study were asked to provide informed consent and a pre-exercise medical clearance from their General Practitioner prior to the collection of any data. Participants were asked not to commence any regular physical activity beyond that of the prescribed program. This study was reviewed and approved by the UniSA Human Research Ethics Committee.

Description of tools and instruments for gathering data

A single-case research design (ABA) was used for the study. The outcome measures were divided into four categories, namely safety, quality of life, sensation and function. Quality of life, sensation and function measures have been found to be reliable and valid as shown in Table 34. All outcome measures were assessed at UniSA in the School of Health Sciences facilities by the principal researcher using standard procedures. The description and protocols for each measurement are described below.

Table 34 Reliability and validity of quality of life, sensation and function outcome measures

Measurement	Validity	Reliability	Data Type	Reference
Quality of Life				
NeuroQol	Criterion: NDS β = 0.165-0.395 Incremental: $r^{2=}$ 0.287-0.350 Construct: r^2= 0.295-0.350 For all domains	Chronbach's α = 0.86-0.95 for all domains	Ordinal	(Vileikyte et al., 2003)
Sensation				
Semmes Weinstein Monofilament	Sensitivity = 87.5% Specificity = 61.4%	Correlation Coefficient Intraobserver = 0.80 Interobserver = 0.77	Nominal	(Valk et al., 1997)
Vibration Perception Threshold (VPT)	SAC sum score r = 0.83	Cohens κ Intraobserver & interobserver = 0.69	Ratio	(Meijer et al., 2005)
Functional Measures				
Maximal Isokinetic Peak Torque	Instrument validity (torque) against a criterion value ICC = 0.99	Knee flexion ICC=0.94 Knee extension ICC=0.95	Ratio	(Drouin et al., 2004, Sole et al., 2007)
Physical Performance Test (PPT)	Construct & concurrent: Katz ADL = 0.50 Rosow-Breslau scale = 0.69 Spector Scale = 0.56	Chronbach's α = 0.79 Interrater reliability *r* = 0.93 (pearson's product-moment correlation)	Ratio	(7-item scale) (Reuben and Siu, 1990)

NDS: Neuropathy Disability Score, QOL = Quality of Life, ADL = Activities of Daily Living, ICC = Intra Class Correlation, SAC = San Antonio Consensus

Quality of life measurement

NeuroQol

Perceived quality of life was measured using the neuropathic specific quality of life instrument, NeuroQol (Vileikyte et al., 2003) which has been described in Chapter 5. The questionnaire refers to the previous four weeks and was therefore administered monthly throughout the five month study period.

Sensation measurement

A Semmes Weinstein Monofilament was used to assess protective sensation, and a biothesiometer was used to assess VPT. It is commonly noted that the combined use of the monofilament and biothesiometer can be a more valid measure of sensation than either instrument alone. When the Semmes Weinstein Monofilament and VPT scores are combined, a substantial increase in specificity has been detected, with little or no reduction in sensitivity (Armstrong et al., 1998). Rahman et al. (2003) concluded that whilst the VPT appeared to be the most valid measure of peripheral nerve function, testing using a combination of VPT and monofilament was more sensitive in identifying neuropathy than either instrument alone. Both instruments are reported as valid and reliable measurement tools which have been extensively used in previous studies.

Protocol for protective sensation testing

In accordance with the International Working Group for the Diabetic Foot (IWGDF) a 10g Semmes Weinstein monofilament was applied to three testing sites on the plantar surface of each foot namely the great toe, first metatarsal and fifth metatarsal as shown in Figure 23 (Apelqvist et al., 2000). Testing occurred at non-calloused sites and if any of the three testing sites were calloused, a point as close as possible was tested instead. Participants were tested in a supine position on an examination bed (Olaleye et al., 2001, Perkins et al., 2001).

To ensure consistency of results and the relaxation of the participant, a standard pre-testing procedure was followed. Prior to testing, participants were shown the monofilament to reduce any anxiety and it was applied to their hand to provide a reference sensation (Apelqvist et al., 2000, Rahman et al., 2003, Simeone and Veves, 1997). Participants were then asked to close their eyes before commencement of the test. The monofilament was applied perpendicular to the

skin with enough force to cause to the filament to buckle as shown in Figure 23. The total duration of the approach, contact and removal of filament was approximately 2 seconds and caution was taken to ensure that the filament did not slide across the skin or make repetitive contact at the site (Apelqvist et al., 2000).



Figure 23 Recommended application and testing site of the monofilament

The standard yes/no method of response was used whereby upon the commencement of testing, participants were asked to indicate if they felt the pressure being applied by responding 'yes' (Armstrong et al., 1998, Miranda-Palma et al., 2005, Pham et al., 2000, Simeone and Veves, 1997). At the time which the participant responded 'yes' they were then asked to determine whether the pressure was applied to the left or right foot (Apelqvist et al., 2000). The application of the monofilament at each site was random, with three applications at each of the three sites equating to a maximum score of nine for each foot.

Protocol for vibration perception threshold (VPT)

VPT was assessed using a biothesiometer (Bio-Medical Instrument Company, Ohio). VPT testing took place with the participants in a supine position on an examination bed in a quiet environment (Goldberg and Lindblom, 1979). A familiarisation test was conducted by placing the stylus on the participant's hand and turning the biothesiometer to the maximum voltage (Bloom et al., 1984, Miranda-Palma et al., 2005, Simeone and Veves, 1997). Participants were tested at the hallux of both the left and the right foot (Armstrong et al., 1998, Bloom et al., 1984, Frykberg et al., 1998, Miranda-Palma et al., 2005, Pham et al., 2000, Simeone and Veves, 1997). The stylus was placed in a vertical position against the skin at the distal aspect of the hallux to ensure the vibration was transferred maximally to the underlying bone (Goldberg and Lindblom,

1979, Miranda-Palma et al., 2005, Pham et al., 2000, Simeone and Veves, 1997). To ensure consistency, the stylus was applied to the skin with no additional pressure as the weight of the unit itself provided firm enough contact with the skin (Bloom et al., 1984, Goldberg and Lindblom, 1979, Simeone and Veves, 1997, van Deursen et al., 2001). During testing participants were required to close their eyes whilst the vibration amplitude was gradually increased at a constant and steady pace until the participant verbally indicated they could feel the vibration (Bloom et al., 1984). The voltage displayed at that point when the participant indicated they could feel the vibration was noted (van Deursen et al., 2001) and a mean of three readings on each foot was recorded as recommended by various authors (Armstrong et al., 1998, Goldberg and Lindblom, 1979, Miranda-Palma et al., 2005). Biothesiometers provide a maximum voltage of 50V and any participant who was unable to detect the vibration at this maximum voltage of 50V, was assigned a voltage of 51V (Pham et al., 2000).

Functional measurement

The functional tests measured in this study included knee and ankle strength using a dynamometer, and a PPT. Isokinetic dynamometers assess muscle performance and are frequently utilised for evaluation, rehabilitation, training and research (Karnofel et al., 1989, Eyigor et al., 2008). Isokinetic dynamometers provide a constant velocity with an accommodating resistance throughout a specified range of motion (Drouin et al., 2004, So et al., 1994). As the dynamometer controls the velocity of the limb movement, it measures forces or torques generated by the muscles. Isokinetic dynamometry has been used to assess the lower limb strength in people with peripheral neuropathy in several studies and has been found to be reliable and clinically informative (Andersen et al., 2004b, Andreassen et al., 2006, Park et al., 2007).

The use of a functional performance test can provide researchers with useful information in order to target physical activity interventions toward populations at risk of declining health and functional status (Malmberg et al., 2002). This study used a version of the PPT adapted by Brandon et al. (2003) which assesses the lower-extremity, as those with Type 2 diabetes and peripheral neuropathy can sustain greater deficits in the lower limb. This modified test consists of a timed-up-and-go (TUGT) test, a 50 foot timed walk, a stair climb and a stair descent. Functional performance that is assessed in these tests includes balance, speed and strength.

Protocol for isokinetic strength testing

Isokinetic peak torque was measured at the knee and ankle using a Biodex System 4 Quick set Dynamometer (Biodex Medical Systems, New York). Flexion and extension of the knee and plantar and dorsi flexion of the ankle was measured. The dynamometer was calibrated prior to use according to the manufacturer's instructions. The non-dominant leg was used for testing unless contraindicated by pain, previous injury or joint replacement as recommended by various authors (Andersen, 1996, Andersen et al., 2004b, Andersen et al., 1996, Andreassen et al., 2006, Olsson et al., 2004).

Participant and dynamometer settings

Participant and dynamometer settings were positioned according to the manufacturer's instructions or individualised to ensure the correct anatomical positioning (Table 35).

Table 35 Dynamometer settings during knee and ankle testing

Dynamometer Setting	Knee	Ankle	
Back rest	85°	70°	
Seat rotation	45°	90° (L)	65° (R)
Dynamometer head rotation	45°	75° (L)	60° (R)
Height of dynamometer head	Individualised	Individualised	
Distance of mechanical level from load cell			
Depth of seat			
Distance of seat from dynamometer head			
Height and depth of thigh support (ankle)	N/A		

L = Left, R = Right

For testing at the knee, participant and dynamometer settings were such that the mechanical axis of the dynamometer was visually aligned with the axis of rotation of the knee, determined to be the lateral epicondyle of the femur (Andersen et al., 1996, Hart et al., 1984, Sole et al., 2007, Stratford et al., 1990). The shin pad of the knee attachment was placed two centimetres above the medial malleoli (Sole et al., 2007). For testing at the ankle, positioning was such that when the foot was rested in the foot attachment, the axis of rotation of the ankle (deemed to be the midway point between the lateral and medial malleolus in the sagittal plane) was visually aligned with the axis of rotation of the dynamometer (Andersen, 1996, Andersen et al., 1996, Karnofel et al., 1989, Salsich et al., 2000). The height of the head of the dynamometer and the height and depth of the thigh support was positioned to ensure the participant was in a seated position with 120^0 of

knee extension measured using a hand-held goniometer (Holmback and Lexell, 2007, Holmback et al., 1999).

During both knee and ankle testing, participants were strapped into the Biodex chair using a series of belts around the pelvis and trunk in order to isolate the joints during movement by stabilising the rest of the body. A further strap was placed around the thigh of the non-dominant leg which secured the thigh to the dynamometer seat (knee testing) or the stabiliser attachment (ankle testing). In addition, during knee testing the shin was strapped around the shin pad of the attachment and during ankle testing, the foot was secured into the foot plate using two straps tightened over the dorsum of the foot (Andersen, 1996, Andersen et al., 1996, Connelly and Vandervoort, 2000, Hart et al., 1984, Karnofel et al., 1989, Salsich et al., 2000, Sole et al., 2007).

Starting position and range of motion

During knee testing, participants were asked to start in a neutral position defined as 90^0flexion and extend their knee maximally to 180^0 or to their greatest range of motion before returning to the neutral position. The defined range of motion of 90^0 was measured using a spirit level attached to the lever arm and confirmed by the Biodex set-up procedures. During ankle testing the ankle started in a neutral positioned defined to be 90^0 using a hand held goniometer where the proximal arm was aligned with the head of the fibula, and the distal arm was parallel to the head of the 5^{th} metatarsal. The range of motion defined using the Biodex set-up procedures was 10^0 dorsi-flexion and 30^0 plantar-flexion from neutral, amounting to 40^0 range of motion. Participants were instructed to move through their full range of motion within this range.

Testing procedures

Gravity compensation was calculated using the Biodex in order to define the effect of gravity on the torque produced during ankle and knee testing (Andersen, 1996, Andersen et al., 1996, Beneka et al., 2005, Connelly and Vandervoort, 2000, Salsich et al., 2000, Sole et al., 2007). Prior to testing, a five minute warm-up was completed on a cycle erogmeter (Monark AB, Sweden). Once seated on the dynamometer, participants were asked to perform a sub-maximal warm-up set of five repetitions prior to data collection (Beneka et al., 2005, Sole et al., 2007).

During testing, participants were asked to cross their arms over their chest during every maximal trial (Connelly and Vandervoort, 2000, Karnofel et al., 1989). Participants were directed to "push and pull as hard and as fast as possible" throughout their full range of motion (Andersen, 1996, Andersen et al., 2004b, Andersen et al., 1996, Karnofel et al., 1989, Salsich et al., 2000). Participants were asked to produce five maximal repetitions (Beneka et al., 2005, Stratford et al., 1990) with a 30 second rest interval between each trial (Salsich et al., 2000, Stratford et al., 1990). During testing, participants were asked to produce maximal torque at 90^0/sec and 60^0/sec at the knee and ankle joint respectively (Andersen et al., 2004b, Beneka et al., 2005, Karnofel et al., 1989, Salsich et al., 2000).

Protocol for the Physical Performance Test (PPT)

The footwear worn by the participants was recorded and the same footwear was used for all testing sessions (Podsiadlo and Richardson, 1991). During all tests, participants were given one familiarisation attempt which was not timed, followed by three recorded trials with a 30 second rest period between each. The outcome measure was the average of the three trials (in seconds), and the sum of these scores resulted in an overall PPT score.

The TUGT required the participants to rise from a standard chair with arm rests, walk three metres and then return to their seated position as quickly and safely as possible (Brandon et al., 2000, Brandon et al., 2003, Levinger et al., 2007a, Morris et al., 2001, Podsiadlo and Richardson, 1991, Whitney et al., 2005). During all trials, participants were asked to start in a standarised sitting position which included their back resting against the chair backrest, their arms placed on the arm rests and their feet placed flat on the floor with their thighs horizontal and knees flexed (Morris et al., 2001, Podsiadlo and Richardson, 1991). Timing commenced on the word 'go' and ceased once the participant returned to the sitting position.

The next component of the PPT was the stair climb and descent whereby a flight of 13 steps with a hand rail was used. During testing, participants were asked to walk as quickly but as safely as possible (Bean et al., 2002, Brandon et al., 2000, Hurley et al., 1998, Tiedemann et al., 2007). Participants would ascend the stair case first and then descend. The participants starting position was standardised, so that participants would begin at either the bottom (ascent) or top (descent) of the landing with both feet square on the ground, and on the command 'go' were required to ascend or descend the stairs whilst only taking one step at a time (Tiedemann et al., 2007).

Timing was commenced on the word ‘go’ and ceased once the participant’s second foot had been placed down either at the top (ascent) or bottom (descent) of the staircase (Hurley et al., 1998, Tiedemann et al., 2007).

The final component of the PPT was the 15 metre (also known as the 50ft) timed walk. Participants were asked to walk as quickly and as safely as possible (Brandon et al., 2000, Brandon et al., 2003, Hurley et al., 1998, Levinger et al., 2007b, Norton et al., 2010, Wang et al., 2005). In order to standardise the starting position, participants were required to begin the test with their feet in a square position against the starting line. On the command ‘go’ participants were asked to walk in a straight line for 7.5 metres, turn, and return to the starting line (Brandon et al., 2003, Reuben and Siu, 1990, Wang et al., 2005). Timing commenced from the word ‘go’ until the participants first foot had crossed the start/finish line (Reuben and Siu, 1990, Wang et al., 2005).

Safety measures (adverse events)

Common Terminology Criteria for Adverse Events (CTCAE)

Adverse events experienced throughout the testing and the exercise intervention were assessed using the CTCAE version 4.0 from the U.S Department of Health and Human Services. This tool uses descriptive terminology for reporting adverse events by using a grading (severity scale) for a range of conditions. Adverse events are defined as any unfavourable and unintended sign, symptom, or disease temporarily associated with the use of a medical treatment or procedure that may, or may not be, considered related to the medical treatment or procedure. Table 36 provides the definitions of the five grades of severity. Safety measures were not assessed in the same manner as other outcomes measures (ABA design) but rather, were documented throughout the exercise program.

Table 36 Common Terminology Criteria for Adverse Events (CTCAE) grades

Grade	Definition
1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL
3	Severe or medically significant but not immediately life-threatening; hospitalisation or prolongation of hospitalisation indicated; disabling; limiting self-care ADL
4	Life threatening consequences; urgent intervention indicated
5	Death related to adverse event

ADL = Activities of Daily Living

Additional measures

Additional measures using standard collection procedures were taken throughout the exercise program (Table 37). Body mass, standing height and seated blood pressure were calculated using the average of two measurements. Demographic details such as, sex, age and date of birth were recorded for each participant during baseline. Participants were also asked to give a detailed summary of any current medications they were currently taking. If medications were altered throughout the five month period, participants were asked to inform the principal researcher and the change to medication was noted. Long term glycemic control (HbA1c) was assessed before and after the intervention by the participant's GP.

Table 37 Additional measures collected in the study and apparatus used for the measurement

Measurement	Apparatus/Technique	Collected by:
Body mass (kg)	Tanita 2000 (Tanita Corporation of America, Inc. Illinios)	Principal researcher
Standing height (cm)	Seca 222 stadiometer (Medizinische Waagen und Messsysteme, Hamburg)	Principal researcher
Blood Pressure, seated (mm/Hg)	Omron SEM-2 automatic blood pressure monitor (Omron Healthcare, Kyoto)	Principal researcher
HbA1c (%)	Venepuncture	General Practitioner

Procedures

Baseline phase (A)

Participants undertook a familiarisation session which included the assessment of all outcome measures in order to reduce variability between testing sessions. Following the familiarisation session, participants were asked to attend the University for the outcome testing session weekly, for four consecutive weeks. During measurement sessions, tests were always conducted in the same order, with that order being monofilament, VPT, PPT, knee strength and ankle strength. Quality of life questionnaires were also completed. Height (for the first session only), body mass and blood pressure were also measured during these sessions. During the final week of the baseline phase, participants were asked to attend their GP clinic for an HbA1c measurement.

Intervention (B) phase

In keeping with the continuous assessment nature of single case research, outcome measures were then assessed once a month throughout the intervention phase using the protocols as previously described. The intervention phase consisted of a 12-week combined aerobic and resistance training program. Participants were asked to attend the UniSA HLS Fitness Centre twice a week for 12 weeks. Exercise sessions were performed on non-consecutive days where possible. Each exercise session went for approximately one hour and all exercise sessions were performed under the supervision of the principal researcher or a staff member of the HLS Fitness Centre. A familiarisation session was conducted prior to the commencement of the exercise program in order to demonstrate safety practices and to teach the participants the correct technique when conducting the exercises. The exercise program was developed using various methodologies from studies which have used aerobic, resistance or combined training programs in adults with Type 2 Diabetes (Balducci et al., 2004, Bhargava, 2008, Cohen et al., 2008, Dunstan et al., 2005, Ibanez et al., 2005, Lambers et al., 2008, Sigal et al., 2007). Consideration was also given to the participant's time and ability to frequent the UniSA HLS Fitness Centre.

One Repetition Maximum (1RM) testing session

Participants completed a 1RM testing session at the beginning of each month of the program to prescribe the resistance component of the training session. For the first 1RM attempt, a heavy weight was selected, guided by the results from the familiarisation session and warm-up sets. The incremental increases in weight were made according to the difficultly with which the

participant executed the previous lift as measured by the RPE value (Borg, 1998), and the observation of technique by the researcher. The participant's 1RM was defined as the maximum weight that could be lifted through a full range of motion using correct technique with no compensatory movements. The 1RM data was recorded and used to calculate the exercise intensity for the following four weeks of the exercise program.

Exercise training

In order to minimise the risks of hypoglycaemia during exercise, participants were asked to measure their blood sugar levels using a monitor provided by Abbott Diagnostics (Abbot Park, Illinois) prior to, and immediately after each exercise session. Management of hypoglycaemic episodes during the exercise program followed protocols already in place at the UniSA Allied Health Clinics. Discussions were held with all participants prior to the exercise program about the signs and symptoms of hypoglycaemia. Participants were asked if they had previously experienced a hypoglycaemic episode and if they were aware of the associated symptoms. After an initial assessment by a podiatrist from the UniSA Allied Health Clinic, participants were also encouraged to monitor their feet throughout the exercise program, and report any alterations or injury to the principal researcher.

Aerobic component

Participants performed aerobic activity at a moderate intensity using a choice of low weight bearing machines, namely a cycle ergometer (Monark Exercise AB, Sweden), a recumbent bicycle (SCIFIT, United Kingdom) or an indoor rowing ergometer (Concept 2, Australia). Participants were asked to work at an intensity between 50-60% HRR, as calculated using the Karvonen Formula (ACSM, 2000b). Low weight bearing activities were deemed most appropriate according to the recommendations from the American Diabetes Association at the time, which was noted in Figure 1, Chapter 2. The participant's resting HR was measured at the beginning of the program, and reassessed every four weeks in order to capture any changes in fitness throughout the program.

Exercise intensity was measured throughout the aerobic component using a Polar S610i heart rate monitor (Polar Electro, Finland) and Borg's 6-20 RPE Scale (Borg, 1998). Previous studies have found that individuals with diabetes and neuropathy may exhibit an increased resting heart rate yet a depressed maximal heart rate and hence the RPE scale has been considered a valid

method to monitor levels of exercise intensity in this population (Colberg et al., 2003). Participants performed a five minute warm-up at a self-selected pace, followed by 20 minutes of moderate intensity exercise at a designated pace, with the resistance manipulated to elicit a heart rate and RPE response equivalent to moderate intensity. Following the 20 minutes of exercise, participants were required to cool down at a self-selected pace for five minutes.

Resistance component

Participants were prescribed a progressive resistance training program at an initial intensity of 50-60% 1RM during the first four weeks, followed by 75-85% 1RM for the remaining eight weeks. A combination of eight exercises were performed for eight to ten repetitions over two sets. A combination of four upper and lower body exercises were performed each week (two upper and two lower body exercises per session). Exercises included seated row, leg press, seated biceps curl, seated calf raise, seated chest press, lying leg curl, triceps extension and abdominal curls. Participants were asked to evaluate each set using the RPE scale and technique was carefully monitored by the principal researcher. A summary of the aerobic and resistance components of the intervention is shown in Table 38.

Table 38 Summary of resistance and aerobic components of the training program.

Wk	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**		**10**		**11**		**12**	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Resistance Training																								
	50-60% 1 RM: 11-13 RPE								**75-85% 1 RM: 11-13 RPE**															
SR	X		X		X		X		X		X		X		X		X		X		X		X	
LP	X		X		X		X		X		X		X		X		X		X		X		X	
BC	X		X		X		X		X		X		X		X		X		X		X		X	
CR	X		X		X		X		X		X		X		X		X		X		X		X	
CP		X		X		X		X		X		X		X		X		X		X		X		X
LC		X		X		X		X		X		X		X		X		X		X		X		X
TE		X		X		X		X		X		X		X		X		X		X		X		X
AC		X		X		X		X		X		X		X		X		X		X		X		X
Aerobic Training 50-60% Heart Rate Reserve: 11-13 RPE 20 minute aerobic exercise using a cycle ergometer, recumbent bicycle or an indoor rowing ergometer																								

Wk: week, SR: seated row, LP: Leg Press, BC: Biceps Curl, CR: Calf Raise, CP: Chest Press, LC: Leg Curl, TE: Triceps Extension, AC: Abdominal Curl, RM: Repetition Maximum, RPE: Rate of Perceived Exertion, X: denotes exercise was performed during that session

Post intervention phase (A)

In accordance with the single case ABA research design, the post intervention phase was identical to the baseline phase. Following the cessation of the 12-week exercise program, participants were asked to attend the University for the outcome testing session weekly, for four consecutive weeks. During measurement sessions, tests were always conducted in the same order as described in the baseline phase. During the first week of the post intervention phase, participants were asked to attend their GP clinic to measure their HbA1c in order to assess the effects of the 12-week exercise program on their long term glycemic control.

Data analysis

Sensation, function and quality of life outcome measures were analysed in accordance with single-case design methodology. As the primary aim of the exercise program was to determine the safety and effect of the exercise program, outcome measures were assessed for change between the baseline and intervention phases. However, if any significant changes occurred between the baseline and intervention phases, the post intervention phase was investigated to see if these changes were ongoing. All variables were assessed using the two standard deviation (2-SD) bandwidth method. In order to achieve this, the standard deviation of the baseline data was calculated, and a horizontal band, the width of 2-SD were extended through the graph. If at least two consecutive intervention data points fell outside the band, the intervention phase (Phase B) was considered to be significantly different than that of the baseline phase (Backman 1999). Where participants missed a measurement session during the weekly baseline or post intervention phase (A), data was treated as missing. Data are presented in graphs, whereby the three sections represent the baseline (A), intervention (B), and post intervention (A) phases as shown in Figure 24 below.

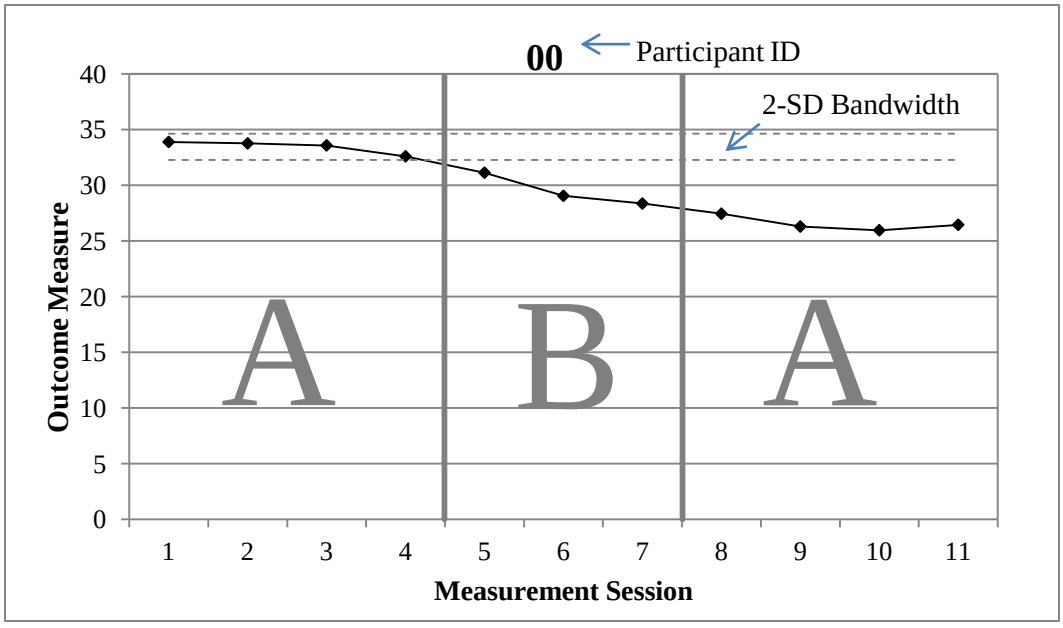


Figure 24 Example of an ABA graph used to present outcome measures

Results

Participant information

There were 59 expressions of interest to partake in the study, 10 (16.9%) of which commenced the program. The most common reason for non-participation in the study was failure to satisfy the inclusion criteria (78%), whereby the majority of respondents had an existing comorbidity or injury (49%), or were not diagnosed with peripheral neuropathy (26%). Of the ten participants who commenced the study, eight completed the program resulting in an attrition rate of 20%. Both participants withdrew during the 12-week exercise intervention with one participant travelling overseas unexpectedly for family reasons, while the other participant had a sudden unrelated decline in health which prevented her from continuing the exercise program. Figure 25 displays the number of participants recruited from each of the recruitment methods and the age and gender of each participant.

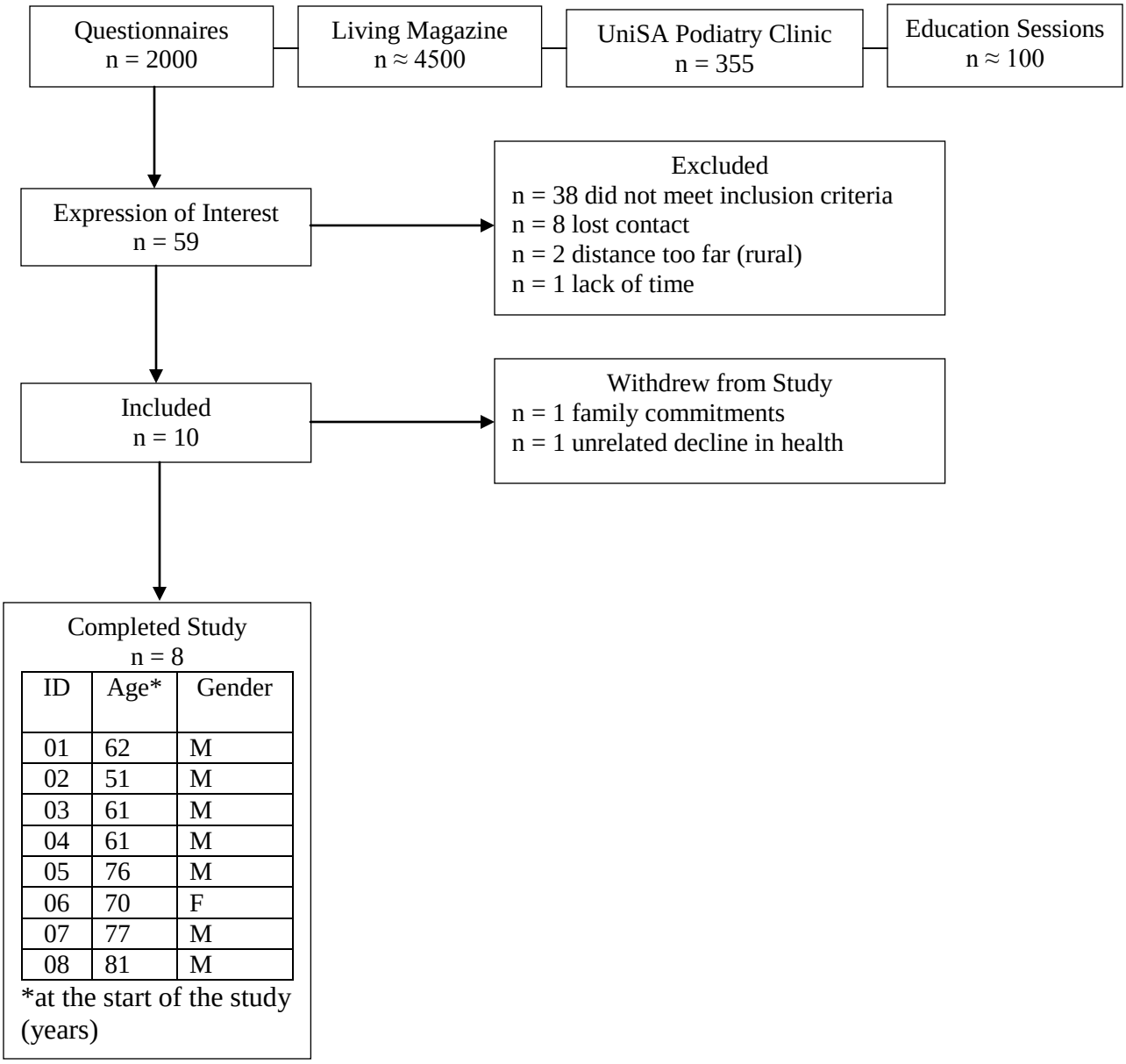


Figure 25 Participant recruitment methods and participant information

M = Male, F = Female, UniSA = University of South Australia

Exercise program

The exercise intervention was well attended by those who completed the study, with an average attendance of 88% (range 79%-100%). No participant ever missed more than two consecutive sessions throughout the 12-week program.

During the aerobic component of the program, participants were asked to exercise at a moderate intensity, that is between 50-60% of the participant's HRR, or between 11 to 13 on Borg's RPE scale (ACSM, 2000b). Due to the use of heart rate lowering medications, the aerobic intensity of four participants was assessed using RPE data only. During the resistance component of the program, participants were asked to exercise at an intensity between 11 and 13 on Borg's RPE scale. Table 39 provides the average RPE values across the 12-week program for both the aerobic and resistance components.

Table 39 Average RPE for aerobic and resistance training across the 12-week program

Participants ID	Aerobic Training	Resistance Training							
		SR	LP	BC	CR	CP	LC	TE	AC
01	12	14	15	13	15	15	14	14	11
02	11	13	12	12	12	12	12	11	11
03	12	14	14	13	12	14	14	13	13
04	14	13	13	12	12	14	14	13	14
05	13	15	14	14	14	14	14	13	13
06	9	10	10	10	10	12	10	9	9
07	12	15	14	12	15	14	14	14	14
08	12	12	13	13	11	13	12	10	13

RPE = rate of perceived exertion, SR = seated row, LP = leg press, BC = biceps curl, CR = calf raise, CP = chest press, LC = leg curl, TE = triceps extension, AB = abdominal curl

Additional measures

Additional measures taken throughout the program included long-term glycemic control, and physiological measures such as height, weight and blood pressure. Table 40 summarises these measurements over the five month period.

Table 40 Participants' height, weight, seated blood pressure[┼] and glycemic control (HbA1c) throughout the different phases of the study

Participant ID	Measure	Average baseline (A)	Average intervention (B)	Average post Intervention (B)
01	Height (cm)	184.7		
	Weight (kg)	77.8	78.1	77.9
	BP (mmHg)	128/68	113/65	112/65
	HbA1c (%)	8.5	7.5	
02	Height (cm)	173.0		
	Weight (kg)	87.3	85.3	84.1
	BP (mmHg)	131/65	112/58	117/60
	HbA1c (%)	5.5	5.7	
03	Height (cm)	186.5		
	Weight (kg)	132.3	132.2	131.9
	BP (mmHg)	132/74	126/68	127/74
	HbA1c (%)	6.8	6.7	
04	Height (cm)	180.9		
	Weight (kg)	92.5	92.2	90.4
	BP (mmHg)	150/84	136/79	127/76
	HbA1c (%)	6.7	6.9	
05	Height (cm)	179.1		
	Weight (kg)	83.8	84.9	86.2
	BP (mmHg)	137/76	124/75	117/69
	HbA1c (%)	7.7	7.6	
06	Height (cm)	161.2		
	Weight (kg)	65.3	65.1	66.2
	BP (mmHg)	132/69	129/79	131/69
	HbA1c (%)	6.8	7.1	
07	Height (cm)	179.6		
	Weight (kg)	92.0	90.6	90.9
	BP (mmHg)*	145/80	130/77	146/82
	HbA1c (%)	5.7	5.7	
08	Height (cm)	170.4		
	Weight (kg)	91.5	92.1	91.7
	BP (mmHg)	116/72	121/68	123/74
	HbA1c (%)	6.3	6.2	

*Participant altered blood pressure (BP) medication between baseline and intervention phases according to GP's instruction. [┼]Blood pressure presented as systolic/diastolic

Outcome measures

Safety measures (adverse events)

Several safety measures were implemented throughout the program and adverse events are presented in Table 41. Participant 03 sustained an upper body musculoskeletal injury during the study period (Grade 2), however the injury occurred outside of the supervised and prescribed exercise training sessions and therefore is not recorded as a consequence of the prescribed exercise program. Participant 02 was absent from training for one session due to illness (Grade 2), but again this was not attributable to the exercise program. Participant 04 was the only participant who experienced an adverse event directly attributable to the exercise program. Table 42 shows the average pre-exercise session and post-exercise session blood glucose levels measured by the participants. Participant 04 experienced three hypoglycemic episodes (Grade 1), all of which were asymptomatic and most likely a result of the participant not participating in this intensity of exercise for some time. As noted in Table 42, Participant 04 decreased his blood glucose levels by an average of over 50% from the beginning to the end of the exercise sessions. Accordingly, the participant altered his dietary intake prior to an exercise session and blood glucose levels were also checked throughout each exercise session as an additional safety measure. Importantly, no adverse events in relation to foot complications of peripheral neuropathy (tissue breakdown, ulceration) were reported throughout the study.

Table 41 Adverse Events reported during the Intervention phase

Adverse Event	Participant ID	# of events	CTCAE Grade	Attributable to program
Blood glucose regulation	04	3	1	Yes
Musculoskeletal	03	1	2	No
Illness	02	1	2	No

CTCAE = Common Terminology Criteria for Adverse Events

Table 42 Average blood glucose levels (mmol/l) measured by participants before and after each exercise session

Participants ID	Pre (mmol/l)	Post (mmol/l)	% change
01	9.42	5.58	- 40.7
02	7.27	6.89	- 5.0
03	11.27	7.91	- 29.8
04	11.64	5.55	- 52.2
05	8.28	6.39	- 22.8
06	12.77	7.77	- 39.2
07	6.57	6.40	- 2.50
08	8.57	6.07	- 29.2

Table 43 provides a summary of the outcome measures assessed using the 2-SD bandwidth method. A green light indicates a significant positive change, a yellow light indicates no change, and a red light indicates a significant change in the opposite direction to that desired between baseline and intervention phases. These coloured 'lights' are also presented in Figures 26-44 whereby individual ABA graphs are presented for each participant. For the purposes of this study, outcome measures with either a green or yellow light are considered to be a positive result, indicating that the exercise program did not result in a deterioration of the variables being measured.

Table 43 Summary of the change in outcome measurement between baseline and intervention phases where a yellow dot indicates no change, a green dot indicates significant positive change and a red dot, a significant negative change

Outcome Measure	01	02	03	04	05	06	07	08
Quality of Life								
Pain								
Pain Domain 'A'								
Lost Feeling								
Lost Feeling Domain 'B'								
SMS								
SMS Domain 'C'								
ADL								
ADL Domain 'D'								
Social								
Social Domain 'E'								
Emotional								
Emotional Domain 'F'								
Effect of foot problems on QOL								
Overall QOL								
Sensation Measures								
Mono left								
Mono right								
VPT left								
VPT right								
Functional Measures								
Knee flexion								
Knee extension								
Ankle DF								
Ankle PF								
PPT								

SMS =Sensory-motor Symptoms, ADL=Activities of Daily Living, Mono =Monofilament, DF =Dorsi flexion, VPT = Vibration perception Threhsold, PF = Plantar-flexion, PPT = Physical Performance Test

Quality of life

The neuropathic specific quality of life measure (NeuroQol) was used to assess quality of life. All domain scale scores, domain summary scores (A-F), and the overall summary scores of the NeuroQol are presented below.

Pain

The average scale scores of the baseline, intervention and post intervention phases for the pain domain of the NeuroQol are shown in Figure 26. According to the 2 S-D bandwidth method for the majority of the participants there was no change in the frequency of painful symptoms as shown through the scale domain score. The majority of the participants had a low scale score during the baseline phase, indicating that the feeling of pain did not have a substantial impact on their life prior to the start of the program. Participant 05 demonstrated a significant increase in the frequency of painful symptoms between baseline and intervention phases.

The summary question of the pain domain ‘A’ asked the participant if any of the painful symptoms had reduced their quality of life. The average domain summary score throughout baseline, intervention and the post-intervention phases is shown in Figure 27. Participants 02 and 04 indicated a significant improvement in whether or not the painful symptoms affected their quality of life. Despite Participant 05 indicating a significant increase in painful symptoms, he did not find that this significantly affected his quality of life.

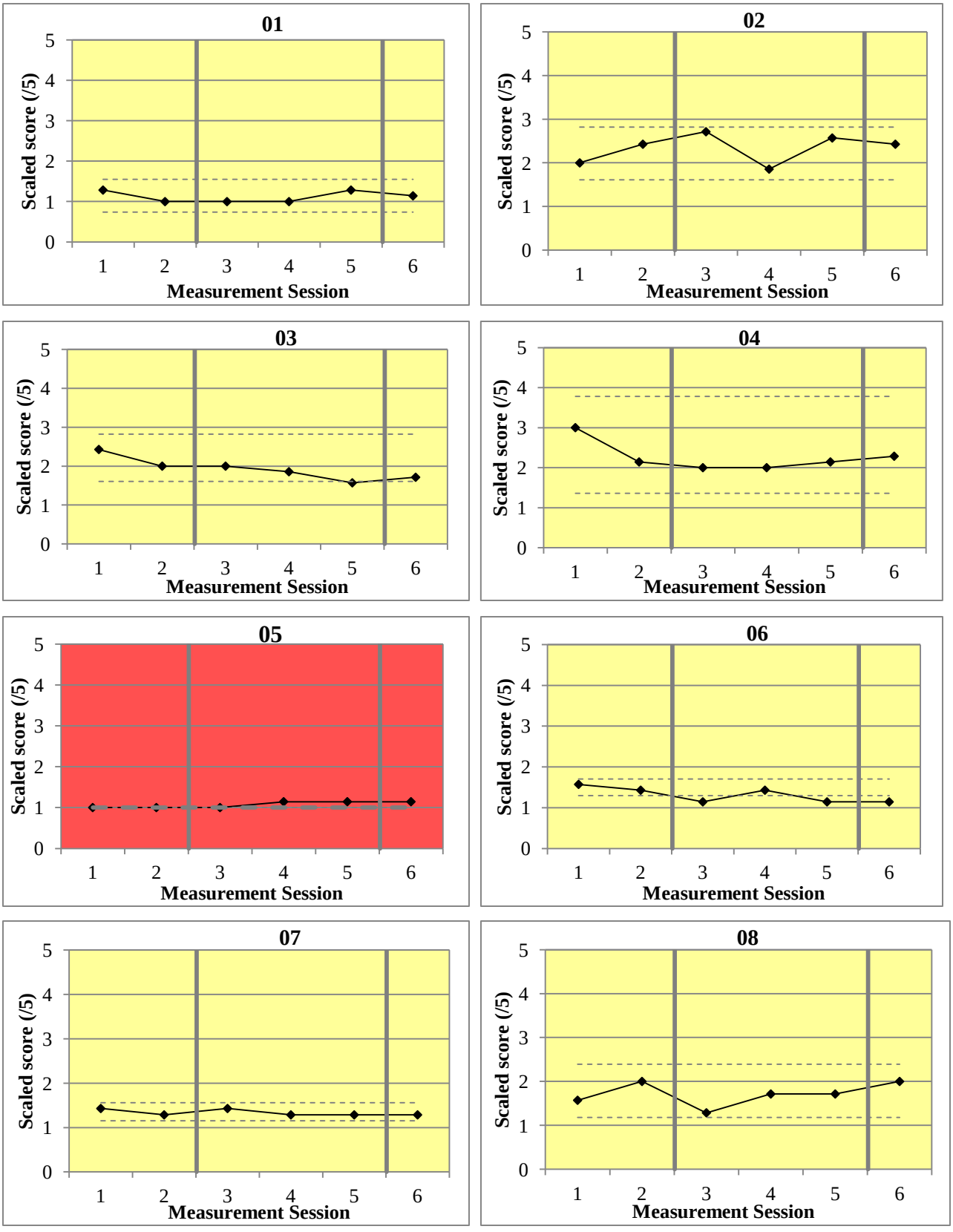


Figure 26 Individual scale scores (/5) for the pain domain of the NeuroQol for all participants

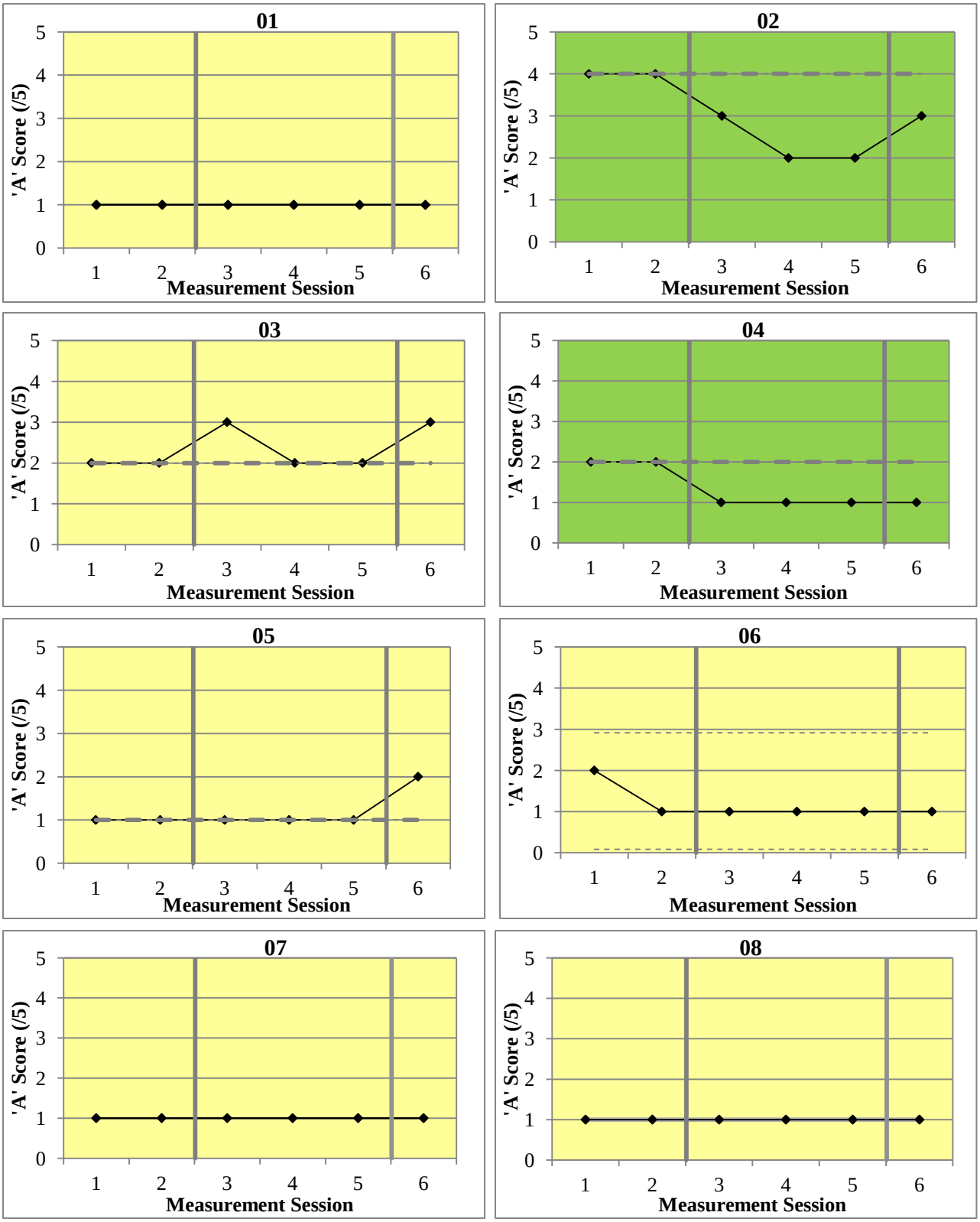


Figure 27 Individual summary score (/5) for the pain domain 'A' of the NeuroQol for all participants

Lost feeling

The lost feeling scale scores of the NeuroQol for baseline, intervention and post intervention phases were averaged for each participant and are shown in Figure 28. Two participants (03 and 04) indicated a significant change between baseline and intervention phases, with Participant 03 indicating a worsening perception of lost feeling in the feet. However, it should be noted that toward the end of the intervention period, there was a decrease in the scale score towards the baseline result. In contrast, Participant 04 who recorded the highest baseline score of all participants had a decrease in the average scale score during the intervention phase indicating a significant improvement in the symptom of lost feeling. All remaining participants indicated there was no change in the perception of lost feeling in the feet throughout the baseline and intervention phases, which is considered to be a positive result.

The summary question of the lost feeling domain 'B' asked the participants if the symptoms of lost feeling had reduced their quality of life. The scores throughout baseline, intervention and post-intervention phases are shown in Figure 29. Participants 03 and 04 indicated a significant change in the perceived effect of lost feeling on their quality of life between the baseline and intervention phases. Again, Participant 03 noted an increase in the domain summary score indicating that the symptoms of lost feeling reduced their quality of life more so during the intervention phase than the baseline phase. Participant 04 reported a decrease between the two phases indicating that during the intervention phase, the lost feeling symptoms did not impact their quality of life as much as during the baseline phase.

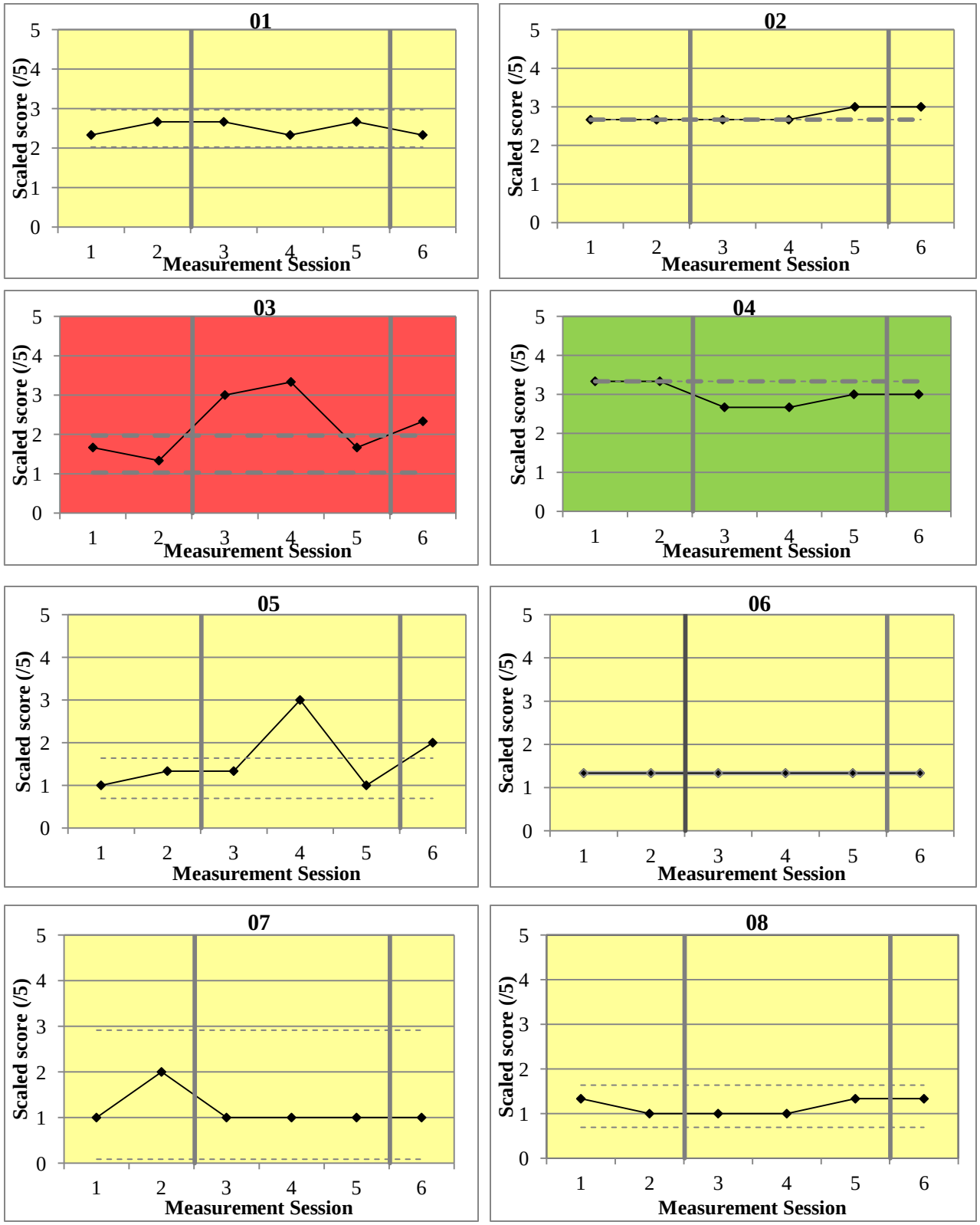


Figure 28 Individual scale scores (/5) for the lost feeling domain of the NeuroQol for all participants

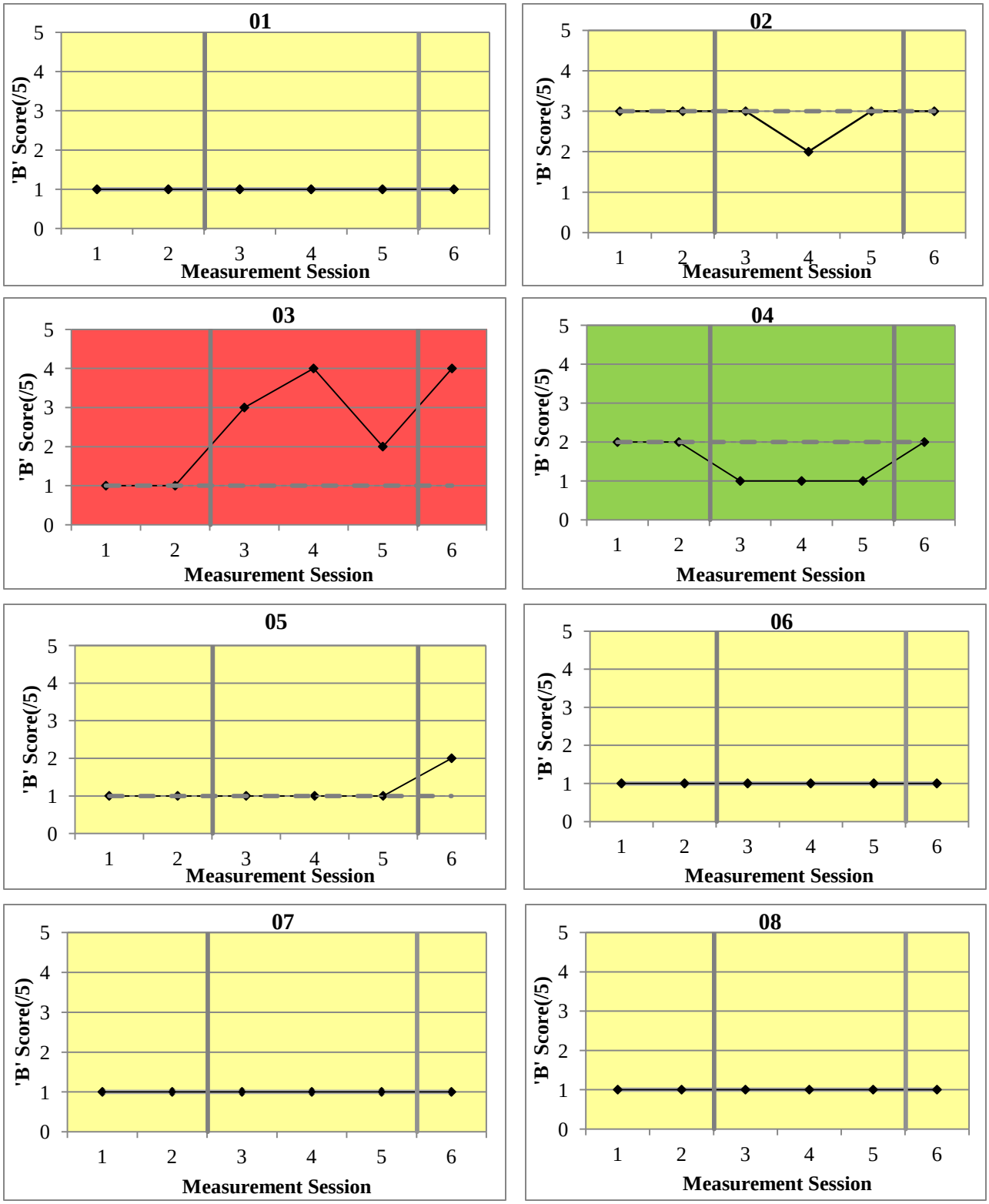


Figure 29 Individual summary score (/5) for the lost feeling domain 'B' of the NeuroQol for all participants

Sensory-motor symptoms

The average baseline, intervention and post-intervention scale scores for the sensory-motor symptoms as measured by the NeuroQol for each participant is shown in Figure 30. Three participants (05, 06 and 07) reported a significant improvement between the baseline and intervention phases as indicated by a decreased scale score. All remaining participants indicated that the exercise intervention did not make their sensory motor symptoms worse, as they reported no change between the two phases. The majority of participants had a low scale score during the baseline phase. The participant who reported the highest baseline score (05) reported a significant improvement throughout the intervention phase.

The summary domain question 'C' asked participants whether or not the sensory-motor symptoms had reduced their quality of life. The baseline, intervention and post intervention results are shown in Figure 31. Despite participants 05, 06 and 07 reporting a significant improvement in the scale score, this did not translate to a significant improvement in their quality of life with respect to this domain. One participant (04) reported a significant improvement in the effect of this domain on their quality of life as indicated by a decreased score during the intervention phase. Despite this participant (04) not reporting a change in the frequency of their sensory motor symptoms (scale score), there was an indication that the sensory motor symptoms did not affect their quality of life as much during the exercise program, compared to baseline. The absence of any significant negative changes across any participant is a positive feature of the exercise program indicating that exercise did not make the participant's quality of life worse with respect their sensory-motor symptoms.

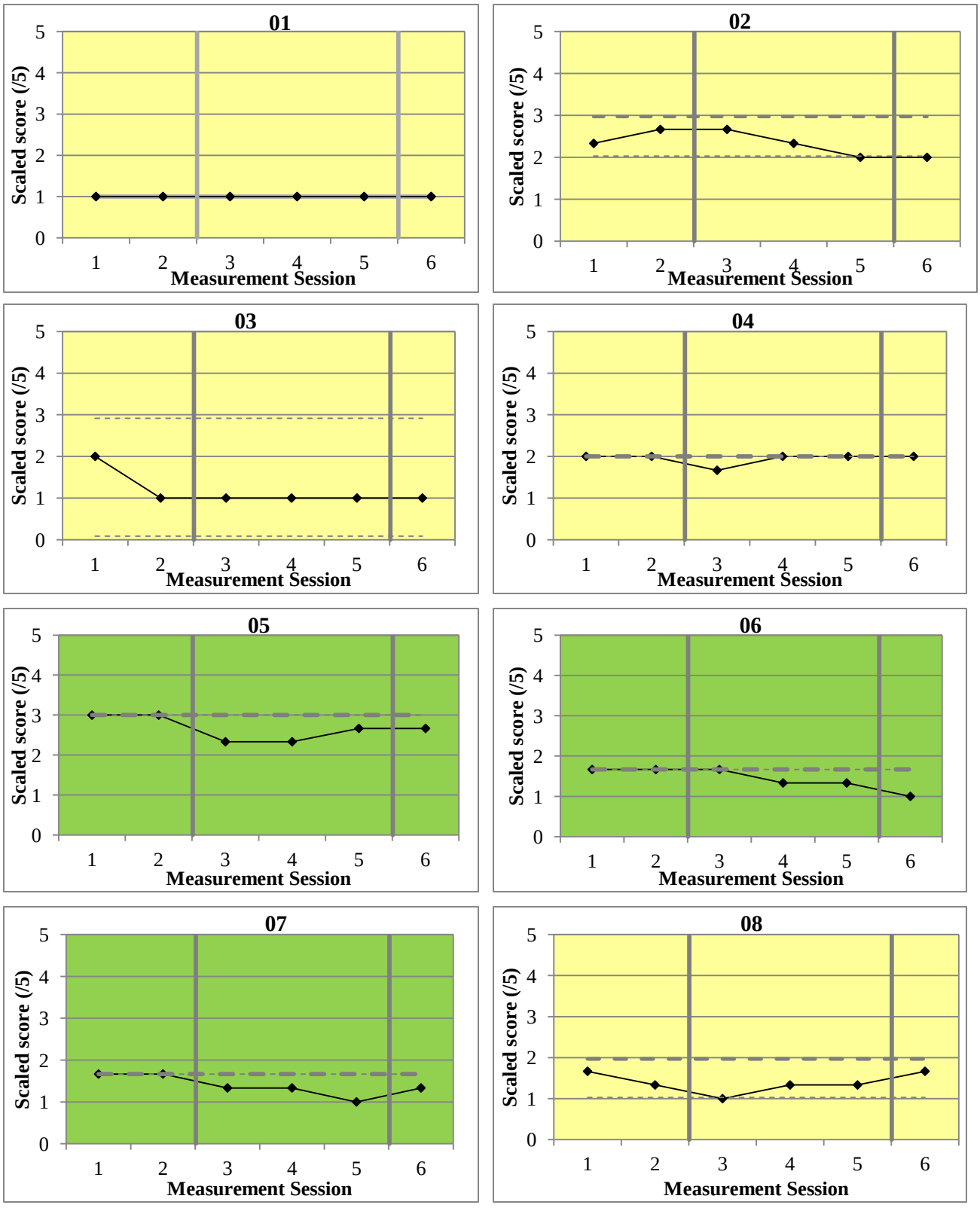


Figure 30 Individual scale scores (/5) for the sensory-motor symptoms domain of the NeuroQol for all participants

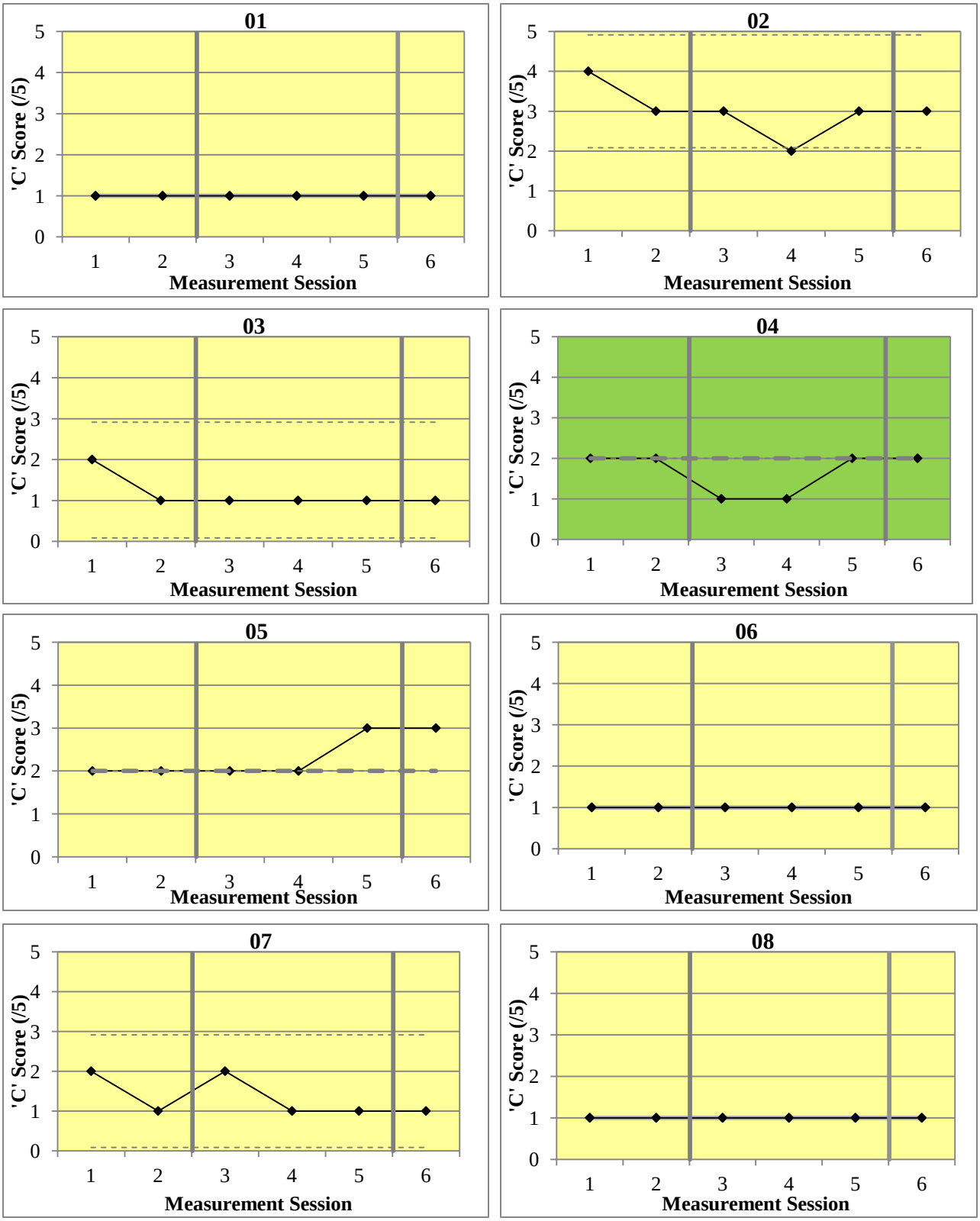


Figure 31 Individual summary score (/5) for the sensory motor symptoms domain 'C' of the NeuroQol for all participants

Activities of Daily Living (ADL)

Figure 32 shows the scale ADL score as measured using the NeuroQol for all participants during baseline, intervention and post intervention phases. Half of the participants' ADL scale score remained stable throughout the study period (01, 06, 07 and 08), with these participants consistently reporting a scale score of one ('not at all'). This indicates that the presence of peripheral neuropathy did not impair the participants' ability to perform activities of daily living. Furthermore, no participants reported an increased score during the intervention period indicating the exercise intervention did not impair their ability to perform activities of daily living.

The ADL domain summary question 'D' asked participants if their ability to perform activities of daily living had reduced their quality of life with the results shown in Figure 33. Similar to the scale domain score, the summary domain score for Participants 01, 06, 07 and 08 all remained stable throughout the study period, and Participants 02, 04 and 05 reported their ability to perform activities of daily living did not affect their quality of life as indicated by a yellow light, which is considered to be a positive outcome. A significant difference between baseline and intervention was found for Participant 03. This was despite this participant not indicating a decrease in his ability to perform activities of daily living as shown in Figure 32.

Social relationships

There were no significant changes in the scale or domain summary scores ('E') of the social relationships domain as measured by the NeuroQol between baseline and intervention phases for all participants. This indicates that the exercise program did not negatively influence the social relationships of the participants. The average scale domain scores and average domain summary scores for the social relationships domain are shown in Figures 34 and 35.

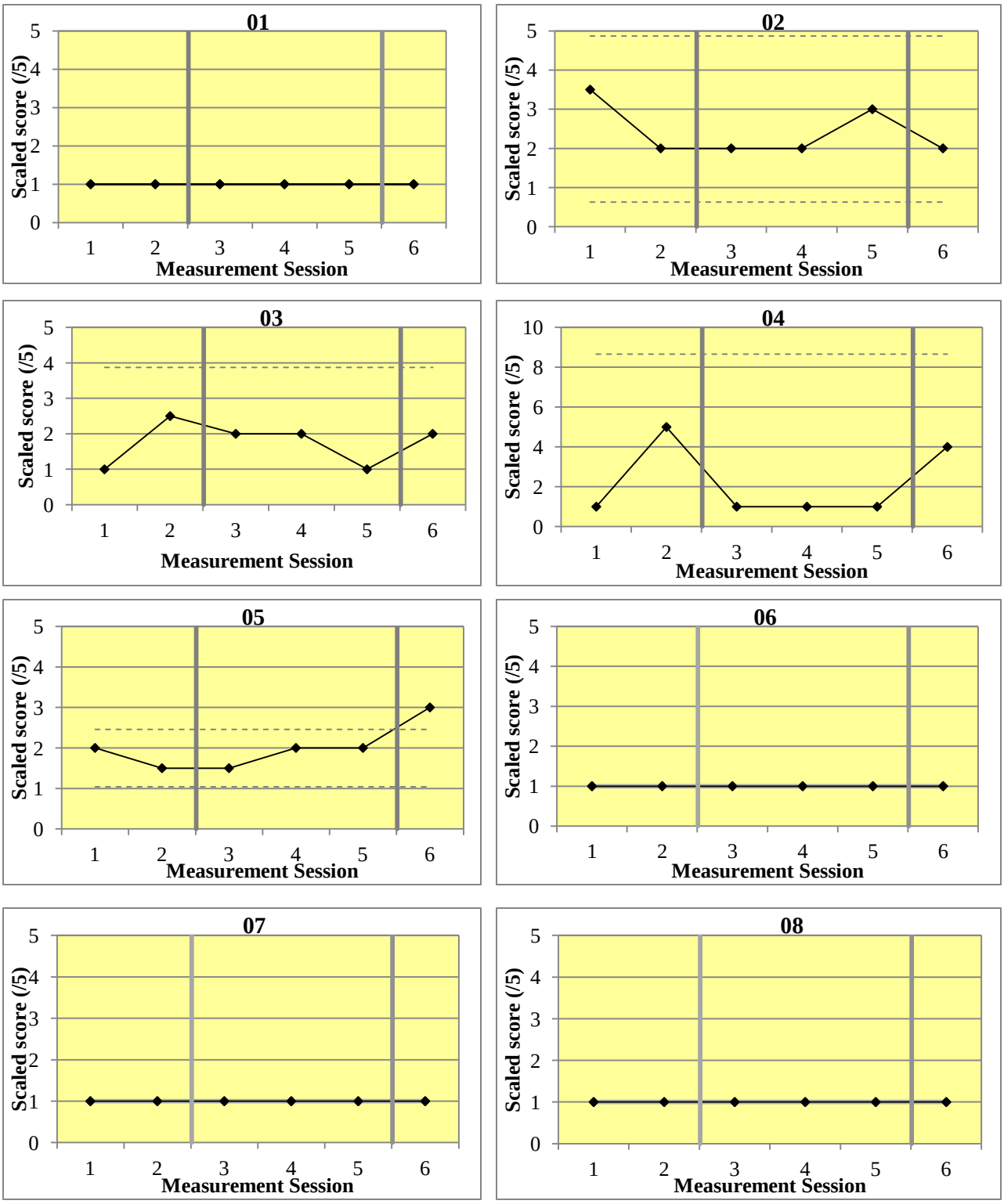


Figure 32 Individual scale scores (/5) for the activities of daily living domain of the NeuroQol for all participants

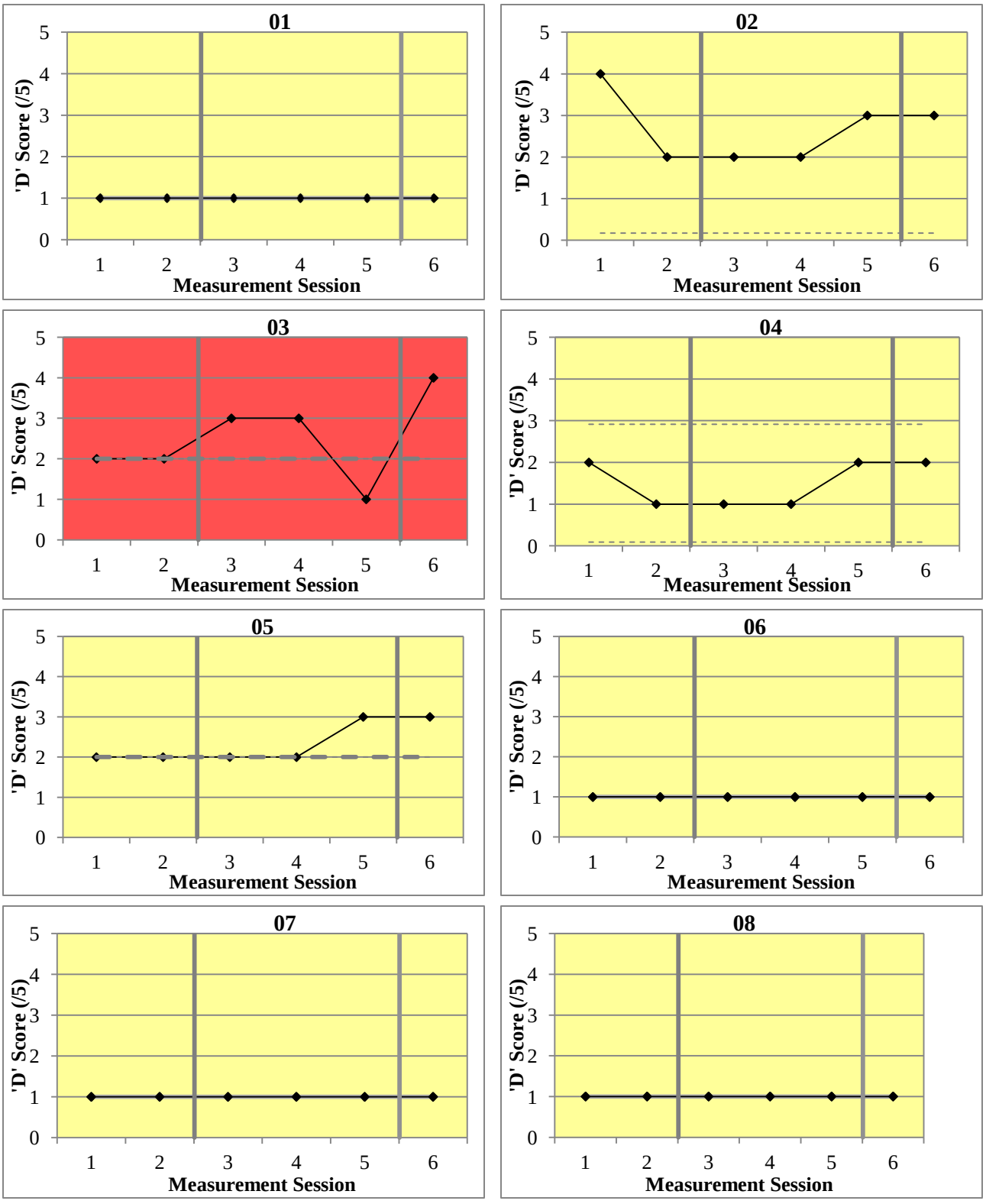


Figure 33 Individual summary score (/5) for the ADL domain 'D' of the NeuroQol for all participants

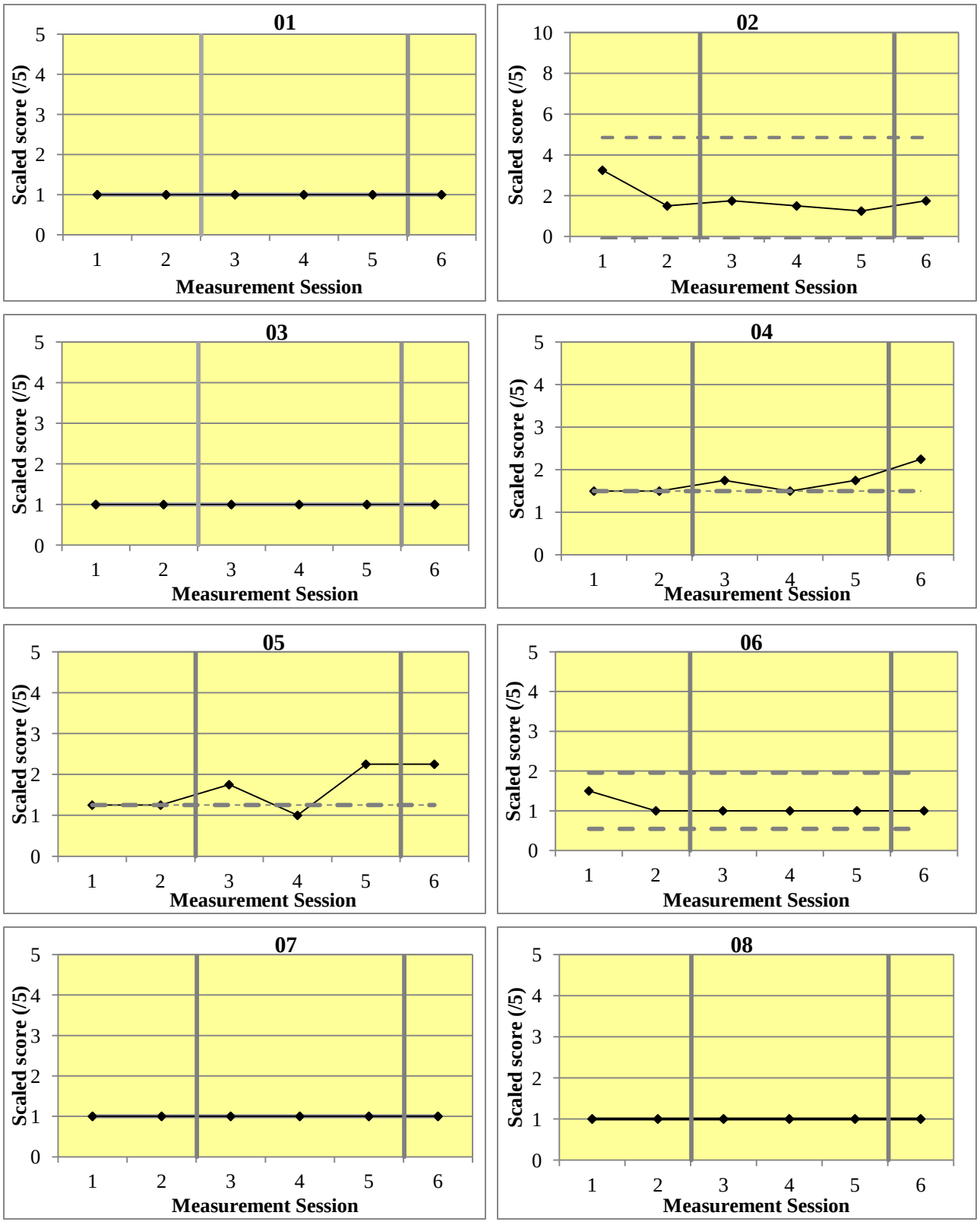


Figure 34 Individual scale scores (/5) for the social relationships domain of the NeuroQol for all participants

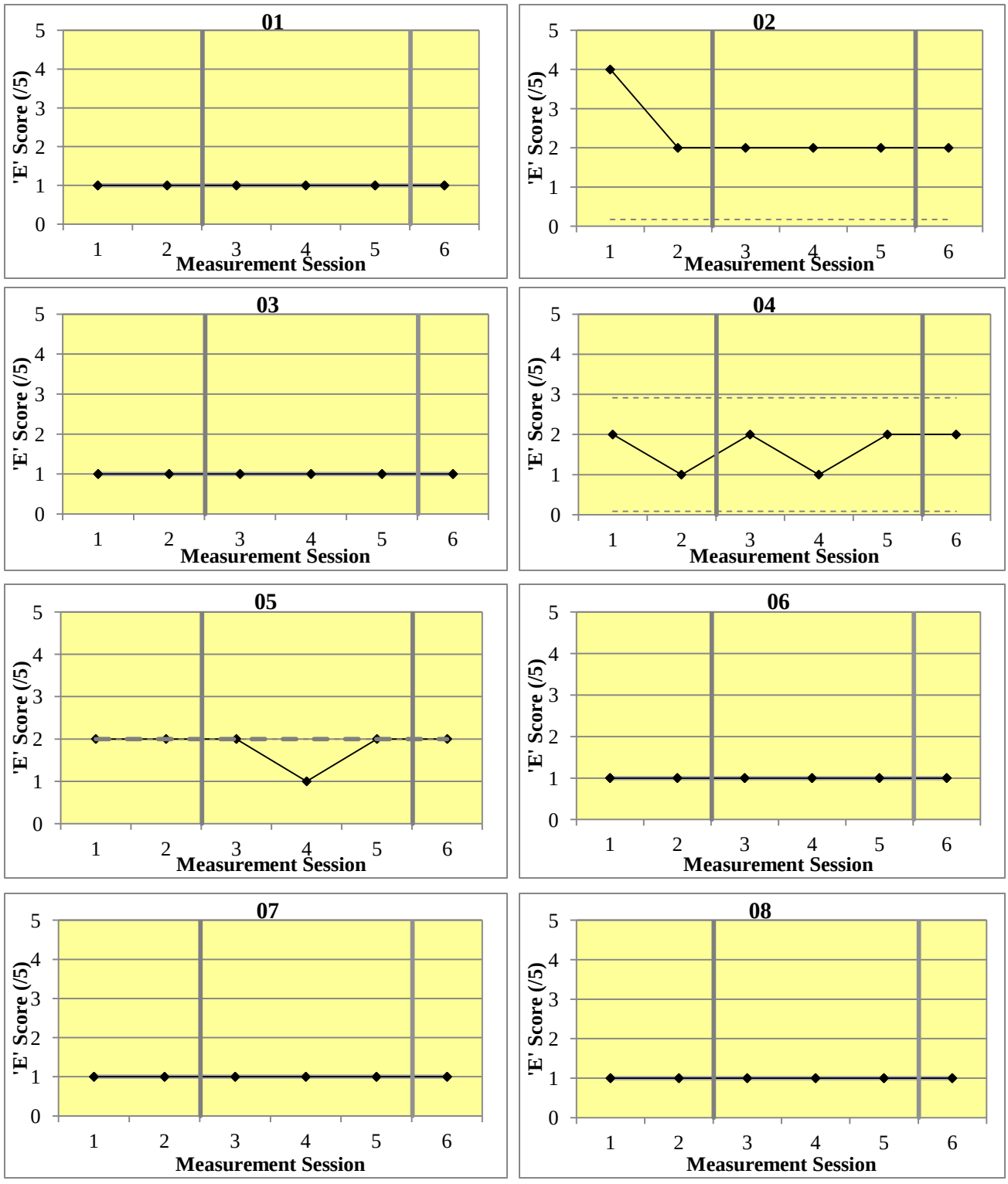


Figure 35 Individual summary score (/5) for the social relationships domain ‘E’ of the NeuroQol for all participants

Emotional distress

The average baseline, intervention and post-intervention scale scores for emotional distress for all participants as measured by the NeuroQol are shown in Figure 36. Participant 05, who reported the highest level of emotional distress during the baseline phase, showed a significant improvement in perceived emotional distress during the intervention phase. All remaining participants reported that their level of emotional distress did not change during the exercise program.

Participants were asked whether the feeling of emotional distress had affected their quality of life in any way (domain summary score 'F'). No participant reported a significant change in perceived quality of life due to emotional distress between the baseline and intervention phases as shown in Figure 37.

Overall quality of life

Question 28 of the NeuroQol asked how the participant's foot problems affected their overall quality of life with higher scores indicating a greater impact. Despite the variation in results, there were no significant differences found between the baseline and intervention phases indicating that the exercise program did not cause a decrease in the participant's perceived quality of life due to problems with their feet as shown in Figure 38.

Question 29 of the NeuroQol asked participants what their overall quality of life was, with higher scores indicating a greater quality of life. The results indicated that there were no significant differences between baseline and intervention phases for any participant, indicating that the introduction of the exercise program did not have any effect on the participant's perceived quality of life (Figure 39).

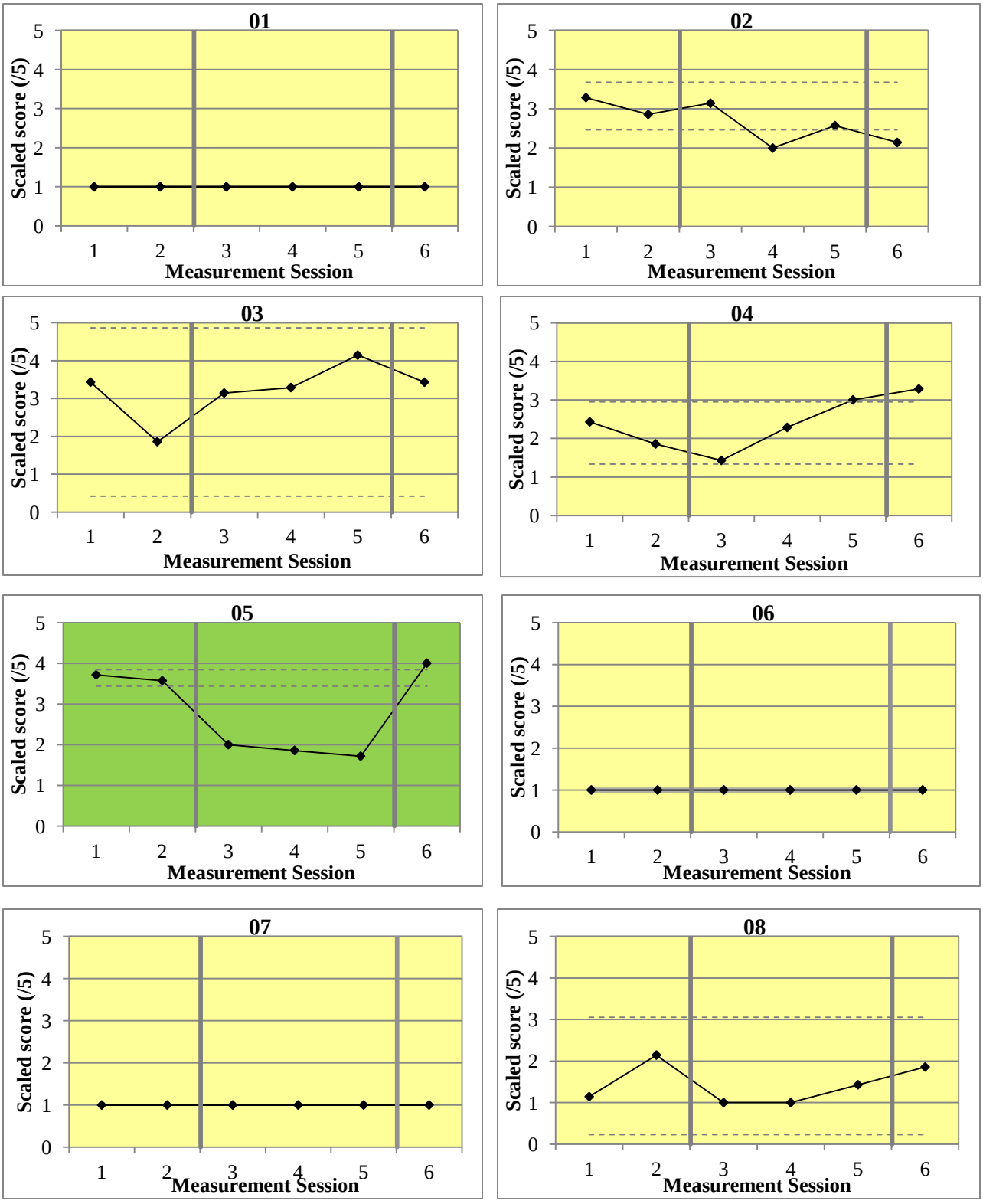


Figure 36 Individual scale scores (/5) for the emotional distress domain of the NeuroQol for all participants

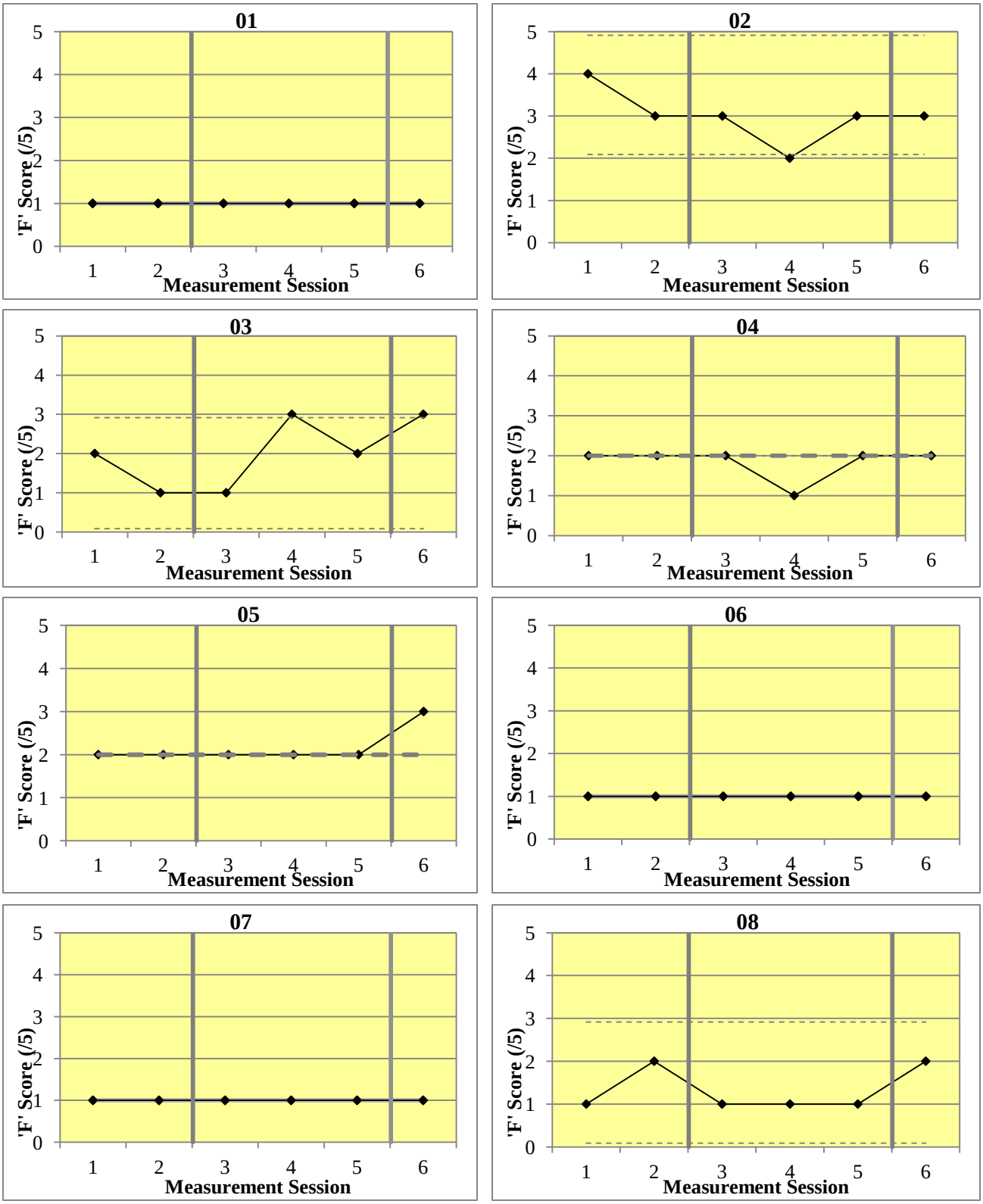


Figure 37 Individual summary score (/5) for the emotional distress domain 'F' of the NeuroQol for all participants

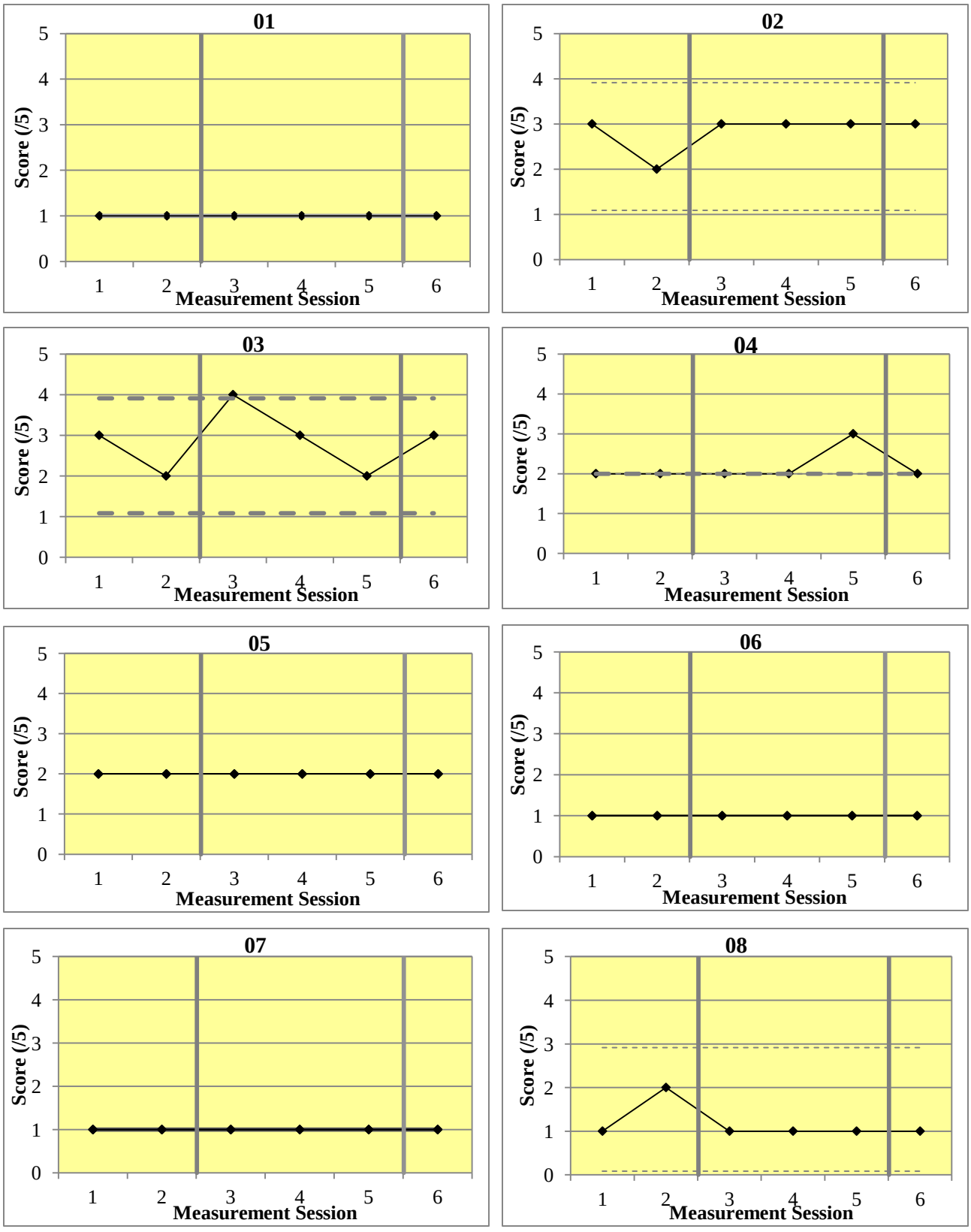


Figure 38 The effect of problems with the feet on individual's quality of life (/5) for all participants

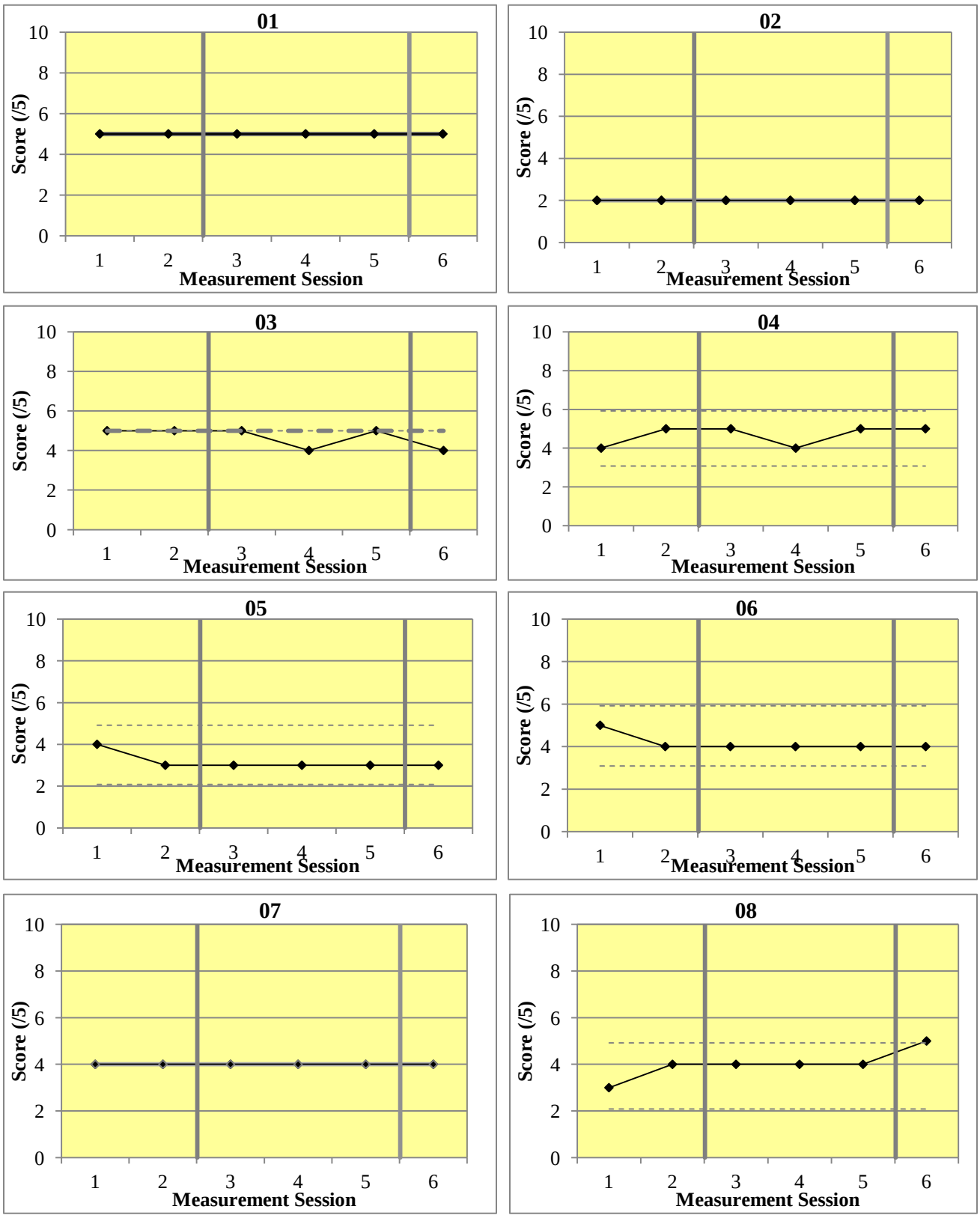


Figure 39 Overall Quality of Life (/5) for all participants

Sensation

Monofilament testing

The scores for monofilament testing (/9) for the left and right foot during baseline, intervention and post-intervention phases for all participants are shown in Figure 40. Participant 01 had a significant increase in their left foot score between baseline and intervention stage, indicating an improvement in protective sensation. Participant 05 had a significant increase in their right foot score between baseline and intervention phases indicating an improvement in protective sensation. It can be noted that this improvement continues into the post intervention phase. No participant reported a significant worsening of protective sensation during the exercise intervention.

Vibration Perception Threshold (VPT)

The average VPT scores for the left and right foot during baseline, intervention and post intervention for all participants are shown in Figure 41. Participant 01 had a significant decrease in left foot scores between baseline and intervention phase indicating an improvement in VPT with this improvement continuing into the post intervention phase. No participant reported a significant worsening of vibration perception threshold during the exercise program.

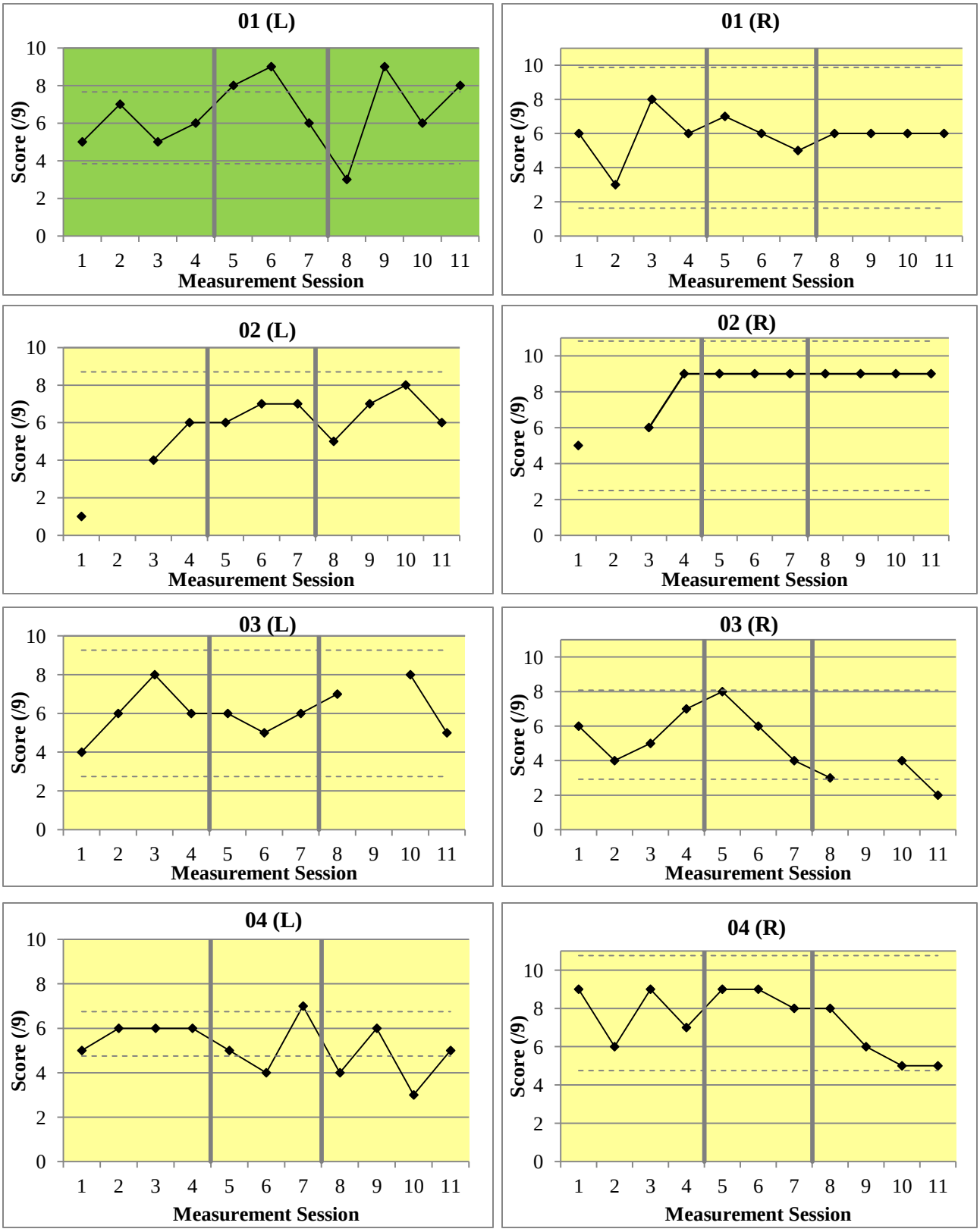


Figure 40 Monofilament score for left (L) and right (R) foot (/9) for all participants

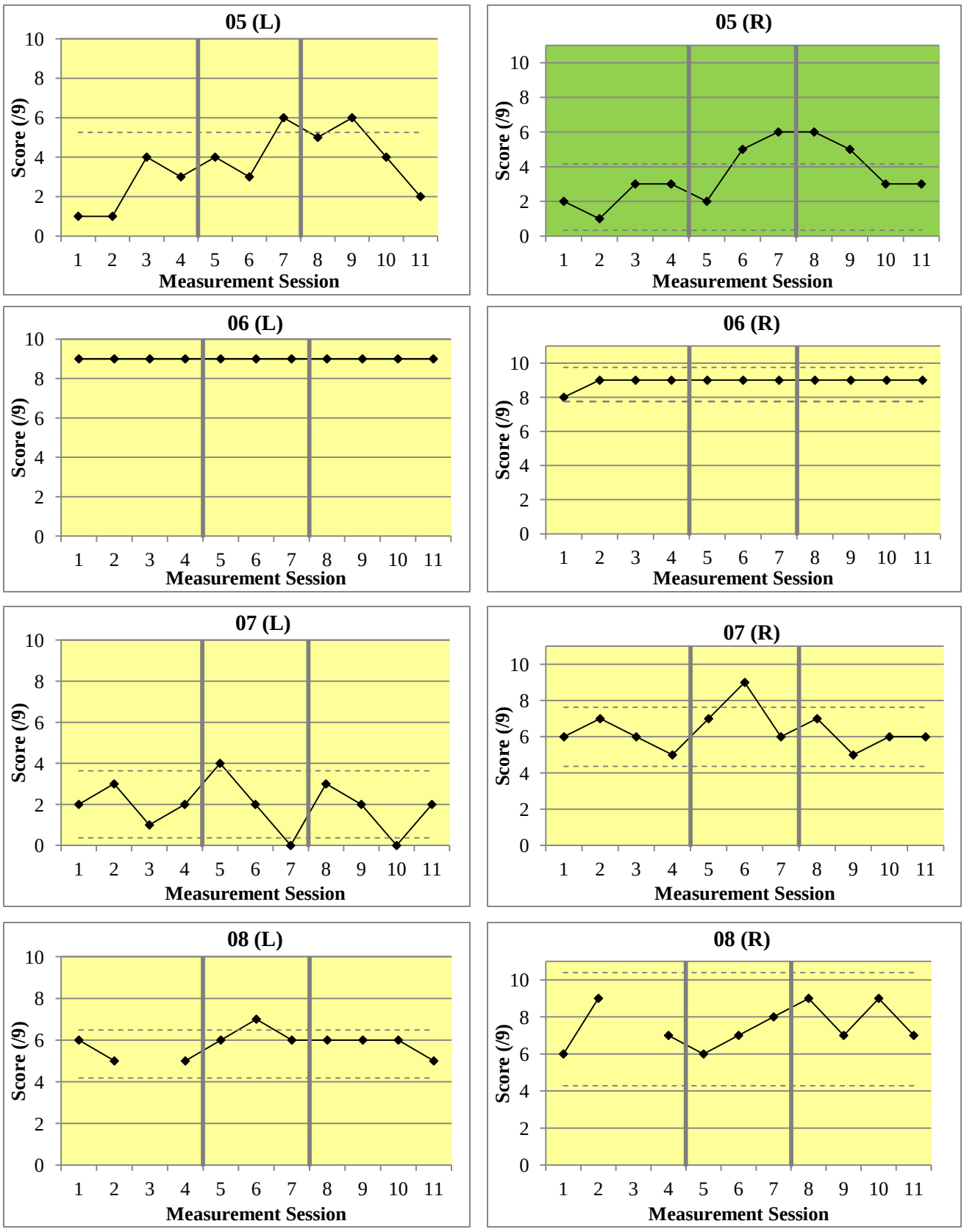


Figure 40 cont. Monofilament score for the left (L) and right (R) foot (/9) for all participants

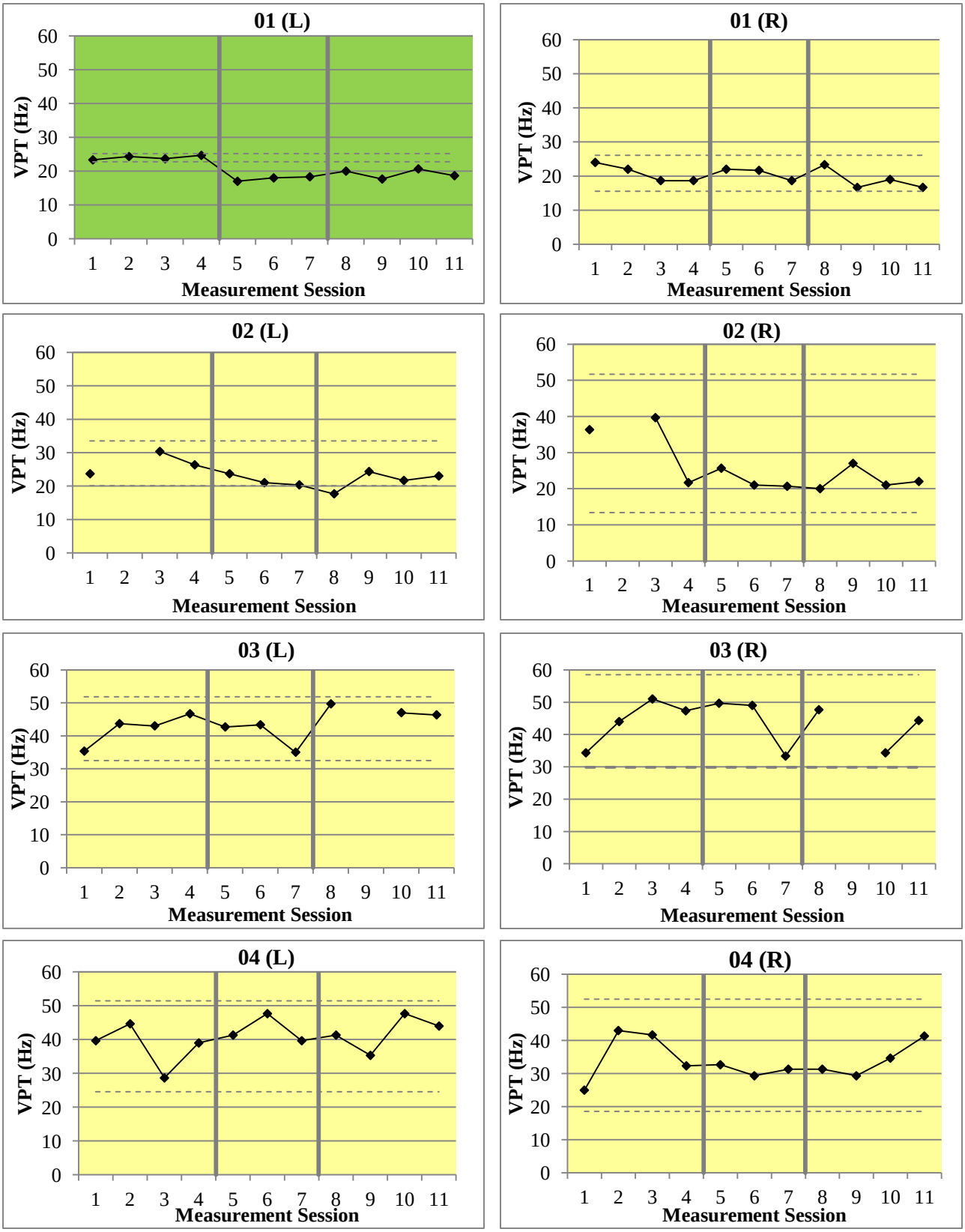


Figure 41 Vibration Perception Threshold scores (Hz) for left (L) and right (R) foot for all participants

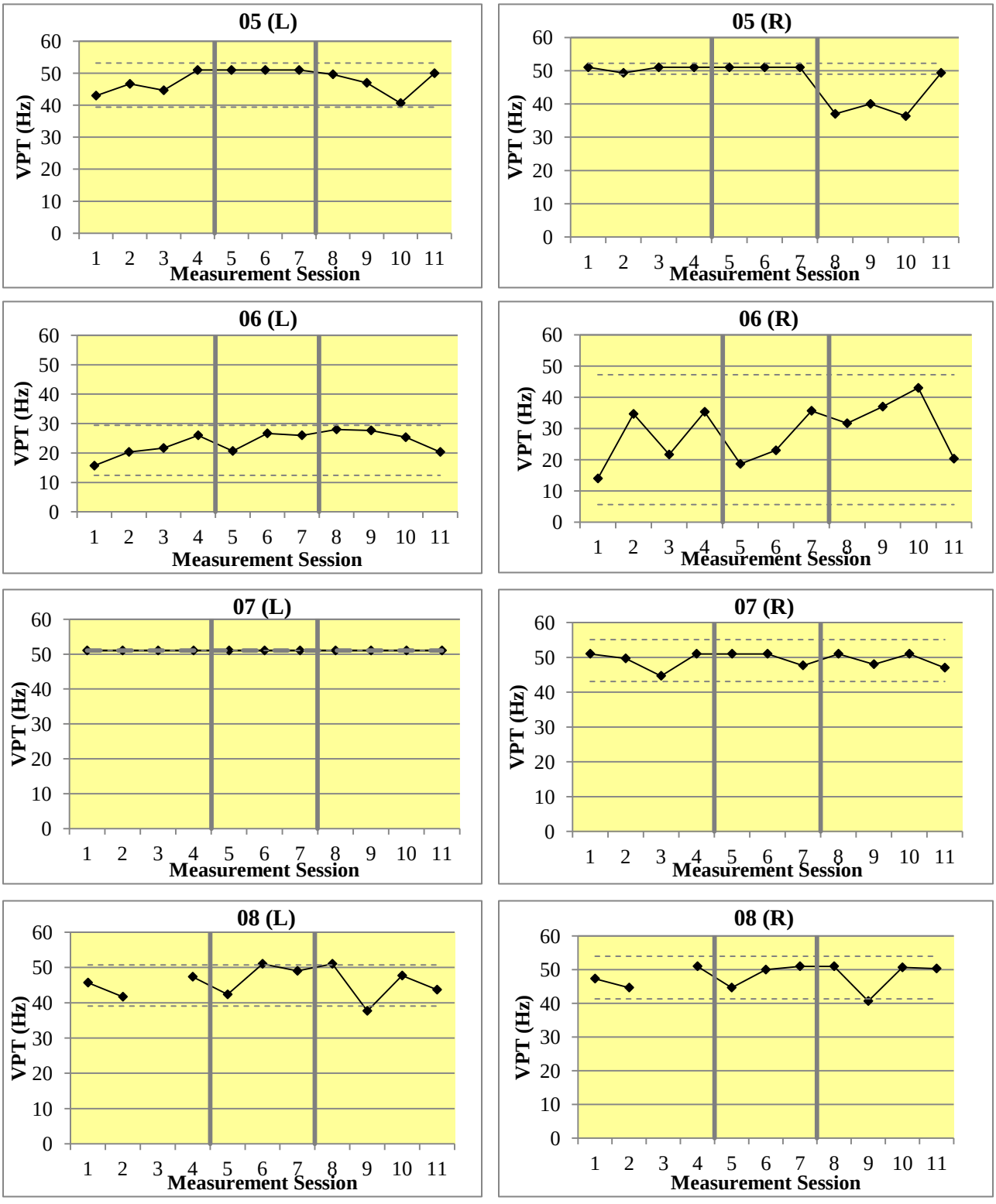


Figure 41 cont. Vibration Perception Threshold scores (Hz) for left (L) and right (R) foot for all participants

Functional measures

Knee strength

Knee flexor and extensor strength for each participant during the baseline, intervention and post-intervention phases are shown in Figure 42. The results of the knee flexion analysis revealed Participants 05, 06 and 08 had a significant increase in strength between baseline and intervention phases, with Participants 06 and 08 continuing this improvement in the post intervention phase. The knee extension results indicated that Participant 07 had a significant decrease in knee extensor strength between baseline and intervention phases. Participants 01 and 08 had a significant increase in knee extensor strength between baseline and intervention phases.

Ankle strength

Ankle strength during baseline, intervention and post intervention phases for ankle plantar-flexion and dorsi-flexion is shown in Figure 43. There were no significant changes in ankle strength (plantar-flexion or dorsi-flexion) between baseline and intervention phases for all participants.

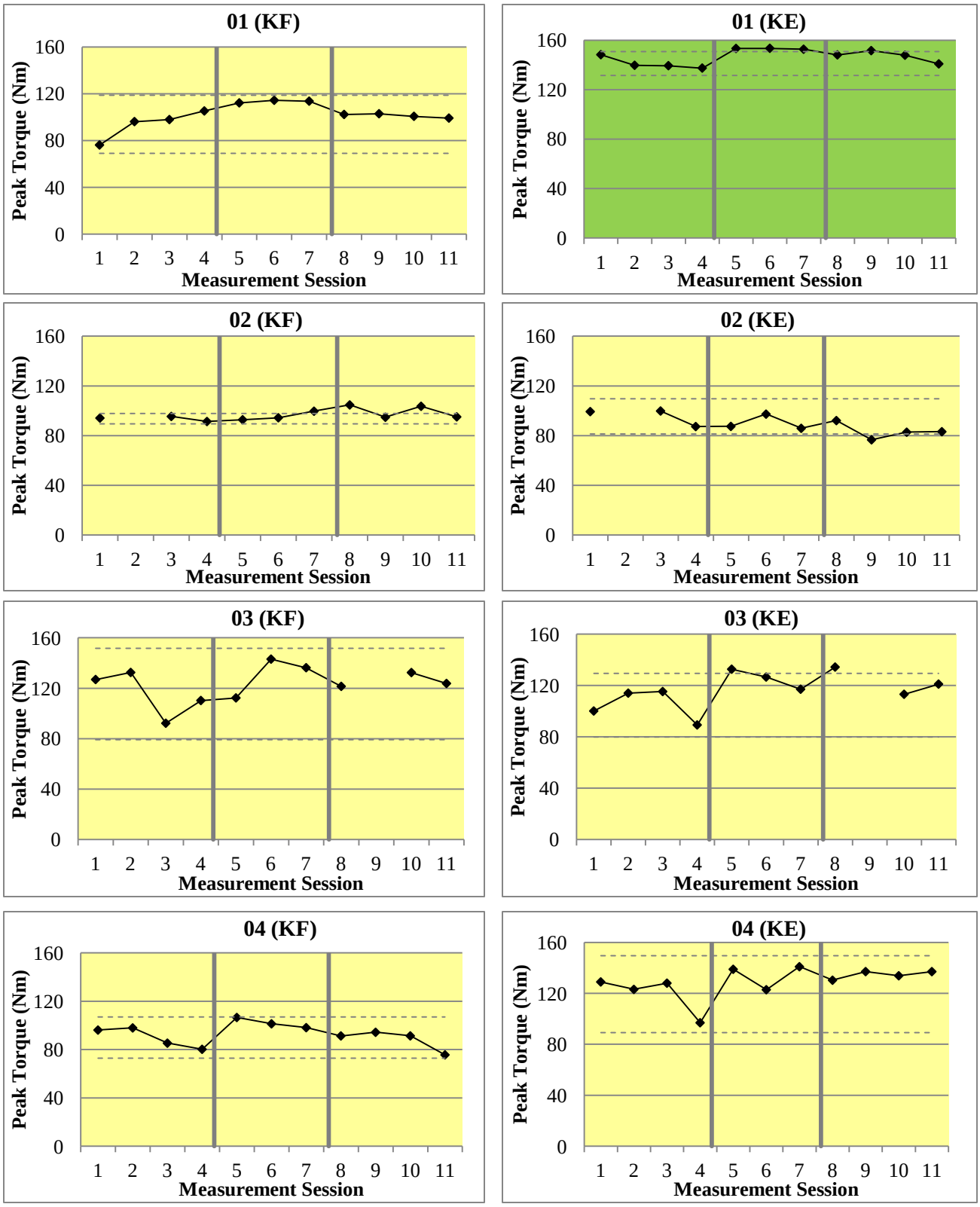


Figure 42 Peak torque (Nm) during knee flexion (KF) and extension (KE) of the dominant leg for all participants

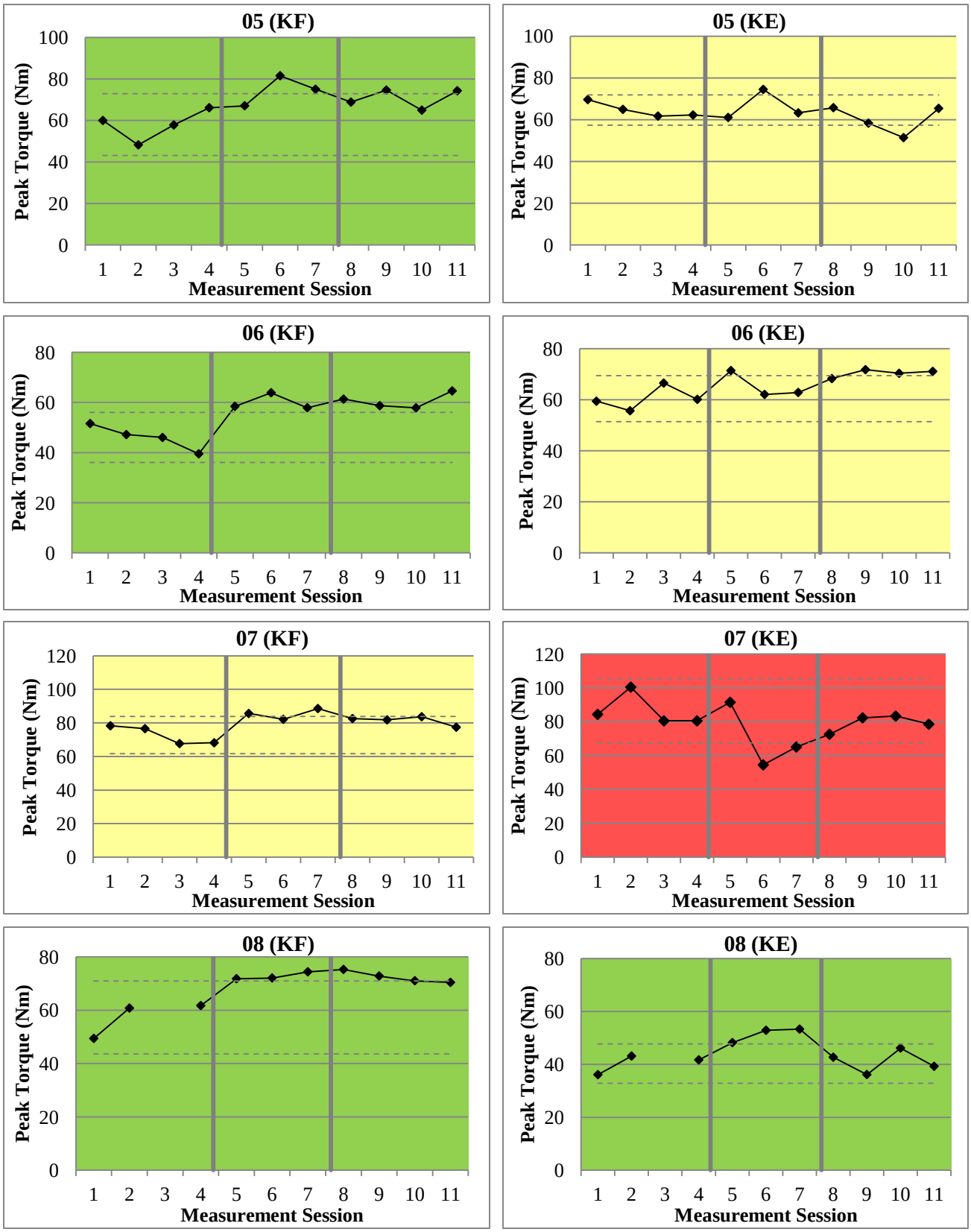


Figure 42 cont. Peak torque (Nm) during knee flexion (KF) and extension (KE) of the dominant leg for all participants

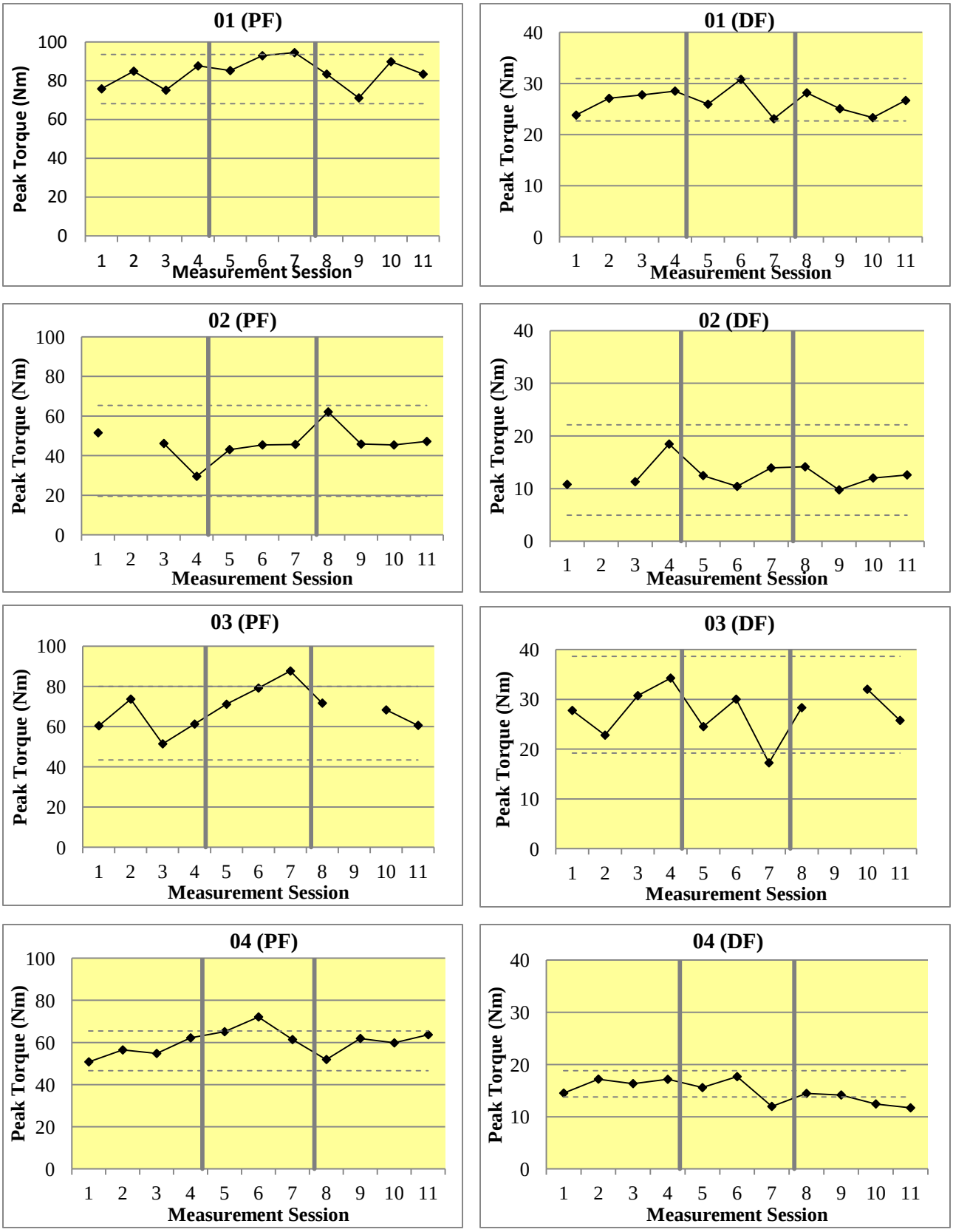


Figure 43 Peak torque (Nm) during ankle plantar (PF) and dorsi (DF) flexion of the dominant leg for all participants

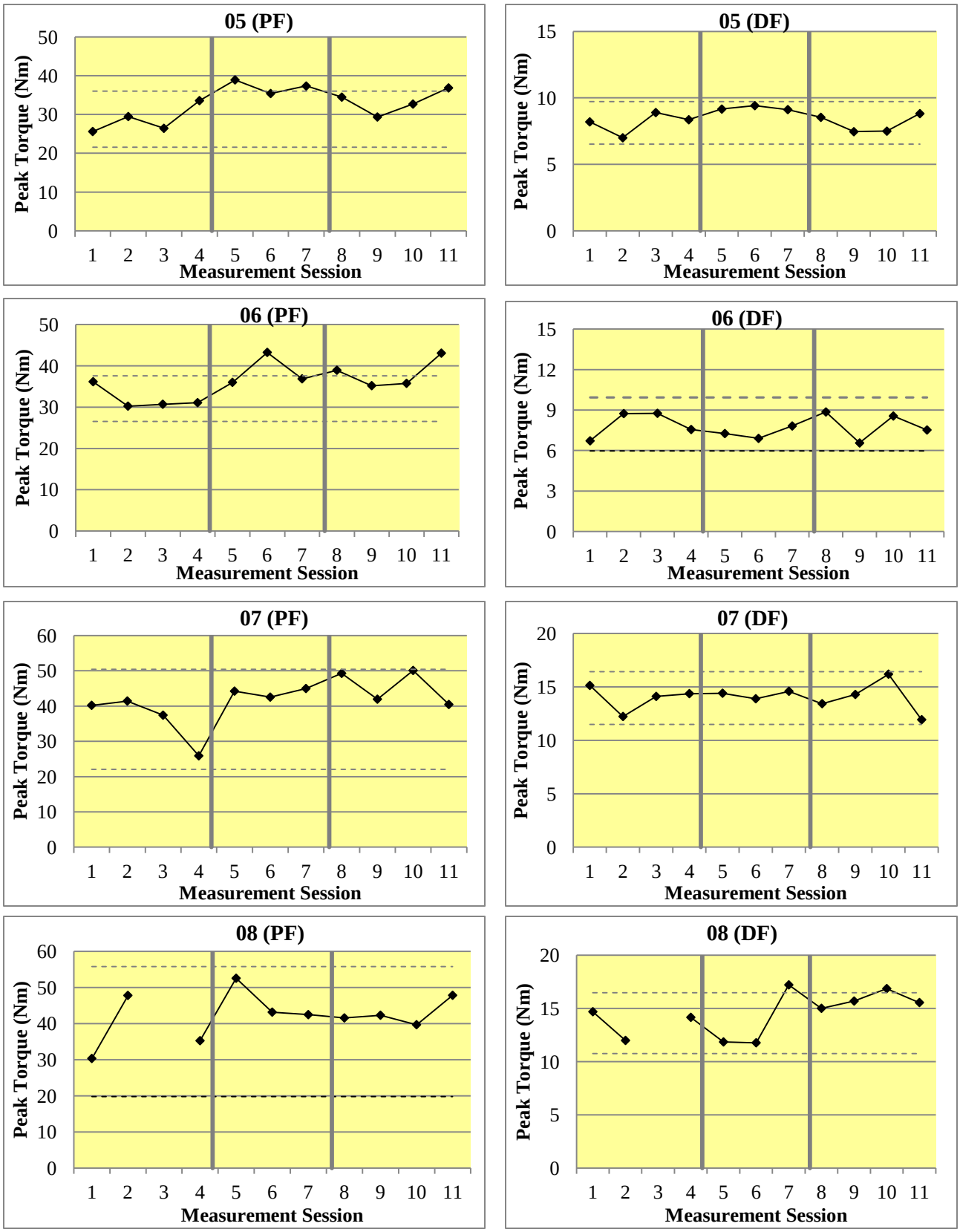


Figure 43 cont. Peak torque (Nm) during ankle plantar (PF) and dorsi (DF) flexion of the dominant leg for all participants

Physical Performance Test (PPT)

The average performance, measured in seconds for the PPT for each participant during the baseline, intervention and post-intervention is shown in Figure 44. Participants 05 and 07 recorded a significant decrease in time to complete the tests between baseline and intervention phases indicating an improvement in performance. Participant 07 continued to improve their performance into the post intervention phase. No participant had a significant decline in performance over time.

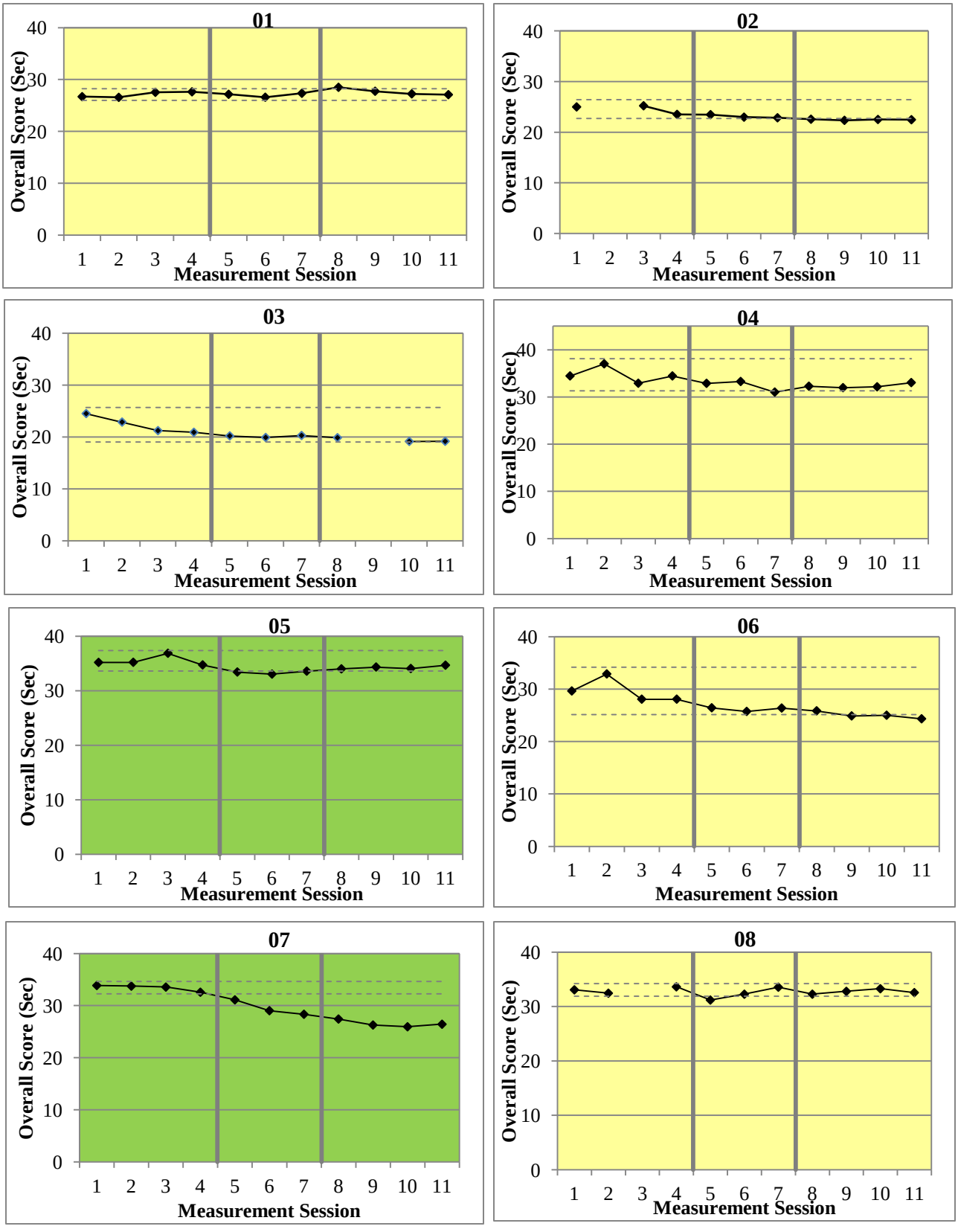


Figure 44 Physical Performance Test (PPT) overall scores (sec) for all participants

Discussion

The results of this study demonstrate that a supervised and prescribed exercise program is a safe intervention in people with Type 2 diabetes and peripheral neuropathy. The outcome measures whereby a significant improvement or no change was reported (quality of life, sensation and function) indicate that the exercise program was beneficial in people with Type 2 diabetes and peripheral neuropathy. At the time when this thesis was proposed, a review of the literature identified that research into the effects of an exercise program in people with Type 2 diabetes and peripheral neuropathy was scarce. Little evidence into the effect of a combined resistance and aerobic training program on outcomes of quality of life, sensation and function was available. However, recently more research has been reported indicating the prescription of exercise for people with Type 2 diabetes and peripheral neuropathy. However, at this time the methods used to collect data, and the results of exercise interventions across these studies are inconsistent.

Safety

Of highest importance to this study was the question of whether a prescribed aerobic and resistance training program was safe for people with Type 2 diabetes and peripheral neuropathy. The prescription of exercise and physical activity, and the effectiveness and safety of supervised and monitored training regimes need to be studied and shared. This exercise intervention study has provided such a regime, using well defined exercise parameters and outcome measures. The single case study design allowed each participant to be their own control with close monitoring undertaken as part of the study. It is encouraging that no adverse events requiring cessation of the exercise program occurred across the 12-week prescribed program.

Although there are known risks associated with exercise for people with Type 2 diabetes and peripheral neuropathy, only recently have authors documented and reported their safety measures and outcomes (Kluding et al., 2012, Otterman et al., 2011). This study has contributed to this documentation, by acknowledging the need for heightened safety measures given the unknown nature of exercise for people with peripheral neuropathy.

Of the eight participants who completed the program, three separate hypoglycemic episodes experienced by one participant were the only adverse events attributable to the exercise program and these were recognised as grade 1 according to the CTCAE. This is similar to Kluding et al. (2012) who indicated that blood glucose control was amongst the most common adverse event throughout their intervention, rated as Grade 2, however it was not specified exactly how many of these adverse events occurred. Similarly, Otterman et al. (2011) found that hypoglycemic events were the most common adverse event during their 24-week program.

In agreement with other studies (Fisher et al., 2007, Richardson et al., 2001, Tuttle et al., 2012, Kluding et al., 2012) there were no instances of tissue breakdown or ulceration in the lower limb throughout this program, which is a positive finding considering the increased risk for this population. This is in contrast to Otterman et al. (2011) who cited five instances of adverse events relating to the foot, however whether or not these were directly attributed to the exercise program was not made clear. Mueller et al. (2013) reported 13 foot lesions and four ulcers throughout their exercise program. Furthermore, LeMaster et al. (2008) reported 48 lesions to the feet of their participants which may have been attributed to the study program. It should be noted however, that the participants in the Otterman et al. (2011), Mueller et al. (2013) and LeMaster et al. (2008) studies were already at a high risk, as previous foot ulcers were not an exclusion criteria compared to the study reported in this thesis whereby the presence of any ulcer deemed the participant ineligible to participate.

Quality of life

A search of the literature failed to find studies that had used the NeuroQol to measure levels of quality of life before and after an exercise program in those with Type 2 diabetes and peripheral neuropathy. As discussed previously, studies which have assessed the effect of an exercise intervention in those with diabetes and peripheral neuropathy typically investigated electrophysical outcomes (Balducci et al., 2006, Fisher et al., 2007) and functional measures such as strength and balance (Otterman et al., 2011, Kruse et al., 2010). Therefore the study reported in this thesis appears to be the first to evaluate the effect of a combined aerobic and resistance exercise program on quality of life in those with Type 2 diabetes and peripheral neuropathy.

In the present study the majority of participants recorded either no change or a significant improvement in domains and overall quality of life scores. One participant (03) indicated the exercise program resulted in a worsening of some domains, however this did not impact the participants overall quality of life. Specifically, this participant indicated a worsening of symptoms of lost feeling, however there was no significant change in the sensation measures (monofilament and VPT) of this participant. The most consistent improvement reported across all participants was in the domain of sensory motor symptoms. The overall summary quality of life questions of the NeuroQol also resulted in no significant change for all participants. This is promising in that the exercise program was reported as not impacting on quality of life, either overall or specifically due to the participant's foot problems.

On the other hand it is interesting to consider why the exercise program was not associated with a significant improvement in quality of life as measured by the NeuroQol. This could be associated with the fact that the group of participants in the study appeared to have a reasonable level of quality of life prior to the commencement of the intervention. Other studies which have used neuropathic specific quality of life instruments have found that peripheral neuropathy was associated with a poorer quality of life and was a risk factor for depression (Currie et al., 2006, Vileikyte et al., 2009). However the results from this study show baseline scores for the domain, domain summary and the effect of foot problems on quality of life (question 28) were generally low which equates to a higher quality of life. In addition, when assessing the participant's overall quality of life (question 29) whereby a higher score indicates a greater quality of life, the baseline scores for all but one participant (02) were between a rating of 'good' to 'very good'. A possible reason for the relatively high baseline quality of life scores for these participants is the fact that they had no foot ulceration which is commonly cited as a reason for the decreased quality of life (Ribu, 2010). Another potential reason for the good quality of life scores at baseline is the fact that the participants also had a reasonably well-controlled HbA1c level prior to the intervention, with only two participants (01 – 8.5%, 05 – 7.7%) recording HbA1c levels above the recommended 7.0% (WHO, 2006). Research has found that those with Type 2 diabetes and a HbA1c level below 7.0% have a better quality of life than those with a higher levels (Sundaram et al., 2007).

Sensation

This study found that sensation and VPT were not made significantly worse by the exercise program. These results are a positive finding and suggest that a 12-week combined aerobic and resistance training program is safe in terms of not increasing sensory loss or foot ulceration, the main precursor of amputation (Bansal et al., 2006, Duby et al., 2004, Vinik and Mehrabyan, 2004). Furthermore, two participants had a significant improvement in sensation, and one participant reported a significant improvement in their vibration perception threshold. A review of the literature failed to find other studies which have assessed a combined aerobic and resistance training program on sensation using a monofilament, and VPT using a Biothesiometer in those with Type 2 diabetes and peripheral neuropathy.

Comparison of the results found in this study are difficult due to differences in instruments used to measure sensation, and variability in the inclusion and exclusion criteria from other studies. Fisher et al. (2007) found a 24-week aerobic exercise program produced an improvement in nerve function through nerve conduction studies. Balducci et al. (2006) assessed VPT at the hallux throughout a four year aerobic training program, and found a significant difference between the exercise and the control group, with the exercise group reducing their mean VPT scores from M = 14.1, SD = 4.0 Hz to M = 13.6, SD = 7.0 Hz. However it is important to note that at baseline, participants were people with diabetes without signs or symptoms of peripheral neuropathy. Furthermore, of the participants within the exercise group, only 6.45% (2 participants) developed sensory neuropathy throughout the study period, and therefore these results cannot be compared the current study (Balducci et al., 2006).

The results of the current study should be interpreted with caution as whilst the 12-week exercise program did not alter the sensation and vibration perception threshold of the majority of participants, the nerve fibres which are affected in those with peripheral neuropathy decline slowly, over a long period of time (Vinik and Mehrabyan, 2004). It has been suggested that scores of VPT testing in those with peripheral neuropathy would decline between one to two vibration units per year (Vinik and Mehrabyan, 2004). This is supported by research from Coppini et al. (2001) who found VPT scores increased from M = 14.2, SD = 4.7 Hz to M = 35.9, SD = 9.5 Hz over a 12-year period. Vinik and Mehrabyan (2004) have estimated that a clinical meaningful loss of vibration perception would take three years, meaning the results from this 12-

week exercise program should be interpreted with caution. However due to the high risk of tissue breakdown and ulceration within this population, it was deemed appropriate to monitor any changes in sensation throughout the intervention for safety purposes.

Physical function

A review of the literature failed to find any previous studies which have assessed the effect of a combined aerobic and resistance training program on the PPT in individuals with Type 2 diabetes and peripheral neuropathy. Results from this study found a significant improvement in performance for two participants as shown by a decrease in the overall time taken to complete the TUGT, the 15m walk and the stair ascend and descend. Whilst it is difficult to make any conclusions about the results of the PPT in this single-case study, together with the apparent lack of literature within this population, the fact that no participants' functional performance significantly declined is a positive of this exercise program given the predisposition of physical limitation and functional impairment in those with diabetes and peripheral neuropathy (Bruce et al., 2005, Eberhardt et al., 2006, Menz et al., 2006, Schwartz et al., 2008).

Kruse et al. (2010) assessed the effect of a 12-month exercise program, aimed at improving lower limb strength and balance in a cohort of people with diabetes and peripheral neuropathy, using the TUGT, which is one of the tests comprising the PPT. The results found that there was no change in the time taken to complete the task between baseline, six months or 12 months. A possible reason for this lack of change may be associated with the adherence rate of 45% for those taking part in the intervention (Kruse et al., 2010) compared to the adherence of the study reported here (88%). More recently however, Song et al. (2011) found a significant improvement in the TUGT in those with diabetes and peripheral neuropathy after an eight week exercise program. The exercise program was a balance specific program and did not contain any aerobic activity or the use of weights, as resistance was provided by a Thera-Band. Mueller et al. (2013) included a secondary measure of a physical performance test which utilised nine items and found no change in performance as a result of the exercise program. A possible reason for this is as well as the PPT items included in this thesis, the nine item test also included writing a sentence, simulated eating, turning 360 degrees, putting on and removing a jacket, lifting a book onto a bookshelf and picking a coin up from the floor; tasks which largely utilise the upper body which is not commonly identified as being problematic for people with peripheral neuropathy.

Other studies have used the same PPT to assess the effectiveness of an exercise program on similar populations. Brandon et al. (2003) conducted a 24-month strength training program in older adults with diabetes and found the only measure to significantly improve was the stair descent, and this improvement was found after 6-months only, but not at 24-months. It was noted however that there was a trend toward improvement for the stair ascent, TUGT and the 15m walk throughout the intervention (Brandon et al., 2003). More recently, a 10-week resistance training program produced a significant reduction in time taken to complete the PPT, however this sample included only those with high metabolic risk factors, and who had not yet been diagnosed with diabetes (Levinger et al., 2007a).

The study presented in this chapter is unique in that it presents the results of the effect of a combined aerobic and resistance training program on knee and ankle strength using isokinetic testing on a dynamometer. The results were mostly positive with several participants significantly improving knee strength, yet there were no significant changes in ankle strength. However one participant (07) recorded a significant decrease in strength between the baseline and intervention phase. This response is difficult to explain and replication of the study with a larger sample size may help to understand if this response is an outlier.

Of the limited research in the field of exercise programs in people with diabetes and peripheral neuropathy, four studies have assessed strength as an outcome measure, however only one of these studies used isokinetic testing on a dynamometer in accordance with the current study (Ruhland and Shields, 1997, Otterman et al., 2011, Kruse et al., 2010, Mueller et al., 2013). Mueller et al. (2013) used isokinetic dynamometry to assess plantar flexion peak torque and similar to the present study, did not find a significant improvement in strength across the exercise program. Otterman et al. (2011) found a 12-week combined aerobic and resistance training program significantly improved knee extension strength. However the Otterman study assessed isometric peak torque on the participant's preferred leg, as opposed to the isokinetic strength of the non-preferred leg as done so in the present study. Ruhland and Shields (1997) also used a combined aerobic and resistance training program over a six week period to demonstrate a significant improvement in strength, but again used different methodology to the current study. Ruhland and Shields (1997) used the average muscle score of knee flexion and extension and plantar dorsi-flexion and plantar-flexion, along with ten other muscle groups using the average of

individual manual muscle tests. In contrast to the above studies, Kruse et al. (2010) found a 12-month strengthening and balance program did not improve ankle dorsi-flexor strength measured using a handheld dynamometer, however being a home based program with a low adherence rate (45%) may have contributed to the lack of change.

Two studies have used similar aerobic and resistance training to assess strength in people with Type 2 diabetes alone, both finding significant improvements in strength (Lambers et al., 2008, Maiorana et al., 2002). Both studies assessed muscle strength using 1RM testing for each of the individual resistance exercises which were performed throughout the program, however Maiorana et al. (2002) did not use any exercises to test ankle strength, and Lambers et al. (2008) only defined testing into upper and lower limb strength and did not provide specific examples of the exercises involved in the testing. Several other studies have used 1RM testing methods to determine changes in strength in those with Type 2 diabetes after a resistance training program, all of which found a significant increase in strength (Castaneda et al., 2002, Cauza et al., 2005, Dunstan et al., 2005, Dunstan et al., 1998). It should be noted that all of the above studies cited changes in glycemic control and metabolic factors as the primary aim of the study, with strength being a secondary outcome measure which may have led to the use of the more clinically viable method of 1RM testing. In the present study, 1RM measurements were assessed throughout the program in order to help inform the prescription of the following month's program.

Limitations

The primary limitation of this study is the small number of the sample. Ten participants commenced the study however only eight completed the baseline, intervention, and post intervention phases. The recruitment took longer than anticipated, and the time frame that recruitment could stay open beyond the original ten participants was limited. As the eight participants were recruited through Diabetes SA and the UniSA Podiatry Clinic, it is hard to determine whether they were representative of the broader population of people with Type 2 diabetes and peripheral neuropathy or not. More participants would have added more cases by which to understand the effect of exercise on people with Type 2 diabetes and peripheral neuropathy.

The single case experimental design was chosen because of the high-risk nature exercise for people with Type 2 diabetes and peripheral neuropathy, and the lack of literature to draw upon about the safety parameters of an exercise program. Whilst the single case method was chosen to allow each participant to provide their own control and to ensure maximum safety and monitoring, there are limitations in its ability to generalise the results to groups. Trends have been identified using the single case study approach and these trends need further investigation in a larger randomised controlled trial. However, the results have shown that in this group of participants with Type 2 diabetes and peripheral neuropathy, there was a varied response to exercise and therefore it may have been premature to make assumptions about a group exercise intervention approach. The outcome measures assessed using the 2-SD bandwidth method, indicated there was little agreement between participants on most measures. No two participants' responses to the exercise program could be categorised as 'similar' and thus the use of a single-case design seems to have been justified.

Another possible limitation of the study was the 12-week intervention period. Twelve weeks may not have been long enough to capture changes in some of the outcome measures, particularly the sensation measures as already discussed. However, these outcome measures were included in order to assess the effect of a short term combined aerobic and resistance training program, and to determine the safety of such a program in this vulnerable population. The lack of change between the baseline and intervention phases of these measures was in fact a positive finding, indicating that the exercise program was safe.

Conclusions

The results of this study have highlighted the heterogeneity of people with Type 2 diabetes and peripheral neuropathy and their response to moderate intensity exercise. However, the one uniform outcome for all participants was that the intervention did not cause any harm as shown by the absence of any tissue breakdown and ulceration in the feet. Various other positive outcomes were noted in areas of quality of life and physical function which are commonly cited as problematic for people with Type 2 diabetes and peripheral neuropathy. The results of this study demonstrate encouraging signs for the prescription of moderate intensity physical activity in people with Type 2 diabetes and peripheral neuropathy. Future research should focus on the prescription of physical activity in a larger sample size so as to be able to generalise findings.

CHAPTER 7: Key Findings and Conclusions

At the conception of this research little literature existed investigating the relationships between physical activity and the biopsychosocial components (biological, social and psychological) which exist in people with Type 2 diabetes and peripheral neuropathy. The aims of this thesis were to determine the level of self-reported physical activity in people with Type 2 diabetes and Type 2 diabetes and peripheral neuropathy; investigate the level of quality of life in people with Type 2 diabetes and peripheral neuropathy and the relationship between quality of life and physical activity; and investigate the effect of a prescribed aerobic and resistance training program on safety, quality of life, sensation and function in people with Type 2 diabetes and peripheral neuropathy. These aims were addressed using various research questions, and the results were presented in Chapters 4, 5 and 6.

In Chapter 4, the assessment of self-reported physical activity revealed that those with Type 2 diabetes and peripheral neuropathy were significantly less active than those with Type 2 diabetes alone. Although those with Type 2 diabetes and peripheral neuropathy were engaging in 150 minutes of physical activity per week, it was found not to be of a high enough intensity to be deemed as meeting recommendations. Walking was found to be the most popular form of exercise within this group. Those participants in Chapter 4 with Type 2 diabetes and peripheral neuropathy then completed a quality of life questionnaire discussed in Chapter 5. It was found that the complications associated with peripheral neuropathy affected the participants' ability to perform activities of daily living, and this impacted their quality of life. As the literature suggested that physical activity may be an effective management tool for people with Type 2 diabetes, and that Chapter 4 identified that people with Type 2 diabetes and peripheral neuropathy were not meeting physical activity recommendations, further analysis was conducted between the results of the self-reported physical activity questionnaire (IPAQ) and the quality of life questionnaire (NeuroQol). The results indicated an association between overall quality of life and meeting physical activity recommendations. The results described in Chapters 4 and 5 demonstrate that physical activity may be a useful tool in improving the quality of life in people with Type 2 diabetes and peripheral neuropathy.

The results in Chapters 4 and 5 supported the engagement of physical activity in people with Type 2 diabetes and peripheral neuropathy, however a review of the literature found a lack of supporting evidence investigating the biological, sociological and psychological effects of

exercise in this population. This dearth of literature prompted the third study using a SCED to determine the value of a moderate intensity exercise program for those with Type 2 diabetes and peripheral neuropathy. The Australian Safety and Quality Framework for Health Care was used due to the unpredictable nature of peripheral neuropathy. Accordingly, an exercise program was devised specifically for the participants using up to date and relevant literature, and was organised to ensure the upmost safety of the participants. The use of a single case design was deemed appropriate due to the infancy of this research and the heterogeneity of the population. This was inevitably justified as the results showed that despite the use of rigorous tools and methodologies, varying outcomes were noted amongst all participants.

Whilst some improvements in outcome measures including physical function, quality of life and sensation were seen among several participants, the most important finding of this research was that a supervised, prescribed exercise program was indeed safe for this population. This thesis has explored the difficulty in the promotion of physical activity to this population due to the lack of peer reviewed evidence and formal recommendations over the years, which have only recently been updated to include the addition of walking and moderate weight bearing activities for those without ulceration (ACSM/ADA, 2010). Although the aerobic component of the program discussed in Chapter 6 included non-weight bearing exercises as a precaution, the resistance training component included activities of a moderate weight bearing nature. However the only adverse events recorded which were attributable to the program, were hypoglycemic episodes which are commonly cited as the main adverse event for this population (Kluding et al., 2012, Otterman et al., 2011). This is an indication that the program was successful in not exacerbating the problems associated with Type 2 diabetes and peripheral neuropathy, and that participants had the assurance that they were being closely monitored and that their safety was a priority.

Considering a moderate intensity exercise program prescribed within the framework noted above appeared safe, attention can now be directed towards the physical and psychosocial outcomes of exercise for this population. The results of the exercise program were mostly positive for outcomes of sensation and functional measures, with the majority of outcomes for all participants indicating either no change, or a significant improvement. The results for measures of quality of life were more variable with two participants indicating some domain scores declining throughout the exercise program, however not to a point where it reduced their overall quality of

life. As various studies have reported positive changes in measures of quality of life, sensation and function in similar populations, it may be concluded that a program of longer duration may eventually elicit similar outcomes for people with peripheral neuropathy. It has been shown that people with Type 2 diabetes and peripheral neuropathy have a greater deficit in quality of life, sensation and functional capacity compared to those without peripheral neuropathy (Bruce D, Davis & Davis 2005; Liedberg & Vrethem 2009; Vileikyte et al 2005). Therefore it may be argued that this population needs a prolonged, sustained intervention to reap the same benefits which may be seen within a shorter time period in those without peripheral neuropathy.

Recommendations for further study

The research presented in this thesis supports the continued research into the effects of physical activity and exercise in people with Type 2 diabetes and peripheral neuropathy. This thesis has shown, in a small number of participants that exercise can be done safely within this population. Therefore the next step forward would be to extend this research further, with a larger cohort over an extended period of time. A larger sample size with the use of control participants may progress the findings within this thesis, and allow generalised statements to be made about physical activity and exercise in people with Type 2 diabetes and peripheral neuropathy. Extending the duration of the exercise intervention would allow greater time for the effects of the exercise program to make an impact on a participant's life, particularly through measures of quality of life and sensation. It would be hypothesised that the benefits of exercise training on measures of strength and physical function would continue to improve over time.

However further careful consideration must be given to the population with Type 2 diabetes and peripheral neuropathy who are not in as good health as those seen within this present study. Due to ethical considerations, participants undertaking this exercise program were required not to have had any ulceration, amputation and other co-morbidities which may impair their ability to exercise safely. Despite the proportion of people with Type 2 diabetes and peripheral neuropathy who have one or a combination of these problems being unknown, of those who expressed an interest in participating in the exercise program, 49% were excluded as they had an existing co-morbidity.

Furthermore, the number of participants required to reach statistical power to conduct a high level research design, including the use of a control group may be problematic considering the difficulty of recruitment experienced in this thesis. As discussed in Chapter 6, despite an exhaustive effort to recruit people with Type 2 diabetes and peripheral neuropathy through member organisations and clinics, there was a poor response rate. This response rate may be indicative of the fluctuations of diagnosis of peripheral neuropathy, complications which may exclude people from participating in a trial, or the lack of motivation and interest in exercise for this population. Despite these difficulties, researchers and clinicians should continue promote physical activity and exercise within this population, knowing the positive outcomes available to those who are able to maintain a structured supervised program.

Final conclusions

Physical activity is widely considered as a management tool for various chronic diseases, and up until recently, people with Type 2 diabetes and peripheral neuropathy were without the knowledge that exercise was a safe management option. This research has aimed to explore the level of physical activity in the lives of people with Type 2 diabetes and peripheral neuropathy, and their quality of life. This prompted further investigation into the effect of a moderate intensity, prescribed and supervised exercise program on the quality of life, functional ability and sensation measures in those with Type 2 diabetes and peripheral neuropathy. This research has concluded that exercise is indeed safe for this population and provides many other positive benefits to a population who were previously overlooked due to their condition. These findings support continued research to promote the use of exercise and physical activity as a safe management tool for people with Type 2 diabetes and peripheral neuropathy.

Contribution of this thesis to the field

Body of knowledge

The study results of this thesis:

- Demonstrated that people with Type 2 diabetes and peripheral neuropathy may not be exercising at an high enough intensity to be considered meeting physical activity recommendations
- Identified that there is a positive relationship between overall quality of life and self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy
- Suggest that a prescribed and supervised aerobic and resistance training program is safe for people with Type 2 diabetes and peripheral neuropathy
- Recommend further research into the effects of physical activity and exercise in people with Type 2 diabetes and peripheral neuropathy

Methodological Rigour

The studies presented in this thesis are underpinned by the Biopsychosocial model and the Australian Safety and Quality Framework for Health Care, and are characterised by:

- A critical examination of the literature
- A combination of subjective and objective measures using valid and reliable tools
- The use of a single case experimental design

Originality

This thesis has made an original contribution to the field by providing:

- An in depth description of the levels of self-reported physical activity in people with Type 2 diabetes and peripheral neuropathy, and whether or not physical activity guidelines were being met
- An examination of the levels of self-reported quality of in people with Type 2 diabetes and peripheral neuropathy, and whether or not there was a relationship between self-reported quality of life and self-reported physical activity
- Evidence that a prescribed aerobic and resistance training program can be safe for people with Type 2 diabetes and peripheral neuropathy

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Appendix 1: International Physical Activity Questionnaire

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** 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. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

   _____ **hours per day**

   _____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days. Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent 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.

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

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

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

Appendix 2: Cover letter (Diabetes SA)

11th January 2010

Dear Member

Seeking Research Participants

Please find enclosed details of a research study seeking participants.

If you do not wish to be involved or you do not fit the criteria simply disregard the information. There is no need to call us to decline; the contact details of the study are enclosed if you are interested in being involved.

Diabetes SA supports ongoing research into the cure and/or management of diabetes and hope that you or someone you know who fits the criteria will consider being involved.

In addition, Diabetes SA wishes to advise that we have not relinquished your details to any third party and are therefore sending this letter on behalf of the researcher to a randomly selected segment of our database.

If you do not wish to be contacted about being involved in research again, please mail your details to:

Diabetes SA
C/- Research participant
Reply Paid 1930
Adelaide SA 5001

Or e-mail estelle@diabetessa.com.au

Thank you for your time.

Kind Regards,

Estelle Mamo
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Appendix 3: Information letter for questionnaires

University of
South Australia

Dear Participant

I am writing to invite you to participate in my PhD study entitled 'Physical activity and quality of life in people with Type 2 diabetes and peripheral neuropathy' being conducted at the University of South Australia (UniSA) with the support of Diabetes SA.

You have been identified as having been diagnosed with Type 2 diabetes. I am interested in looking at the relationship between factors of physical activity and quality of life. The two questionnaires I am using have been used extensively in other research studies and are presented in their published format to ensure they remain valid.

It has been reported that people with Type 2 diabetes do varying amounts of physical activity. This is no different to the population without diabetes. However, what I am interested in looking at is the relationship between the amount and type of physical activity done and perceived quality of life in people with Type 2 diabetes and peripheral neuropathy.

The first page asks you to answer some basic questions regarding your demographic data. Below that is a slip which asks for your personal details if you wish to be included in future studies at UniSA involving exercise interventions. If you choose to fill out this slip, an assistant within the School of Health Sciences will separate your details from the questionnaires to ensure anonymity.

The first questionnaire is called the International Physical Activity Questionnaire (IPAQ) and focuses on how much physical activity you have done in the past week. If you have Type 2 diabetes then I would appreciate it if you would fill out the IPAQ which has been printed on **yellow** paper. This will take you no longer than 10 minutes.

The second questionnaire is called the NeuroQol and is only for those who have been told by their health professional that they have Type 2 diabetes **and** peripheral neuropathy. If this applies to you, then I would appreciate if you could also fill out the NeuroQol which has been enclosed separately on **blue** paper. The NeuroQol focuses on your quality of life across areas such as symptoms, daily activities, relationships and work and will only take a further 10 minutes to complete.

Participation in this study is anonymous and voluntary and whether you chose to participate in this study or not your availability to services provided by UniSA will not be affected. If you choose to participate, could you please return all relevant papers using the enclosed replied paid envelope within 2 weeks.

The University of South Australia's Human Research Ethics Committee has reviewed this study and should you wish to discuss any details of this study with someone not directly involved, in particular in relation to matters concerning policies, the conduct of the study or your rights as a participant, please contact the UniSA Ethics Officer:
Ms Vicki Allen on 8302 3118; fax 8302 3921
email Vicki.allen@unisa.edu.au.

If you require any further information regarding the specific details of the study, please contact myself using the details below.

Kind Regards

Rebecca Nolan

Rebecca Nolan
PhD Student
School of Health Sciences
Adelaide
South Australia 5000

GPO Box 2471
Adelaide
South Australia 5001
Australia

t: 8302 1373

www.unisa.edu.au
Rebecca.nolan@unisa.edu.au

CRICOS Provider Number
00121B

Professor Esther May
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Appendix 4: Demographics sheet

Physical activity and quality of life in people with Type 2 diabetes and peripheral neuropathy

Demographic Data

1. **Age**

   _____years

2. **Gender (please tick)**

   ☐ Male ☐ Female

3. **How long have you been diagnosed with Type 2 diabetes?**

   _____years

4. **Has your General Practitioner or Medical Specialist ever told you that you have peripheral neuropathy? (please tick)**

   ☐ Yes If you have answered 'yes' please fill out the IPAQ (yellow questionnaire) and the NeuroQol (blue questionnaire)

   OR

   ☐ No If you have answered 'no' please only fill out the IPAQ (yellow questionnaire).

Would you be interested in being contacted to participate in an exercise research program at the University of South Australia?

If so, please fill out your details below.

Name……

Address……

……

E-mail Address……

Contact phone number……..

This form will be separated from your questionnaires when opened to ensure anonymity of your questionnaires.

Please send to Rebecca Nolan, School of Health Sciences, University of South Australia, in the return paid envelope. If you have any questions, please ring 8302 1373.

Appendix 5: Example reminder letters for Member of Diabetes SA for return of the questionnaire

University of
South Australia

Date xxxxxx

Dear Diabetes SA Member

In conjunction with Diabetes SA you recently received a questionnaire from me regarding my PhD research. You were randomly selected from the Diabetes SA database for people with Type 2 diabetes.

The questionnaires asked for some demographic details, as well as your physical activity habits over the past 7 days. Additionally a questionnaire was included for those people who also have been diagnosed with peripheral neuropathy (loss of feeling in your feet).

If you were still interested in participating in my study, could you please return the relevant papers as soon as possible. If you have lost or misplaced your questionnaire but would still like to participate, please contact me and I will send you another.

The questionnaires are voluntary and anonymous. This research has been approved by the UniSA Human Research Ethics Committee.

I look forward to receiving your response in the near future.
Kind Regards,

Rebecca Nolan
(PhD Student)

School of Health Sciences

Adelaide
South Australia 5000

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Australia

t: +61 8 8302 1373
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CRICOS Provider Number
00121B

Appendix 6: Additional data for Chapter 4

Table 44 Age and years since diagnosis of Type 2 Diabetes for those who completed physical activity during the past 7-days

	n[†]	Age (years) M ± SD	95% CI	Years since diagnosis M ± SD	95% CI
All	450	63.03 ± 8.64	62.21 – 63.84	8.21 ± 6.51	7.60 – 8.83
Male	269	63.95 ± 7.95	63.00 – 64.90*	8.75 ± 6.62	7.95 – 9.55
Female	166	61.49 ± 9.47	60.04 – 62.95	7.34 ± 6.25	6.38 – 8.30
With PN	51	66.06 ± 8.27	63.69 – 68.44*	11.23 ± 8.44	8.76 – 13.71*
Without PN	383	62.64 ± 8.62	61.78 – 63.50	7.84 ± 6.14	7.22 – 8.46

[†] n = 15 did not provide their gender, n = 16 did not provide their PN status, *statistically significant (95% CI)

Table 45 Age and years since diagnosis of Type 2 diabetes for those who completed moderate physical activity during the past 7-days, by gender

	n	Age (years) M ± SD	95% CI	Years since diagnosis M ± SD	95% CI
Male	167	64.43 ± 8.34	63.16 – 65.70*	8.60 ± 6.94	7.55 – 9.66
Female	96	61.06 ± 9.43	59.15 – 62.97	6.80 ± 4.96	5.79 – 7.81

*statistically significant (95% CI)

Table 46 Age and year since diagnosis of Type 2 diabetes for those who walked during the past 7-days, by gender

	n	Age (years) M ± SD	95% CI	Years since diagnosis M ± SD	95% CI
Male	258	64.04 ± 8.02	63.06 – 65.02*	8.63 ± 6.51	7.82 – 9.43
Female	161	61.46 ± 9.19	60.03 – 62.89	7.29 ± 6.23	6.32 – 8.27

*statistically significant (95% CI)

Table 47 Vigorous percentage contribution to the physical activity profile (mean ± SD)

	n[†]	Vigorous (%)	95% CI
All	450	18.59 ± 24.22	15.38-22.62
Males	269	20.48 ± 25.01	15.22-24.78
Females	166	16.06 ± 22.68	10.42-21.58
With PN	51	13.20 ± 23.33	3.77-22.23
Without PN	383	19.57 ± 24.28	15.99-24.01

[†]n = 15 did not provide their gender, n = 16 did not provide their PN status

Table 48 Moderate percentage contribution to the physical activity profile (mean ± SD)

	n[†]	Moderate (%)	95% CI
All	450	24.66 ± 26.62	20.05-27.95
Males	269	25.03 ± 26.19	19.83-30.17
Females	166	24.00 ± 27.52	17.50-30.50
With PN	51	24.38 ± 30.98	12.28-35.72
Without PN	383	24.72 ± 26.07	20.66-29.34

[†]n = 15 did not provide their gender, n = 16 did not provide their PN status

Table 49 Walking percentage contribution to the physical activity profile (mean ± SD)

	n[†]	Walking (%)	95% CI
All	450	56.75 ± 34.46	52.43-61.57
Males	269	54.49 ± 34.85	48.04-59.96
Females	166	59.94 ± 33.85	52.55-67.45
With PN	51	62.41 ± 38.10	48.68-75.32
Without PN	383	55.71 ± 33.98	51.03-60.97

[†]n = 15 did not provide their gender, n = 16 did not provide their PN status

Table 50 Demographics of those who met PA recommendations

	n[†]	Age (years) M ± SD	95% CI	Years since diagnosis M ± SD	95% CI
All	276	63.4 ± 8.6	62.3 – 64.4	8.3 ± 6.6	7.5 – 9.1
Male	174	64.0 ± 8.1	62.8 – 65.2	8.8 ± 7.0	7.7 – 9.8
Female	95	62.5 ± 9.2	60.6 – 64.3	7.5 ± 5.8	6.3 – 8.6
With PN	27	66.6 ± 8.0	63.5 – 69.8	11.2 ± 9.0	7.6 – 14.8
Without PN	242	63.0 ± 8.6	61.9 – 64.1	8.0 ± 6.2	7.2 – 8.8

[†]n = 7 did not provide their gender, n = 7 did not provide their PN status

Table 51 Demographics of those who did not meet PA recommendations

	n[†]	Age (years) M ± SD	95% CI	Years since diagnosis M ± SD	95% CI
All	205	62.9 ± 8.7	61.6 – 64.1	8.4 ± 7.1	7.4 – 9.4
Male	109	64.3 ± 7.5	62.9 – 65.8	8.3 ± 5.7	7.3 – 9.4
Female	87	61.0 ± 9.7	58.9 – 63.0	8.5 ± 8.5	6.7 – 10.3
With PN	28	66.7 ± 8.6	63.2 – 70.1	11.9 ± 10.2	7.8 – 16.0
Without PN	166	62.2 ± 8.6	60.9 – 63.5	7.8 ± 6.3	6.9 – 8.8

[†]n = 9 did not provide their gender, n = 11 did not provide their PN status

Appendix 7: NeuroQol

NEUROPATHY-SPECIFIC QUALITY OF LIFE Questionnaire Instructions

- These questions ask about the effect your **FOOT PROBLEMS** may have on your daily life and well-being. By **foot problems** we mean **lost or reduced feeling** in your extremities**, pain, discomfort** and/or **ulcers (open sores) on your feet** and, in some cases **unsteadiness** while walking or standing.
- Please note that many **questions have two parts**. Answer every question by ticking one box for each part (tick two boxes per line). Please make sure you answer all questions.
- Please concentrate on how you have felt **IN THE PAST 4 WEEKS** for all of the questions.
- There are no right or wrong answers. If you are unsure about how to answer a question, you can ask the person who gave you the questionnaire. Please **DO NOT** ask a relative or friend to help you.
- **All of your responses will be held strictly confidential.**

In the past 4 weeks how often have you experienced the following symptoms?	All the time	Most of the time	Some of the time	Occasionally	Never	**How much bother did this cause you?**		
						Very much	Some bother	None
1. Burning in your legs or feet								
2. Excessive heat or cold in your legs or feet								
3. Pins and needles in your legs or feet								
4. Shooting or stabbing pain in your legs or feet								
5. Throbbing in your legs or feet								
6. Sensations in your legs or feet that make them jump								
7. Irritation of the skin caused by something touching your feet, such as bedsheets or socks								

A. Have these **painful symptoms** reduced your quality of life?	Very much	Quite a lot	Somewhat	A little	Not at all

In the past 4 weeks how often have you experienced the following symptoms?	All the time	Most of the time	Some of the time	Occasionally	Never	**How much bother did this cause you?**		
						Very much	Some bother	None
8. Numbness in your feet								
9. Inability to feel the difference between hot and cold with your feet								
10. Inability to feel objects with your feet								

B. Have these **last three symptoms** reduced your quality of life?	Very much	Quite a lot	Somewhat	A little	Not at all

In the past 4 weeks how often have you experienced the following symptoms?	All the time	Most of the time	Some of the time	Occasionally	Never	**How much bother did this cause you?**		
						Very much	Some bother	None
11. Weakness in your hands								
12. Problems with balance or unsteadiness while walking								
13. Problems with balance or unsteadiness while standing								

C. Have these **last three symptoms** reduced your quality of life?	Very much	Quite a lot	Somewhat	A little	Not at all

The following questions ask about how your FOOT PROBLEMS affect your daily activities, relationships and feelings.

Are you in <u>PAID WORK</u>?	Yes	No	If **YES** please go to Question 14. If **NO** please go to Question 15.

In the past 4 weeks, HOW MUCH have your foot problems interfered with your:	Very much	Quite a lot	Some what	A little	Not at all	**How important is this aspect of your life to you?**		
						Very much	Some what	Not at all
14. Ability to perform your paid work?								
15. Ability to perform tasks around the house or garden?								
16. Ability to take part in leisure activities?								

D. Have these changes in **daily activities** as a result of your foot problems reduced your quality of life?	Very much	Quite a lot	Somewhat	A little	Not at all

In the past 4 weeks:						How important is this aspect of your life to you?		
	Very much	Quite a lot	Some what	A little	Not at all	Very much	Some what	Not at all
17. How much have your foot problems interfered with your relationships with people close to you?								
18.Have you felt more physically dependent than you would like to be on people close to you as a result of your foot problems?								
19.Have you felt more emotionally dependent than you would like to be on people close to you as a result of your foot problems?								
20. has your role in the family changed as a result of your foot problems?								

E. Have these changes in **relationships with other people** as a result of your foot problems reduced your quality of life?	Very much	Quite a lot	Somewhat	A little	Not at all

						How much bother did this cause you?		
How much do you agree with the following statements:	Completely agree	Partly agree	Neither agree or	Partly disagree	Completely disagree	Very much	Some bother	None
21. People treat me differently from other people as a result of my foot problems.								
22. I feel older than my years as a result of my foot problems.								
23. My self - confidence is affected as a result of my foot problems.								
24. My foot problems make my life a struggle.								

25. I generally feel frustrated because of my foot problems.								
26. My foot problems cause me embarrassment.								
27. I feel depressed because of my foot problems								

F. Have these **feelings about yourself** as a result of your foot problems reduced your quality of life?	Very much	Quite a lot	Somewhat	A little	Not at all

	Very much	Quite a lot	Somewhat	A little	Not at all
28. Overall, I would say problems with my feet reduced my Quality of Life:					

	Excellent	Very good	Good	Fair	Poor
29. Overall, I would rate my quality of life as:					

Appendix 8: Additional data for Chapter 5

Table 52 Scale, weighted and summary scores of the 6 NeuroQol domains (mean ± SD)

	n[†]	Scale (/5)	p	n[†]	Weighted (/15)	p	n[†]	Domain Summary (/5)	p
Pain								**A**	
All	64	2.18 ± 0.86		49	4.40 ± 2.68		67	2.55 ± 1.26	
Male	40	2.09 ± 0.91	0.21	31	4.29 ± 2.91	0.76	45	2.44 ± 1.24	0.31
Female	23	2.30 ± 0.77		17	4.47 ± 2.91		21	2.81 ± 1.33	
Lost Feeling								**B**	
All	71	2.65 ± 1.22		60	5.46 ± 3.77		72	2.40 ± 1.30	
Male	46	2.80 ± 1.24	0.23	40	5.64 ± 3.68	0.44	47	2.40 ± 1.28	0.93
Female	23	2.42 ± 1.16		19	5.09 ± 4.12		23	2.39 ± 1.34	
Sensory-Motor symptoms								**C**	
All	73	2.18 ± 0.99		59	4.53 ± 3.24		71	2.48 ± 1.42	
Male	47	2.07 ± 0.99	0.13	39	4.19 ± 3.18	0.32	46	2.39 ± 1.39	0.42
Female	24	2.43 ± 0.98		19	5.19 ± 3.43		23	2.70 ± 1.52	
ADL's								**D**	
All	68	2.56 ± 1.36		59	6.23 ± 4.27		68	2.63 ± 1.40	
Male	47	2.32 ± 1.23	0.02*	42	5.47 ± 3.74	0.80	45	2.42 ± 1.31	0.07
Female	20	3.09 ± 1.52		17	8.13 ± 4.97		21	3.14 ± 1.53	
Social Relationships								**E**	
All	52	1.71 ± 1.13		33	3.42 ± 3.18		68	2.13 ± 1.37	
Male	34	1.60 ± 0.99	0.52	23	3.39 ± 3.09	0.89	44	1.89 ± 1.32	0.05
Female	16	1.95 ± 1.44		10	3.48 ± 3.56		23	2.57 ± 1.41	*
Emotional Distress								**F**	
All	70	2.57 ± 1.30		57	4.97 ± 3.89		73	2.40 ± 1.22	
Male	45	2.50 ± 1.27	0.59	39	5.06 ± 4.11	0.89	47	2.28 ± 1.21	0.24
Female	23	2.66 ± 1.32		17	5.01 ± 3.46		24	2.63 ± 1.21	

*statistically significant ($p<0.05$), [†]Some participants did not indicate their gender

Table 53 Comparison of scaled, weighted and domain summary scores between those who met (met) physical activity recommendations and those who did not (not met) (mean ± SD)

	n	Scale Score (1-5)		n	Weighted (1-15)		n	Domain Summary (1-5)	
Pain								**A**	
Met	24	2.05 ± 0.67	0.97	20	3.94 ± 2.29	0.84	25	2.40 ± 1.29	0.38
Not met	23	2.22 ± 1.11		18	4.71 ± 3.58		25	2.72 ± 1.34	
Lost Feeling								**B**	
Met	26	2.56 ± 1.22	0.80	23	5.00 ± 3.50	0.92	25	2.20 ± 1.26	0.41
Not met	25	2.48 ± 1.08		19	4.98 ± 3.28		26	2.50 ± 1.36	
Sensory-Motor symptoms								**C**	
Met	26	2.05 ± 0.96	0.24	23	3.78 ± 3.06	0.06	25	2.12 ± 1.45	0.04*
Not met	26	2.41 ± 1.07		20	5.60 ± 3.43		24	2.92 ± 1.44	
ADL's								**D**	
Met	23	2.33 ± 1.30	0.37	21	5.73 ± 4.50	0.35	23	2.35 ± 1.27	0.27
Not met	24	2.73 ± 1.43		19	6.70 ± 4.10		25	2.84 ± 1.52	
Social Relationships								**E**	
Met	20	1.41 ± 0.86	0.18	16	2.59 ± 2.71	0.04*	24	1.83 ± 1.24	0.25
Not met	17	1.84 ± 1.19		9	4.58 ± 3.33		24	2.29 ± 1.40	
Emotional Distress								**F**	
Met	23	2.30 ± 1.25	0.28	21	4.94 ± 4.19	0.79	24	2.36 ± 1.15	0.86
Not met	25	2.71 ± 1.34		20	5.02 ± 3.82		23	2.46 ± 1.30	

*statistically significant ($p<0.05$)

Appendix 9: Information sheet for participants recruited via Diabetes SA

Dear……..,

During March, a questionnaire was sent out through Diabetes SA as apart of research being conducted at the University of South Australia. In your response, you expressed an interest in participating in future exercise interventions being conducted at the University. As such, below are the details of an intervention we would hope you would be interested in participating in.

BACKGROUND INFORMATION

The current prevalence of Type 2 diabetes in Australia is estimated at 7.4% and is higher than the average global prevalence. One of the most devastating complications of Type 2 diabetes is peripheral neuropathy which can lead to the loss of lower limbs due to ulcers and infections. To minimize the risk of complications of peripheral neuropathy, it is important to maintain good glycemic control. Exercise has been well established as a method of lowering blood sugar levels and is often prescribed to those with Type 2 diabetes. As such, the use of exercise may also help to reduce the complications and progression of peripheral neuropathy. Whilst some evidence has shown a positive relationship between aerobic exercise and peripheral neuropathy, there is little evidence on the effect of a combined resistance and aerobic training program.

PURPOSE OF THE STUDY

This study will investigate the effects of a 12-week moderate intensity combined aerobic and resistance training program on measures of strength, function and sensation in those with Type 2 diabetes and peripheral neuropathy.

DETAILS OF THE STUDY

Selection of Participants

For inclusion in the program you must satisfy the following criteria:

- Aged 18 years and over
- Have Type 2 diabetes for greater than 6 months controlled by diet and or hypoglycaemic agents
- Have peripheral neuropathy as diagnosed by your medical practitioner
- Not currently participating in regular aerobic exercise or resistance training nor had been during the previous 6 months.

However, if you meet any of the following criteria will be excluded from the program:

- Type 1 diabetes or Type 2 controlled by insulin.
- A history of recurrent hypoglycaemic episodes within past 6-months
- The presence of any co-morbidities which would inhibit physical activity such as severe cardiovascular disease, retinopathy, severe arthritis
- The presence of lower-limb ulceration, amputation or gangrene.

Program Details

The intervention program will be conducted at the School of Health Sciences, University of South Australia. During the 12-week exercise program, you will be required to attend the University twice weekly to perform a variety of exercises including aerobic and resistance training under the supervision of an accredited exercise physiologist. Each session is expected to last 1 hour. You will also be required to attend the University once during the month prior, and month post the intervention for baseline and post-intervention measurements. These testing sessions will also take place each month during the exercise intervention, meaning a total of 5 measurements will be taken throughout the 5 month period. The measurements to be recorded include a series of strength, balance, sensation and vibration tests as well as the same quality of life questionnaire which you completed previously.

Health/Safety Issues
Failure to obtain a clearance, or non-clearance, from your medical practitioner will preclude you from this study.

As you will be required to undertake some physical activity in this study, there will be an increased risk of hypoglycaemia if you are taking oral medication. To minimise the risk of hypoglycaemia, you will undertake a blood glucose test prior to commencement of testing and at the completion of testing. Complex carbohydrate will be provided on completion of testing where necessary. If you are found to have an excessively low (≤ 4 mmol/l) or excessively elevated (> 15 mmol/l) blood sugar level prior to commencement of testing, you will not be permitted to undertake the testing session until levels have returned to within their normal range. If you are found to have an excessively low blood sugar level at the completion of testing you will not be permitted to leave the test area until a normoglycaemic measure (4-8 mmol/l) is achieved.

Management of hypoglycaemic episodes during testing will be undertaken using the clinical protocols already in place in the UniSA podiatry clinic. Glucose Tablets and gel will be made available and both you and the researchers will be made well aware of the early symptoms of hypoglycaemia in order to ensure that appropriate intervention is undertaken.

ETHICAL ISSUES RELATED TO THIS STUDY
Your participation in this study will be on a strictly voluntary basis, with informed consent being provided prior to the commencement of the study. Non-participation in this study will in no way affect future access to services provided by the UniSA podiatry clinic or Diabetes South Australia. You will be free to withdraw from the study at any time without prejudice if you wish to do so.

Your confidentiality will be preserved by using codes in the recording and analysis of all the data with all information provided and the data collected being treated as strictly confidential. While research data gathered for this study may be published, no name or other identifying information related to the participant will be used.

All information collected as part of the study will remain the property of the named researchers and will be retained for a minimum of five years, and securely stored in the office of the Chief Investigator at the School of Health Science, University of South Australia.

The University of South Australia's Human Research Ethics Committee has reviewed this study and should you wish to discuss any details of this study with someone not directly involved, in particular in relation to matters concerning policies, the conduct of the study or your rights as a participant, please contact the UniSA Ethics Officer:

Ms Vicki Allen on 8302 3118; fax 8302 3921
email Vicki.Allen@unisa.edu.au.

FURTHER INFORMATION
If you require any further information regarding the specific details of the study, please contact Rebecca Nolan on the details below.

CONTACT DETAILS AND AFFILIATIONS OF RESEARCHERS

School of Health Sciences, University of South Australia

Rebecca NOLAN	PhD Student	8302 1373	Rebecca.Nolan@unisa.edu.au
Professor Esther MAY	Head of School	8302 2910	Esther.May@unisa.edu.au
Assoc. Prof. Annette RAYNOR	Assoc. Head of School	8302 1418	Annette.Raynor@unisa.edu.au

Diabetes South Australia

Estelle MAMO	Diabetes SA	8354 5803	Estelle@diabetessa.com.au

Appendix 10: Letter on invitation - UniSA Podiatry Clinic

VOLUNTEERS WANTED!

We are looking for volunteers to be involved in a study investigating the effects of exercise on those with Type 2 diabetes and peripheral neuropathy (loss of feeling in your feet)

As a client of the UniSA Podiatry Clinic, you are invited to participate in a study assessing the effects of exercise on strength, quality of life and sensation in your feet in people with Type 2 diabetes and peripheral neuropathy. It is expected this research will commence in early 2010.

Are you eligible?

To take part in this study you will need to meet the following requirements:

- Be aged 18 years and over
- Have Type 2 diabetes for greater than 6 months controlled by diet and or medication (not including insulin)
- Have peripheral neuropathy (loss of feeling in your feet) as diagnosed by your medical practitioner such as your GP or Podiatrist
- Not currently participating in regular exercise, nor have been in the previous 6 months
- No presence of lower-limb ulceration, amputation or gangrene.

What will be involved?

- Testing will take place for a total of 5 months and include measurements of lower-limb strength, balance, sensation, vibration and quality of life. A total of 12 measurements will be taken over the 5 month period.
- Those participants who choose to undertake the exercise component will also partake in a 12-week combined aerobic and strength training program at the UniSA HLS Fitness Centre.

Where and When?

- All sessions will be conducted at the School of Health Sciences, University of South Australia, corner of Frome Rd and North Terrace, Adelaide. Participants will have to fund their own mode of transport.
- All sessions will be on Monday-Friday at times convenient to the participants.

Who do you contact?

For more information about this study or to register your interest please contact:

Rebecca Nolan	**PhD Student**	**8302 1373**	**Rebecca.Nolan@unisa.edu.au**

This research has been approved by the UniSA Human Research Ethics Committee. Non-participation in this study will in no way affect future access to services provided by the UniSA podiatry clinic.

Appendix 11: Information letter for participants recruited through the UniSA Podiatry Clinic

Dear ,

My name is Rebecca Nolan and I am a PhD student at the University of South Australia. You have been invited to participate in research in people with Type 2 diabetes and peripheral neuropathy (loss of feeling in your feet). As such, below are the details of an intervention we would hope you would be interested in participating in. The research will aim to commence early in 2010.

BACKGROUND INFORMATION

The current prevalence of Type 2 diabetes in Australia is estimated at 7.4% and is higher than the average global prevalence. One of the most devastating complications of Type 2 diabetes is peripheral neuropathy which can lead to the loss of lower limbs due to ulcers and infections. To minimize the risk of complications of peripheral neuropathy, it is important to maintain good glycemic control. Exercise has been well established as a method of lowering blood sugar levels and is often prescribed to those with Type 2 diabetes. As such, the use of exercise may also help to reduce the complications and progression of peripheral neuropathy. Whilst some evidence has shown a positive relationship between aerobic exercise and peripheral neuropathy, there is little evidence on the effect of a combined resistance and aerobic training program.

PURPOSE OF THE STUDY

This study will investigate the effects of a 12-week moderate intensity combined aerobic and resistance training program on measures of strength, function and sensation in those with Type 2 diabetes and peripheral neuropathy.

DETAILS OF THE STUDY

Selection of Participants

For inclusion in the program you must satisfy the following criteria:

- Aged 18 years and over
- Have Type 2 diabetes for greater than 6 months controlled by diet and or hypoglycaemic agents
- Have peripheral neuropathy as diagnosed by your medical practitioner
- Not currently participating in regular aerobic exercise or resistance training nor had been during the previous 6 months.

However, if you meet any of the following criteria you will be excluded from the program:

- Type 1 diabetes or Type 2 controlled by insulin.
- A history of recurrent hypoglycaemic episodes within past 6-months
- The presence of any co-morbidities which would inhibit physical activity such as severe cardiovascular disease, retinopathy, severe arthritis
- The presence of lower-limb ulceration, amputation or gangrene.

Program Details

The intervention program will be conducted at the School of Health Sciences, University of South Australia. During the 12-week exercise program, you will be required to attend the University twice weekly to perform a variety of exercises including aerobic and resistance training under the supervision of an accredited exercise physiologist. Each session is expected to last 1 hour. You will also be required to attend the University weekly during the month prior, and month post the intervention for baseline and post-intervention measurements. These testing sessions will also take place each month during the exercise intervention. The measurements to be recorded include a series of strength, balance, sensation and vibration tests as well as a quality of life questionnaire.

Health/Safety Issues
Failure to obtain a clearance, or non-clearance, from your medical practitioner will preclude you from this study.

As you will be required to undertake some physical activity in this study, there will be an increased risk of hypoglycaemia if you are taking oral medication. To minimise the risk of hypoglycaemia, you will undertake a blood glucose test prior to commencement of testing and at the completion of testing. Complex carbohydrate will be provided on completion of testing where necessary. If you are found to have an excessively low (≤ 4 mmol/l) or excessively elevated (> 15 mmol/l) blood sugar level prior to commencement of testing, you will not be permitted to undertake the testing session until levels have returned to within their normal range. If you are found to have an excessively low blood sugar level at the completion of testing you will not be permitted to leave the test area until a normoglycaemic measure (4-8 mmol/l) is achieved.

Management of hypoglycaemic episodes during testing will be undertaken using the clinical protocols already in place in the UniSA podiatry clinic. Glucose Tablets and gel will be made available and both you and the researchers will be made well aware of the early symptoms of hypoglycaemia in order to ensure that appropriate intervention is undertaken.

ETHICAL ISSUES RELATED TO THIS STUDY
Your participation in this study will be on a strictly voluntary basis, with informed consent being provided prior to the commencement of the study. Non-participation in this study will in no way affect future access to services provided by the UniSA podiatry clinic or Diabetes South Australia. You will be free to withdraw from the study at any time without prejudice if you wish to do so.

Your confidentiality will be preserved by using codes in the recording and analysis of all the data with all information provided and the data collected being treated as strictly confidential. While research data gathered for this study may be published, no name or other identifying information related to the participant will be used.

All information collected as part of the study will remain the property of the named researchers and will be retained for a minimum of five years, and securely stored in the office of the Chief Investigator at the School of Health Science, University of South Australia.

The University of South Australia's Human Research Ethics Committee has reviewed this study and should you wish to discuss any details of this study with someone not directly involved, in particular in relation to matters concerning policies, the conduct of the study or your rights as a participant, please contact the UniSA Ethics Officer:

Ms Vicki Allen on 8302 3118; fax 8302 3921
email Vicki.Allen@unisa.edu.au.

FURTHER INFORMATION
If you require any further information regarding the specific details of the study, please contact Rebecca Nolan on the details below.

CONTACT DETAILS AND AFFILIATIONS OF RESEARCHERS

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